"TOWARDS THE SYNTHESIS OF ALKOXY-SUBSTITUTED [2.2] *PARA*-CYCLOPHENES AND [2.2] *PARA*-CYCLOPHANE-1-ENES; TAILORED MONOMERS FOR THE PREPARATION OF WELL-DEFINED, FUNCTIONALISED PPV".

Thesis Submitted for the Degree of
Doctor of Philosophy
At the University of Leicester

by

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Statement

This thesis is based on work conducted by the author, in the Departments of Chemistry at the University of Leicester and the University of Durham, during the period July 2001 to August 2004.

All the work described in this thesis is original, unless otherwise acknowledged in the text or references. None of this work has been submitted for any other degree in this or any other university.

Signed: Date:

This thesis is dedicated to the
memory of my late Grandmother,
Margaret Hickman (1924-2006).

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Abstract

This thesis describes a potential route for the synthesis of alkoxy-functionalised [2.2] *para*-cyclophenes and [2.2]-*para*-cyclophane-1-enes, *via* ring-closing of appropriately derivatised alkoxy-functionalised stilbenes, as possible monomers for the preparation of functionalised poly(*para*-phenylenevinylene)s {PPVs} *via* ROMP.

Firstly, the concepts behind conducting and electroluminescent organic polymers are introduced, with particular emphasis upon polyacetylene and PPV, the first electroluminescent polymer to be discovered. The chemistry of stilbenes is subsequently discussed highlighting details of their structure, preparation, and reactivity. Finally, an overview of cyclophanes and cyclophanes is presented, illustrating the wide variety of these fascinating compounds that are currently known. [2.2] *para*-Cyclophane and its derivative [2.2] *para*-cyclophene are discussed in depth, since these molecules form the focus for this PhD thesis.

A series of alkoxy-substituted benzaldehydes (**111, 114,** and **115**) was synthesised, either *via* reaction of various hydroxy-substituted benzaldehydes with an appropriate haloalkane, or by formylation of a previously alkoxy-functionalised arene or toluene derivative. These methods provided a simple route into readily functionalised precursors to alkoxy-substituted stilbenes. The substituted benzaldehydes were subsequently transformed into the desired stilbenes (**122, 127,** and **131**) through the application of either the McMurry reaction, using titanium tetrachloride and activated zinc, or the Wittig and Horner-Wittig reactions, employing the corresponding phosphonate esters (**130**) as co-reagents. Further transformations of the dibutyloxy stilbenes **131** were then explored; diformylation through a Vilsmeier reaction yielding the stilbene dialdehyde **143,** and a dihydroxylation reaction transforming the stilbene into a 1,2-ethanediol (**156**). This latter reaction was carried out to allow for free rotation about the central carbon-carbon bond, potentially facilitating ring-closing to furnish the desired [2.2.] *para*-cyclophenes.

The diformyl alkoxy-substituted stilbene precursor **143** was also used to synthesise an oligomeric analogue of PPV (**145**) containing four aromatic rings. Compound **145** was fully characterised, its photophysical properties measured and compared to those of the parent stilbenes. Oligomer **145** and diformyl stilbene **143** showed significant red-shifts in both their emission and absorption spectra in comparison to precursor stilbenes **131** and **147,** due to their having longer conjugation path lengths.

Finally, an alternative method of [2.2] *para*-cyclophene synthesis was explored, employing a modified Ramberg-Bäcklund rearrangement of functionalised cyclic dithioethers (**166**). These dithioethers were prepared through the cyclisation of dibromomethyl dialkoxy compounds **164** with benzenedimethanethiol in reasonable yield, and subsequently oxidised to the corresponding sulfone **167**. Compound **167** proved insoluble in all common organic solvents hence the final Ramberg-Bäcklund step has not yet been achieved.

Hazel Alice Hickman, August 2005

Abbreviations

2,4-DNP: 2,4-Dinitrophenyl hydrazine

AD: Asymmetric Dihydroxylation

AIBN: 2,2'-Azo-bis(isobutyronitrile)

Ar: Aryl

Bu: Butyl

COSY: Correlation Spectroscopy

DCM: Dichloromethane

DDQ: 2,3-Dichloro-5,6-dicyanobenzo-1,4-quinone

DEPT: Distortionless Enhancement by Polarization Transfer

DFT: Density Functional Theory

$(DHQD)_2PHAL$: 1,4-bis(9-*O*-Dihydroquinidinyl)phthalazine

DHFR: Dihydrofolate Reductase

DME: Dimethoxyethane

DMF: Dimethylformamide

DMSO: Dimethyl sulfoxide

ECL: Effective Conjugation Length

ee: Enantiomeric Excess

EI: Electron Ionisation

EL: Electroluminescence

ES: Electrospray

ESR: Electron Spin Resonance

Et: Ethyl

FAB: Fast Atom Bombardment

FWHM: Full Width at Half Maximum

GC-MS: Gas Chromatography-Mass Spectrometry

HETCOR: Heteronuclear Correlation Spectroscopy

HOMO: Highest Occupied Molecular Orbital

Hückel/SSH: Hückel/Su-Schrieffer-Heeger

IR: Infra-Red

ITO: Indium-Tin-Oxide

LUMO: Lowest Unoccupied Molecular Orbital

mCPBA: *m*-Chloroperoxybenzoic Acid

Me: Methyl

MEH-PPV: 2-Methoxy-5-(2-ethylhexyloxy)-*p*-phenylenevinylene

MO: Molecular Orbital

MP: Melting Point

MW: Molecular Weight

NBS: *N*-Bromosuccinimide

NCS: *N*-Chlorosuccinimide

NMF: *N*-Methyl Formanilide

NMR: Nuclear Magnetic Resonance

nOe: Nuclear Overhauser Effect

OAc: Acetate

oLED: Organic Light-Emitting Diode

OTf: Triflate

PDI: Polydispersity Index

Ph: Phenyl

pLED: Polymer Light-Emitting Diode

PMEH-PPV: poly[Phenylenevinylene-*alt*-2-methoxy-5-(2-ethylhexyloxy)-*p*-phenylenevinylene

PP: Polyphenylene

PPE: poly(Phenyleneethynylene)

PPP-Hubbard: Pariser-Parr-Pople-Hubbard

PPV: poly(*para*-Phenylenevinylene)

PT: Polythiophene

PTSA: *para*-Toluenesulfonic Acid

RCM: Ring-Closing Metathesis

ROMP: Ring-Opening Metathesis Polymerisation

RT: Room Temperature

S_N2: Bimolecular Nucleophilic Substitution

TBDMS: Tertiary Butyl Dimethylsilyl

TFA: Trifluoroacetic Acid

THF: Tetrahydrofuran

TMEDA: Tetramethylethylenediamine

TMS: Trimethylsilyl

UV: Ultra-Violet

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CHAPTER ONE

INTRODUCTION

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1.1: Introduction

The aim of this thesis is to explore generic routes for the preparation of suitably derivatised [2.2] *para*-cyclophane-1-enes. These compounds have the potential to be used as monomers for ring-opening metathesis polymerisation (ROMP). Such a process can make up a route to alkoxy-functionalised poly(*para*-phenylenevinylene), or PPV, via a precursor polymer approach.

Section A: Conducting Polymers.

A1: Structure, Properties and Conductivity

For many years 'plastics', or organic polymers, have been well known for their insulating properties towards both heat and electricity, being used, for example, as coatings for electrical wires and appliances. In 1968, however, it was shown that an organic polymer, namely polyacetylene (**1**), could become semiconducting when doped with a suitable oxidant or reductant, work which has led to the development of a whole range of organic polymers that can conduct electricity.[1] Polyacetylene is the simplest of these so-called 'conducting polymers,' having the formula $(CH)_n$ *(Figure 1),* and can be prepared using a number of well-established methods that will be discussed later in this section.

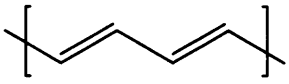

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Figure 1: Polyacetylene.

Examination of the structure of polyacetylene reveals that it is fully conjugated, *i.e.* it has alternating single and double bonds along the main chain and an extended, delocalized, π system. These properties in themselves are not sufficient to confer conduction; in fact, in pure form, these types of polymer are, at best, described as semiconductors and more usually, as insulators.[2] In order to exhibit conductance polyacetylene must be doped, this is achieved by exposure to a suitable reducing or oxidizing agent, for example iodine or AsF_5,[3] in order to introduce electrons or holes into the system. Suitable doping of polyacetylene with iodine can give rise to a polymer with a similar conductivity to that of copper, and indeed it has been shown theoretically that a perfect single crystal of doped polyacetylene should exhibit room-temperature conductivity of around 2×10^6 S cm^{-1}.[4] For

reference, a comparison of the conductivity values of some conducting polymers with metals, semiconductors and insulators is shown in *Figure 2.*

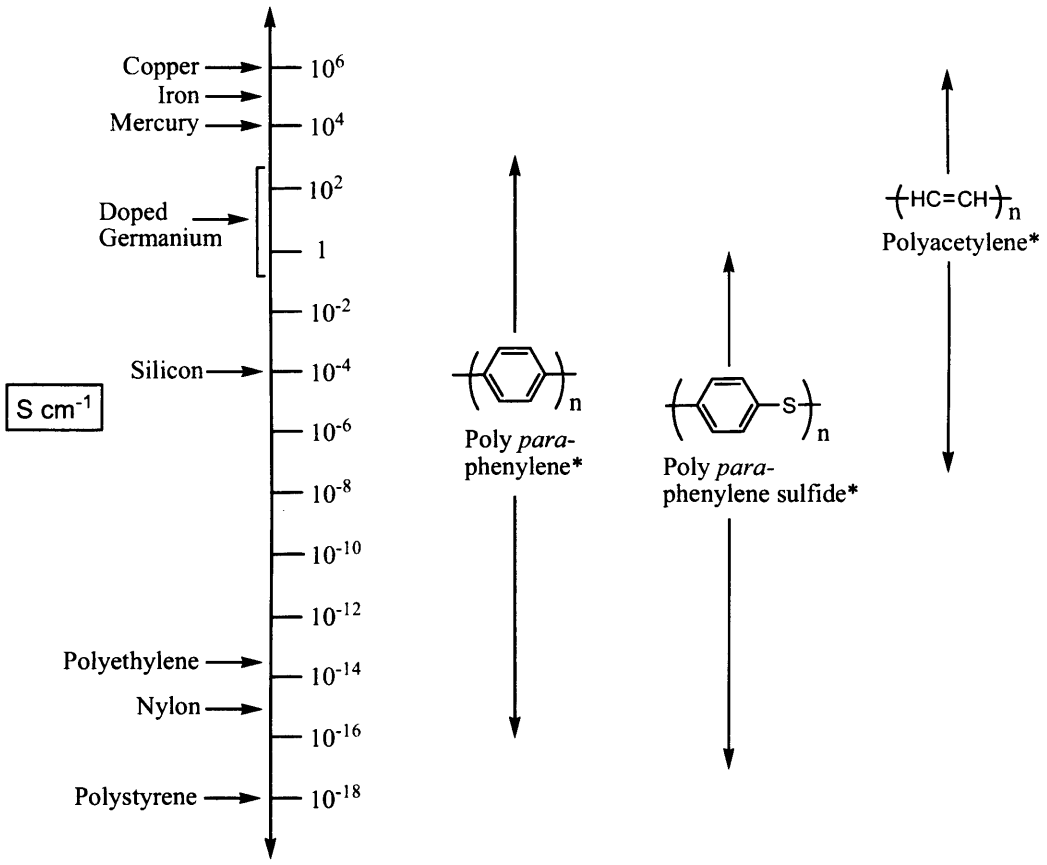


Figure 2: Comparison of Room-Temperature Conductivity Values of Some Doped Polymers with Metals, Insulators and Semiconductors.[5]

Electrical conductivity, σ, arises from the existence of charge carriers within a material, and the ability of these charge carriers to move (*Equation 1*).[6]

$$\sigma = ne\mu$$

n = number of charge carriers per unit volume

e = electronic charge (C)

μ = charge carrier mobility ($cm^2V^{-1}s^{-1}$)

Equation 1: Definition of Electrical Conductivity.

Doped conjugated, "conducting" polymers are good electrical conductors for two reasons. Firstly, because every repeat unit in the polymer chain is a potential site for oxidation or reduction, it means that the polymer can be doped to afford a high density of charge carriers. Secondly, because the delocalized π-electron system allows for high charge carrier mobilities, these can move easily through the polymer matrix.

The behaviour of conducting polymers is best regarded as being related to that of semiconductors as opposed to that of metallic materials, as they possess a band gap in their electronic structure. This can be illustrated by a band theory diagram as shown in *Figure 3*.

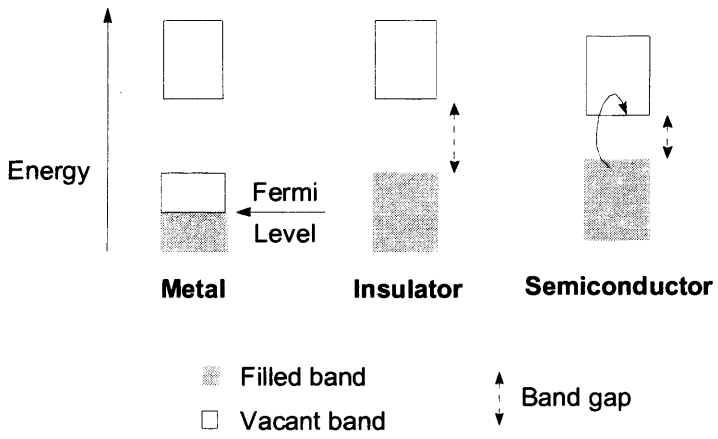


Figure 3: Band theory diagram comparing metals, insulators and semiconductors.

In the solid state, the outer atomic orbitals in atoms or molecules are split into filled bonding orbitals and vacant antibonding orbitals. These split again to form two discrete energy levels, known respectively as the *valence* and *conduction* bands. In bulk compounds these bands are made up of many overlapping molecular orbitals, or MOs. In the case of a metal, the valence and conduction bands are only partially filled with electrons, with the highest occupied molecular orbital, or HOMO, at 0 K being known as the Fermi level. The difference in energy between the HOMO, and the lowest unoccupied molecular orbital, or LUMO, in the solid state is termed the *band gap*. For metals, this difference is so small that there is essentially no gap. At temperatures above 0 K, thermal energy and entropic disorder in the system are enough to move electrons close to the Fermi level and into the vacant MOs lying above, where some of the electrons will become mobile and give rise to an electrical current on application of a potential across the material. Thus, it can be seen that the ability to conduct electricity is a feature of materials with partially filled valence and conduction bands.

Experimentally, the band gap is related to the wavelength of the first absorption band in the electronic spectrum of a material. The energy condition shown in *Equation 2* must be fulfilled in order for a photon of wavelength λ to promote an electron from the HOMO to the LUMO.

$$\Delta E = E(LUMO) - E(HOMO) = h\upsilon = hc/\lambda$$

ΔE = Change in Energy
E(LUMO) = Energy of LUMO (eV)
E(HOMO) = Energy of HOMO (eV)
h = Planck's Constant (6.626068×10^{-34} m^2 kg s^{-1})
υ = Frequency (Hz)
c = Speed of Light (299 792 458 m s^{-1})
λ = Wavelength (nm)

Equation 2: Energy condition for conductance.

Hence, it can be seen that if sufficient electron excitation energy can be applied to a system, the band gap can be overcome and the material becomes conducting, as electrons are promoted from the HOMO to the LUMO across the band gap. Such a material is termed a semiconductor.

The properties and behaviour of conducting polymers, although they are classed as semiconductors, differ greatly from those traditionally associated with a classical inorganic, crystalline semiconductor such as silicon. In these latter materials, the energy levels can be seen as forming bands originating from the electronic levels of the atoms present.[7] The bands are generated as the atomic levels split upon the atoms approaching one another. Adding an electron to, or removing an electron from, these bands *via* doping generates a free electron or hole in the conductance band. Hence, the compound conducts electricity as the charge carrier created moves through the material. In contrast, a conducting polymer can be viewed as originating from a one-dimensional system where there is one electron per carbon atom. Addition or removal of an electron from such a system causes a partial oxidation or reduction of a polymer molecule, from which conduction can then originate. For example, addition of iodine to a sample of polyacetylene will create a 'hole' where an electron has been removed. This hole does not then delocalize over the whole structure as would have been predicted by band theory, but

is instead localized upon one discrete carbon atom forming a radical cation or *polaron* (*Equation 3*).

$$\{CH\}_n + 3x/2\ I_2 \longrightarrow \{CH\}_n^{x+} + xI_3^-$$

Equation 3: Polaron formation upon addition of iodine to polyacetylene **(1)**.

The alternating single bond - double bond structure of polyacetylene gives rise to another form of charge carrier, the *soliton*. The structure of the polymer cannot be thought of as a *quasi*-1D metal with all bonds of equal length and the π electrons fully delocalised.[8] Instead, the adjacent CH units move toward one another creating an alternating short-long-bond arrangement. This can be related to the alternating double bond and single bond structure observed for polyacetylene, and can be either looked upon from a physics viewpoint as a manifestation of Peierls' instability, or in a chemical sense as a form of Jahn-Teller distortion.[9] Symmetry rules state that the single and double bonds can be interchanged *(Figure 4)*, giving rise to two degenerate ground states of the system.[10] This two-fold degeneracy leads to what are known as "nonlinear topological excitations," or *solitons*.

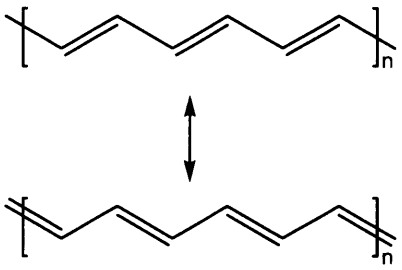


Figure 4: Interchange between single and double bonds in polyacetylene.

Theoretical modelling of the conductance in polyacetylene and related materials has proved harder than was expected, as the models consider only 'ideal', infinitely long polymer chains. Analysis has shown that both electron-phonon (where a phonon is a quantum of vibrational energy in a solid-state lattice) and electron-electron interactions are likely to be of equal importance in a degenerate ground-state polymer such as polyacetylene, with polarons and solitons the possible quasi-particles generated. Neither the Hückel/SSH or PPP-Hubbard models are sufficient to provide a complete description of the observed behaviour of doped, π-conjugated, conducting, polymers.[11]

In practice, polymer morphologies and, as a result electrical properties, are affected by such factors as crystallinity; chain length; chain breakages and defects; and weak inter-chain interactions, the extent of their influence depending largely on the preparation technique used to synthesise the polymer. On the microscopic scale, conducting, conjugated polymers possess a strongly anisotropic structure. This is a consequence of the chain-like molecules exhibiting strong covalent bonding along the length of the chain, and only weak van der Waals interactions between chains. Theoretical calculations give a value for the conduction bandwidth in polyacetylene of approximately 10 eV *along* the polymer chains, but only 0.1 eV perpendicular to them,[12] demonstrating that the material conducts far more efficiently along the polymer chains. Furthermore, polymer chains are not straight and flat; rotation about single bonds causes defects. These shorten the conjugation path length, as do saturated sp^3 centres present in the chain, reducing the energy at which the lowest energy optical absorbance of the polymer will occur, (*i.e.* the $\pi \rightarrow \pi^*$ transition). The longer the conjugation path length of the polymer chain, the lower the energy at which this transition will occur.[13] The longest fully-conjugated sections of polyacetylene observed are approximately 100 carbon atoms.[14]

A2: Examples, Synthesis and Applications of Polyacetylene.

Although polyacetylene is by far the best known of the conducting polymers, there is today a vast range of these types of material, which vary greatly in structure and synthesis, but that still all exhibit conductivity after doping. A short review such as this cannot hope to detail each and every conducting polymer; hence, a selection of examples will be reviewed in the subsequent section in order to give a 'flavour' of this diverse area of research.

A2.1: Polyacetylene.

Polyacetylene is the simplest of all conjugated polymers, having the formula $(CH)_n$, and is often considered as the prototype for other organic conducting polymers, employed in for example polymer light-emitting diodes (pLEDs), nonlinear optical materials and molecular electronics devices.

There are four possible structures for polyacetylene, although in actual fact only two of them are observed experimentally *(Figure 5)*.

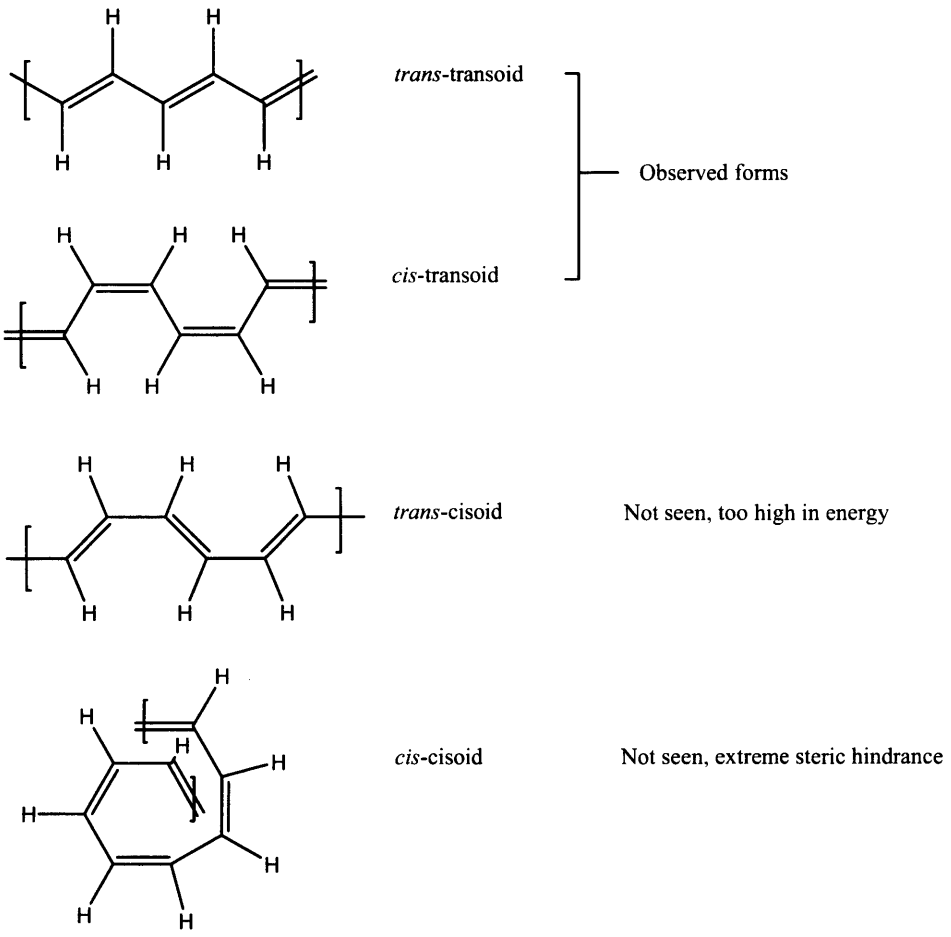
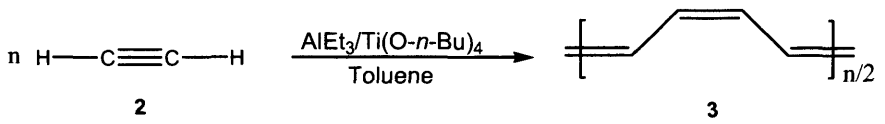


Figure 5: Possible structures of polyacetylene.[15]

A2.1.1: Synthesis of Polyacetylene

Historically, there has been some considerable difficulty in preparing linear, stereoregular polyacetylene from acetylene itself, something which can be attributed to the electronic structure and hence chemistry of this monomer. The C-C triple bond is characterized by high symmetry, high electron density and low polarisability, as well as having increased reactivity with respect to electrophilic reagents when compared to, for example, a C=C double bond.[16] Thus, although polyacetylene was first prepared as early as the 19th century, as "cuprene", it was a highly crosslinked and poorly defined product.[17] Natta *et al.* successfully prepared the first sample of stereoregular, highly ordered and crystalline polyacetylene in 1958, by bubbling acetylene gas through a hexane solution of the polymerisation initiator $AlEt_3/Ti(O\text{-}i\text{-}Pr)_4$.[18] However, at the time there was little interest in this material, because no matter how it was prepared, the polyacetylene product was always obtained as an insoluble, infusible and air sensitive black powder.

It was not until the 1970s that interest in polyacetylene was really awakened, when Shirakawa and co-workers discovered that polymerization of acetylene (**2**) using a concentrated solution of $AlEt_3/Ti(O\text{-}n\text{-}Bu)_4$ under inert atmosphere conditions could, using the right technique, afford well-ordered, free-standing films of silvery-coloured, predominantly *cis*, polyacetylene (**3**) *(Scheme 1)*.[19] These mechanically strong, reasonably stable films could be handled far more easily, and allowed the first studies into the effects of polymer doping (with agents such as halogens or AsF_5) to be undertaken. Indeed, this work led to the first observations of the high conductivity of this material following its doping.[20]



Scheme 1: Shirakawa's route to polyacetylene.

The general method employed by Shirakawa *et al.* involves preparation of the catalyst solution in toluene, followed by an 'aging' step, whereby the solution is allowed to stand for 45 minutes at 20°C. The mixture is then cooled to -78°C, placed under vacuum, and the initiator solution allowed to wet the walls of the reaction flask. Gaseous acetylene is then introduced, at which point a film of polyacetylene begins to form immediately on the walls of the vessel. Repeated washing with either hexane or toluene purifies the polymer, which can then be dried and stored under an inert atmosphere. Judicious alteration of the reaction time, temperature and acetylene pressure can alter the thickness of the film produced from 10^{-5} cm to 0.5 cm, while an increase in initiator concentration and variation in the Al/Ti ratio allows the polymer to be obtained as a powder, a gel-like mass, or a thin film, respectively.[21,22]

Films prepared using the Shirakawa method consist of predominantly *cis*-polyacetylene, which can subsequently be isomerised to the *trans* form by heating for one hour at 150°C. In its pure, undoped state, *trans*-polyacetylene has the higher conductivity of the two forms, with the conductivity of essentially all-*trans,* undoped, polymer being 4.4×10^{-5} S m^{-1} compared to undoped *cis*-polyacetylene at 1.7×10^{-9} S cm^{-1}. Conductivity of doped forms of the polymer vary widely depending on the method of preparation and the dopant used. For example Shirakawa *et al.* give a value of 0.5 S cm^{-1} for bromine-doped polyacetylene, which rises to 560 S cm^{-1} upon doping with AsF_5. Physical alteration of the polymer also increases conductivity. Naarman *et al.* prepared highly stretched, well-

ordered films of polyacetylene by using what is essentially the Shirakawa route, but with an extra reductant (for example *n*-butyl lithium) included in the initiator mixture.[23] Mechanical alignment of the polymer chains increased the order in the material by a factor of six, and it was discovered that carrying out the polymerization reaction using a mixture of the initiator and silicon oil facilitated the stretching process. The polymer thus produced contains a significantly lower proportion of sp^3 defects, and shows a conductivity of over 100,000 S cm^{-1} following iodine doping.[24] Finally, it has been shown that by 'templating' the polymerisation process using an oriented matrix of chiral nematic liquid crystals produces a helical form of polyacetylene, which displays an electrical conductivity of up to 12,000 S cm^{-1}.[25]

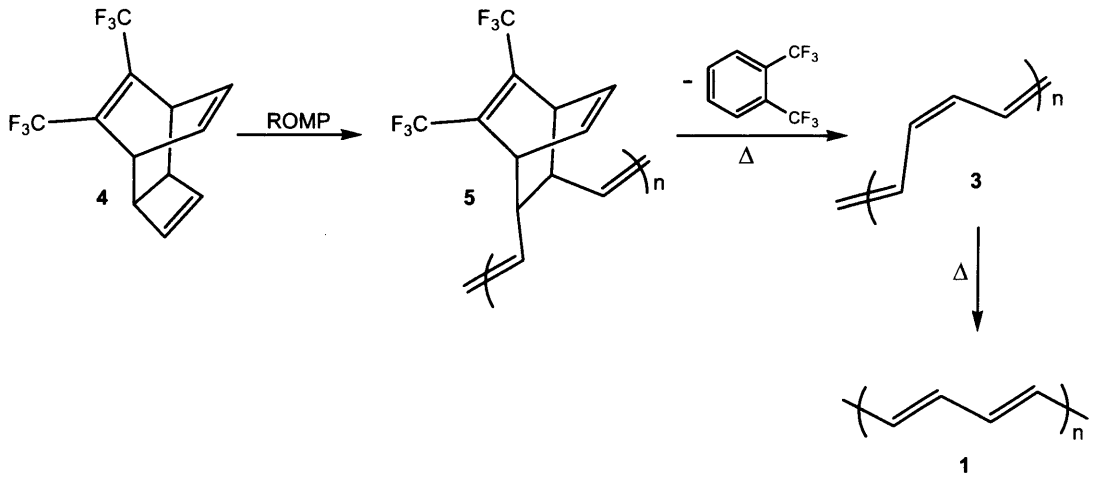
From a materials chemistry viewpoint, polyacetylene is a difficult substance to characterise. Its strong π-π interactions lead to a low entropy of dissolution, which coupled with enthalpic contributions gives polyacetylene a very high free energy of dissolution.[26] This renders it essentially insoluble in any solvent, and also totally infusible. Hence, fundamental properties such as molecular weight (MW), MW distribution (PDI), and details of the chemical structure are difficult to determine, something that has limited any evaluation of their effect on the properties of the polymer. In addition to these characterisation problems, attempts to utilize this material in devices have also been hampered by its sheer intractability.

Thus, it can was evident that a route to soluble, processible polyacetylene and related derivatives was needed, something that was approached in two ways. Firstly by the addition of solubilising groups to the polymer itself, achieved through the polymerisation of functionalized monomers. Secondly, a precursor polymer approach was established, whereby a more tractable precursor material can be prepared initially, which can subsequently be processed and converted to polyacetylene *in situ*.

The first, direct type of approach for preparing polyacetylene has achieved only limited success, as was mentioned earlier the polymer produced is extremely intractable. Although polymers such as methyl- and phenyl-substituted polyacetylene have been synthesized, and were indeed shown to be more soluble in organic solvents than their non-functionalised counterpart, upon doping, these polymers showed very low conductivities. This is thought to be due to the effect of the substituents on the polymer backbone inducing chain twisting, something that dramatically reduces the conjugation path length.[27] Acetylene-

methylacetylene copolymers have also been prepared and again show enhanced solubilities (compared with polyacetylene itself), but are highly sensitive to oxidation and so have found very little in the way of practical application.[28]

The precursor polymer approach to polyacetylene has, however, found much more success, and is generally known as the 'Durham route' as it was discovered at the University of Durham by Edwards and Feast.[29, 30] The overall reaction is shown in *Scheme 2.*



Scheme 2: The 'Durham route' to polyacetylene.

This route essentially involves the polymerization, *via* Ring Opening Metathesis Polymerisation (ROMP), of the monomer 7,8-bis(trifluoromethyl)tricyclo-[4.2.2.$0^{2,5}$]deca-3,7,9-triene (**4**) to afford the high MW, non-conjugated precursor polymer **5**, which is readily soluble and processible in common organic solvents. After purification and processing, this precursor polymer can simply be converted to *cis*-polyacetylene (**3**) upon application of heat, inducing evolution of 1,2-bis(trifluoromethyl) benzene. Further application of heat can be used to isomerise the material to all-*trans* polyacetylene (**1**).

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A3: Electroluminescent Polymers

A3.1: Introduction

The next significant advance in the field of conducting polymers came about in 1990, when Friend *et al.* tested unsubstituted PPV (**6**), for electrical conductivity (*Figure 6*).[31] It was observed that application of an electric current to this polymer resulted in the emission of visible light in the yellow/green region of the electromagnetic spectrum, a phenomenon that was termed electroluminescence. Thus, PPV and other electroluminescent polymers are now being developed for a range of applications including polymer LED's (PLED's), flat screen displays, and chemical sensors.[32]

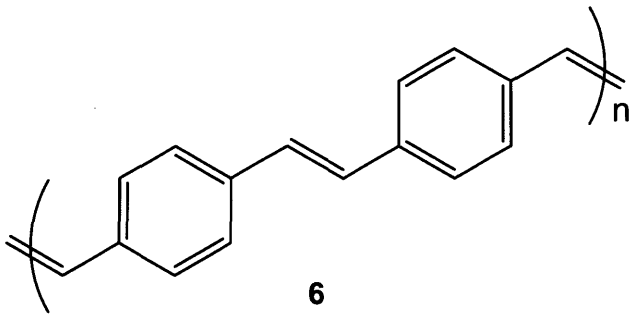

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Figure 6: Structure of unsubstituted PPV.

Electroluminescent (EL) polymers have many advantages over traditional semiconductor technologies. They are cheaper to prepare, more energy efficient and easier to process. For example, it is now possible to make flexible displays by application of the polymer directly to a suitable substrate.[33] Also, these polymers allow a wider viewing angle, faster response times, low operating voltages and easy tuning of the emission wavelength.[34]

As a result of considerable research interest being directed into the field of light-emitting organic compounds over the last fifteen years, there is now a substantial library of electroluminescent compounds known to the chemist. In addition to strictly polymeric systems, the field has expanded to encompass oligomers and even small electroluminescent molecules. Examples of electroluminescent polymers are shown below in *Figure 7*, and small-molecule examples in *Figure 8.* The polymeric examples shown illustrate the wide range of compounds available, encompassing both all-carbon and heterocyclic polymer backbones. This diversity enables tuning of polymer properties through extensive manipulation of substituents R. For example, the unsubstituted form of PPV (**6**), when

incorporated into a pLED, emits light at a wavelength of around 520 nm, unsubstituted polyphenylene (**7**) emits at 459 nm, and polythiophene (**8**) at 530 nm, however these values can be changed dramatically through the incorporation of various functionalities within the polymers, as will be discussed in greater detail later in this section.

The small molecule emissive species **9**, illustrated in *Figure 8,* is one of a range of relatively new systems which incorporate one or more pyrimidine moieties. These electron-deficient heterocycles impart improved electron-transport properties upon the compounds, making them ideal for use as electron conducting / hole blocking layers in organic LEDs. The compound illustrated possesses a HOMO-LUMO gap of 3.13 eV, and when incorporated into a device emits blue-green light at a wavelength of 500 nm.

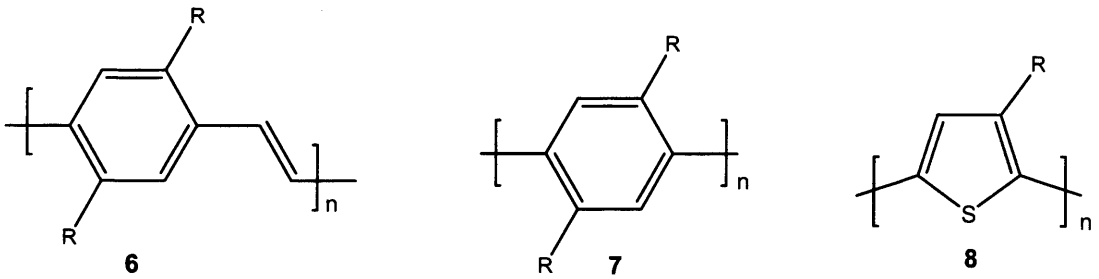

Figure 7: Examples of well-known electroluminescent polymers.

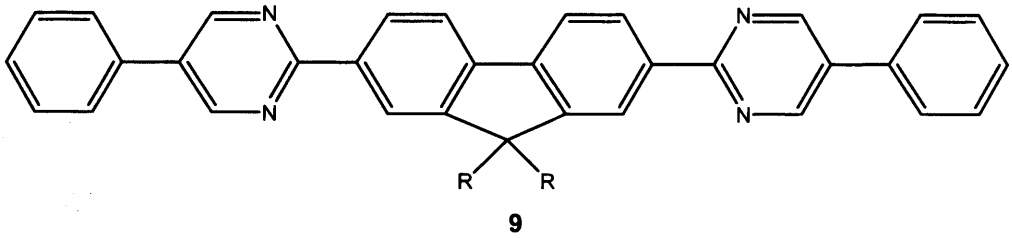

Figure 8: Fluorene-pyrimidine-based oligo(arylene), a small-molecule emissive species.[35]

A3.2: Poly(*para*-phenylenevinylene), PPV

Being the first electroluminescent polymer to be discovered, and hence the most comprehensively studied, PPV is probably the best known member of the family of electroluminescent polymers. A whole 'library' of derivatives is now available encompassing the whole spectrum of colours from red- through to blue-emitters. In recent years, PPV has begun to be incorporated into commercially available devices for example the Philips "Philishave Sensotec" electric razor, which incorporates a polymer LED display

to monitor battery life.[36] In order to exploit this type of technology, the company 'Cambridge Display Technology' was set up in 1992, soon after the discovery of PPV-based polymer LEDs.[37]

A3.2.1: The Origin of Electroluminescence

In order to observe conductance, and thus electroluminescence, in PPV, the polymer must be incorporated within an electrode. This comprises an electron-injecting cathode, usually a low work function metal such as calcium, a thin layer of the polymer, and a hole-injecting anode which is usually indium-tin oxide (ITO) (*Figure 9*).

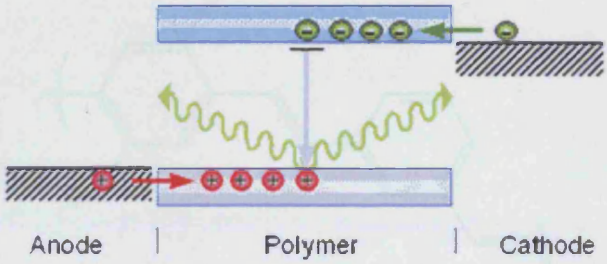

Figure 9: Structure of a polymer LED.

Emission of light occurs when a hole combines with an electron within the polymer, producing an *exciton*. This exciton can best be visualised as an electron which is removed from the HOMO, but is placed in the LUMO instead of having been removed from the system entirely. The emission wavelength depends on the band gap of the polymer, and also on the effective π-conjugation path length, or ECL. Control of the band gap is achieved at a molecular level by variation of the substituents on the polymer chain;[38] the nature, positioning and number of these functionalities has a significant effect on the conductivity and light emission of the bulk material.

The ECL is defined as the number of monomer units at which saturation of conjugation occurs, and can be relatively easily controlled by the polymer morphology, as the π-conjugation length can be varied by changing both the nature of the substituents on the polymer chain, and the orientation of the polymer backbone within the solid-state structure. In general, it can be seen that the shorter the conjugation path length, the shorter the wavelength emitted and the more blue-shifted the electroluminescence. For example, as shown in *Figure 10*, by introducing *ortho-* and *meta*-linkages to the polymer, thus effectively putting a 'kink' in the PPV chain, Ahn *et al.* have been able to significantly

shorten the π-conjugation path length of poly[phenylenevinylene-*alt*-2-methoxy-5-(2-ethylhexyloxy)-*p*-phenylenevinylene], PMEH-PPV.[39] This decreases the absorption maximum from 430 nm for *p*-PMEH-PPV to 390 nm for the *m*-PMEH-PPV, and also causes a blue shift in the emission spectrum from an emission maximum of 550nm in *p*-PMEH-PPV to 490 nm in *m*-PMEH-PPV.

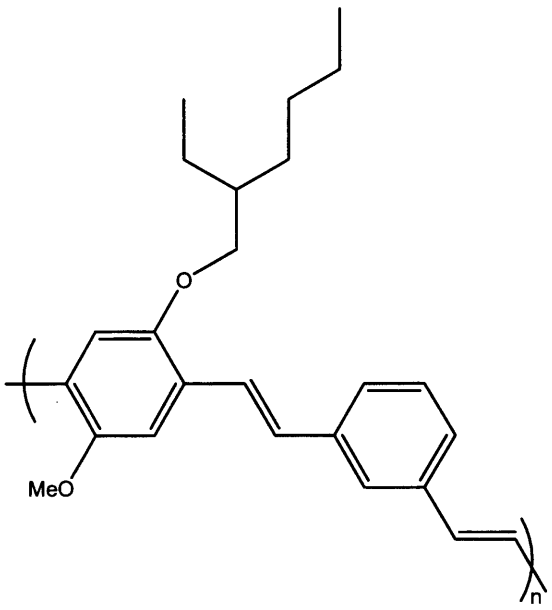

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Figure 10: 'Kinked' section of PMEH-PPV with shorter conjugation length.

A3.2.2: Structure of PPV

The solid-state structure of PPV has been inferred from studies of its soluble oligomeric analogues. Indeed, a large number of the properties of high molecular weight polymers can be estimated from calculations on oligomers of increasing chain length (n = 2-15, *etc.*) and subsequent extrapolation to infinite chain length (the so-called 'oligomer extrapolation technique').[40] These shorter-chain derivatives have a more accessible molecular structure and are easier to manipulate, being much more soluble than their higher polymeric counterparts in most organic solvents, aiding both synthesis and characterisation, while possessing the same/related electronic and optical properties as true polymers.

The crystal structure of unsubstituted PPV oligomers displays a 'herringbone' arrangement (*Figure 11*). As substituents are added to the chains, packing is disrupted and the structure becomes non-planar, bulky pendant phenyl groups on the aromatic rings disrupting the packing to such a degree that the material becomes amorphous and displays no melting or thermotropic behaviour. This interruption of the packing shortens the conjugation path

length of the PPV by twisting of the polymer chains, and hence the emission is blue-shifted.

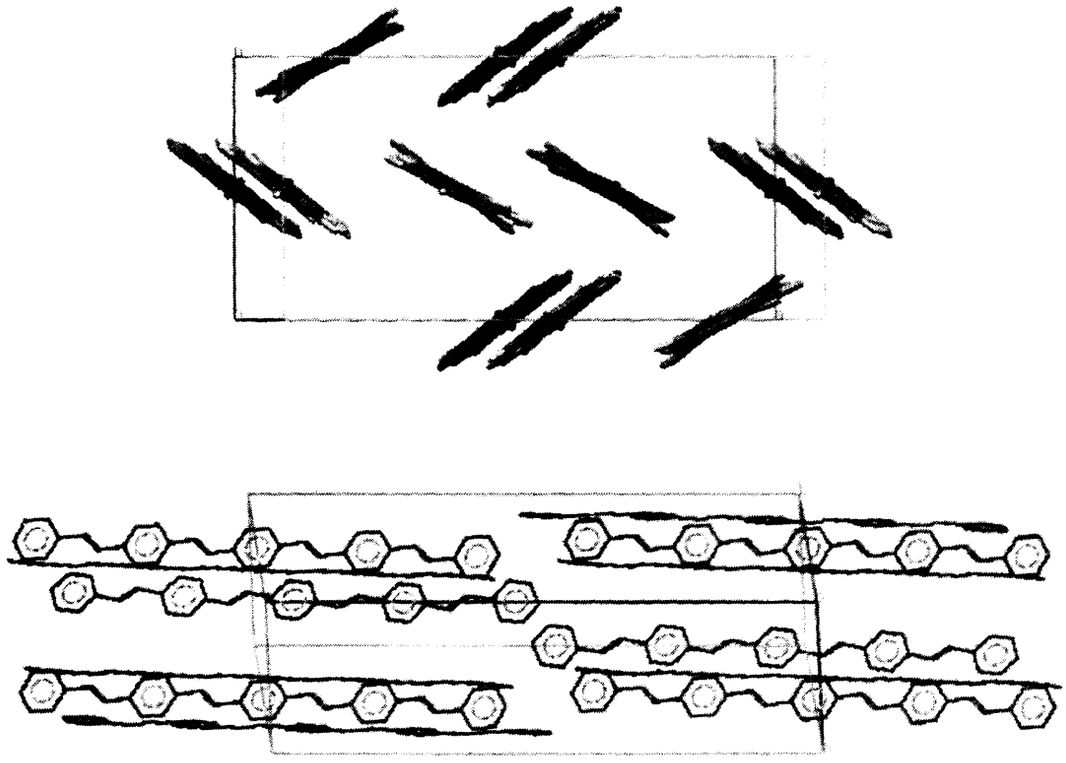
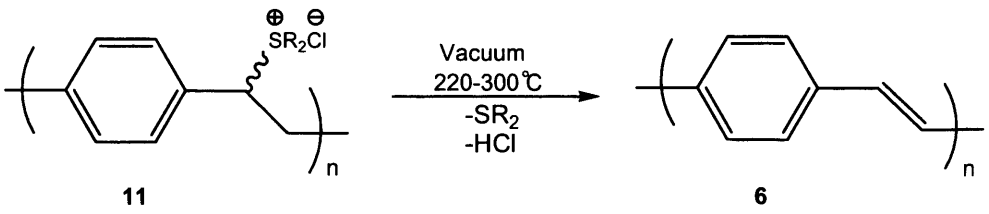


Figure 11: Solid-state structures of oligomeric PPV, illustrating the 'herringbone' arrangement of the chains.[41]

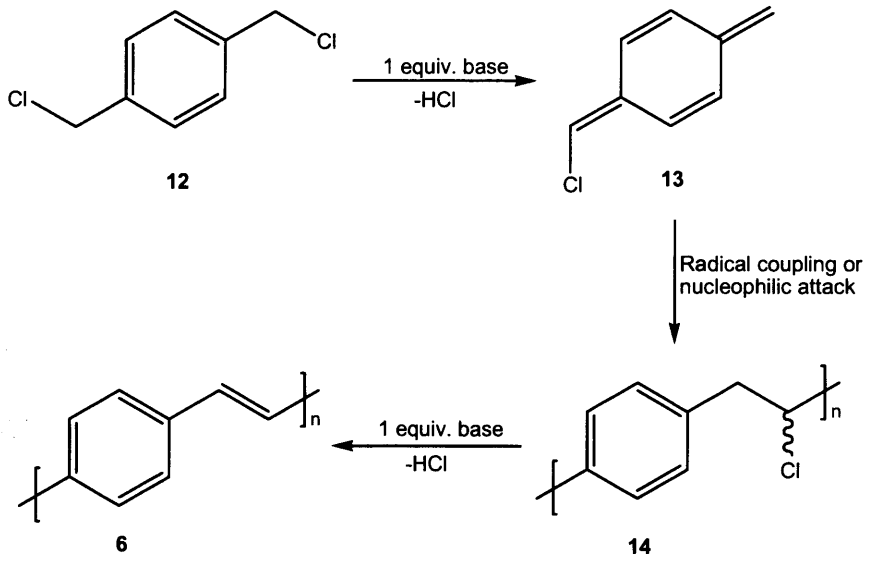
A3.2.3: Synthesis of PPV

The synthesis of PPV has been achieved in a variety of ways, and similarly to the case for polyacetylene there are both 'direct' and 'precursor' routes available. The precursor routes hold the advantage over the direct routes as they allow easier processing of the polymer, due to the enhanced solubility of a non-conjugated precursor material as compared to fully conjugated PPV, the latter being almost insoluble in all common organic solvents. The best known route of this 'precursor' type is that developed by Wessling and Zimmerman which involves a polyelectrolyte intermediate in which the charged species are sulfonium groups.[42] These functionalities serve a duel role, both helping to solubilise the precursor polymer (**9**) in protic solvents, and serving as leaving groups that are eliminated on heating to yield the conjugated PPV (*Scheme 3*). This route produces precursor polymers that can be processed reasonably easily, however control over the polymerisation process is limited and the degree of polymerisation in the final PPV material can be variable.



Scheme 3: The Wessling and Zimmerman route to PPV.

Another well-known 'precursor' route to PPV is the Gilch polymerisation, involving the polymerisation of benzylic halides as shown in *Scheme 4*. First discovered in 1966,[43] this reaction has been shown to proceed *via* a carbanionic step-growth mechanism to yield a halide-substituted precursor polymer (**14**). Opinions vary as to whether the polymerisation step proceeds *via* radical coupling or nucleophilic attack, mechanistic studies by Vanderzande and coworkers pointing to the former.[44] Base-induced dehydrohalogenation is carried out on the precursor polymer in order to yield the desired PPV. The actual monomer involved in the polymerisation is not the 1,4-bis(halomethyl)benzene starting material **12**, but a quinomethane derivative (**13**) produced *via* an initial dehydrohalogenation of the 1,4-bis(halomethyl)benzene.



Scheme 4: The Gilch Polymerisation.

The Gilch method of polymerisation has been modified to allow for the introduction of various functional groups at the aromatic rings of the polymer, which can be used to give some degree of control over both the emission wavelength, and also the solubility of the PPV produced. For example, the modified Gilch route described by Lee and coworkers provides a method of synthesising the well-known PPV derivative poly(1-methoxy-4-(2-

ethylhexyloxy)-*p*-phenylenevinylene) or MEH-PPV (**15**) (*Figure 12*) from α,α'-dibromo-2-methoxy-5-(2-ethylhexyloxy)xylene. This route involves the use of DMF as solvent in place of the more commonly used THF, which prevents the problem of gel formation due to the increased solubility of MEH-PPV in DMF.[45] Also, although the precursor polymers are far more soluble than PPV itself, addition of long solubilising alkyl chains to the aromatic rings further enhances their solubility aiding processing, purification and characterisation. The MEH-PPV prepared via this method has molecular weights of up to 32,000 and a polydispersity index (PDI) of between 1.5 and 4.7. The PDI is a measure of the distribution of molecular weights in a given polymer sample, and is calculated by dividing the weight-average molecular weight by the number average molecular weight. As the polymer chains approach uniform chain length, the PDI approaches unity.

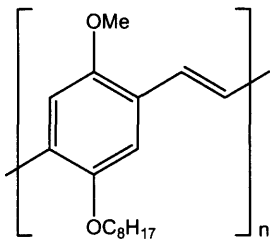


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Figure 12: Poly(1-methoxy-4-(2-ethylhexyloxy)-*p*-phenylenevinylene) (MEH-PPV).

Although the Wessling and Zimmerman and Gilch processes are the most popular methods for making large quantities of PPV for industrial applications,[46] the two syntheses both suffer from a degree of irreproducibility, and the polymers produced are often of low purity. Imperfections in the polymer backbone can arise through 'head-to-head' couplings of the monomer, which on conversion of the precursor polymer to PPV, lead to what are known as tolane-*bis*(benzyl) defects (*Figure 13*), which can account for between 1.5 and 6 percent of the final polymer.[47] After elimination of the sulfonyl or chloride leaving groups to generate PPV, significant impurities can arise because the products arising from elimination of leaving groups become incorporated into the polymer matrix. The actual polymerisation itself is also poorly controlled in these methods; being radical-initiated the technique offers little in the way of control over parameters such as molecular weight, polydispersity and degree of conjugation.

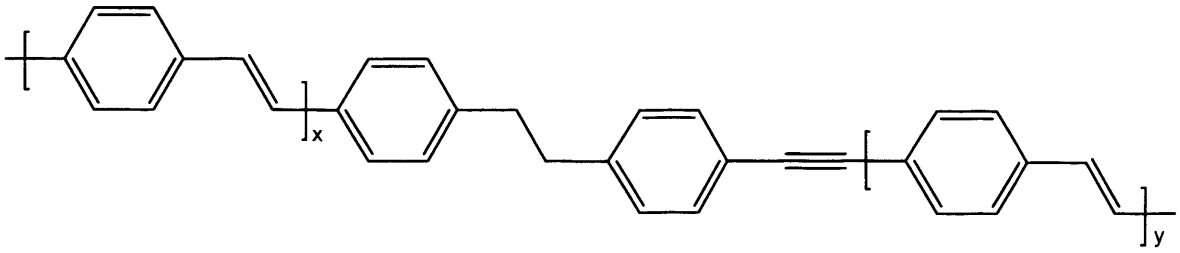
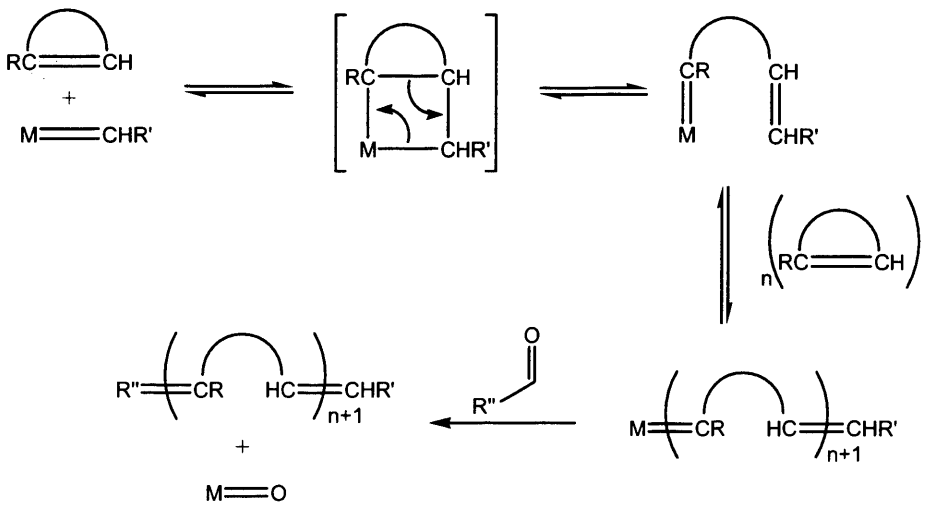


Figure 13: Tolane-*bis*(benzyl) defect in a PPV chain.

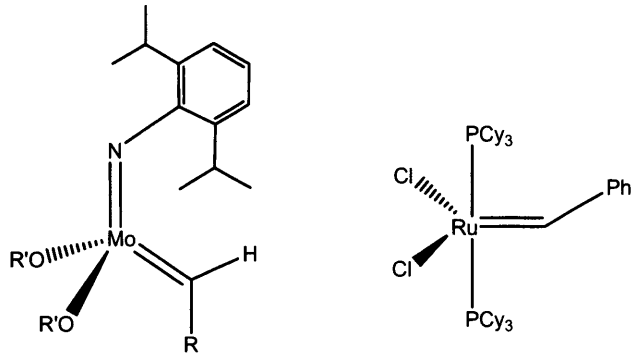
Alternatively, more controllable processes have been developed in order to prepare precursor polymers to PPV, the two most notable using 'living' ROMP.[48] This type of polymerisation was first discovered by Natta during an attempt to polymerise cyclopentene using transition metal catalysts such as $MoCl_3$ and WCl_4 in conjunction with aluminium alkyls. It was observed that instead of poly-(cyclopentene), a linear chain polymer was produced consisting of alternating trimethylene and vinylene units. It was thus evident that opening of the cyclopentene ring had occurred, and the mechanism was postulated to be similar to that of alkene metathesis.

As is illustrated in *Scheme 5*, ROMP is catalysed by a metal alkylidene species which undergoes a [2+2] cycloaddition with strained cyclic olefins in such a way as to exchange the substituents at the double bonds *via* a metallocyclobutane transition state.[49] This metallocyclobutane rearranges in such a way as to generate a new metal alkylidene at the end of the growing polymer chain, which can then go on to react with another molecule of monomer to continue the polymerisation process.



Scheme 5: Mechanism of ROMP, including termination *via* addition of an aldehyde.

ROMP is termed a *living* polymerisation, as there is no chain termination step in the mechanism. Each initiator molecule produces only one polymer chain, the length of which is proportional to the amount of monomer used. These chains all grow at essentially the same rate, thus the polymers produced *via* ROMP are of a controlled molecular weight and have a low PDI.[50] Polymerisation is terminated by adding an excess of either an aldehyde, which reacts with the metal alkylidene in a similar fashion to an alkene and produces a metal oxo compound and a polymer capped with an alkene functionality, or a diene, which terminates the polymerisation through chain transfer.[51] Many initiators have been developed which catalyse ROMP, two of the best known being the Schrock initiator (**16**) and the Grubbs initiator (**17**) (*Figure 14*). The choice of initiator for a particular reaction is largely determined by the nature of the substrate; the Grubbs initiator **17** is significantly more tolerant towards polar functional groups.



16

Schrock Initiator

R = alkyl or aryl

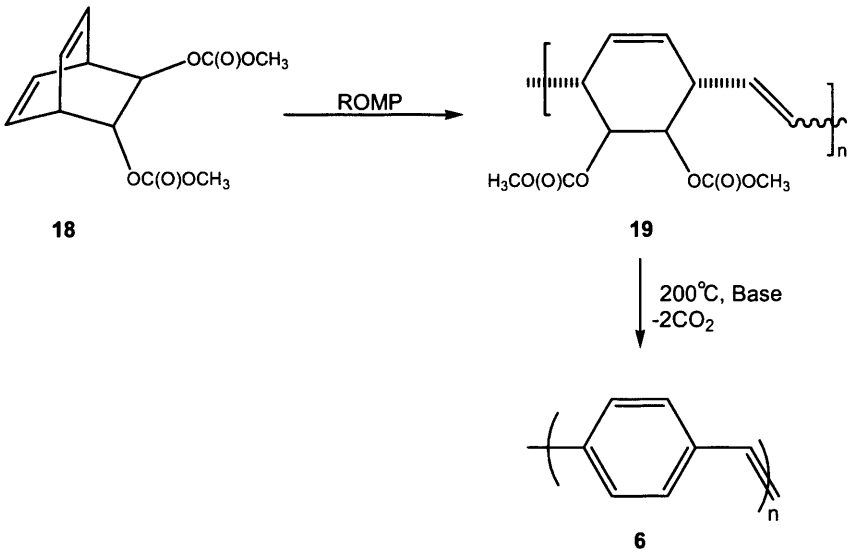
R'=$(CF_3)_2CH_2$

17

Grubbs Initiator

Figure 14: Two well-known initiators used in ROMP.

A route based around ROMP of substituted bicyclo[2.2.2]octadienes (**18**) has been developed by Grubbs *et al.*, using the initiator $[Mo(=NAr)(=C(H)CMe_2Ph)\text{-}(OCMe_2(CF_3)_2)_2]$ (*Scheme 6*).[52] Subsequent elimination of the carboxylate groups of polymer **19** *via* thermolysis yields PPV with a PDI of 1.2-1.3, although the conditions are severe (200°C in the presence of a basic catalyst).

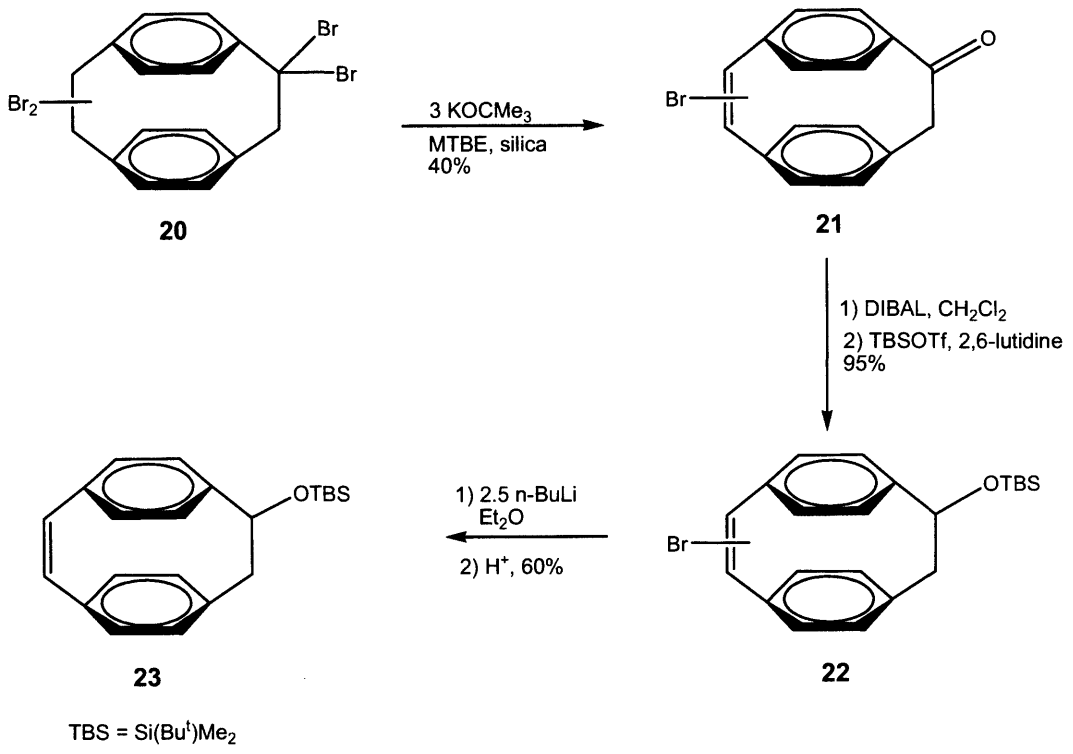


Scheme 6: Grubbs' route to PPV *via* ROMP of bicyclooctadienes.

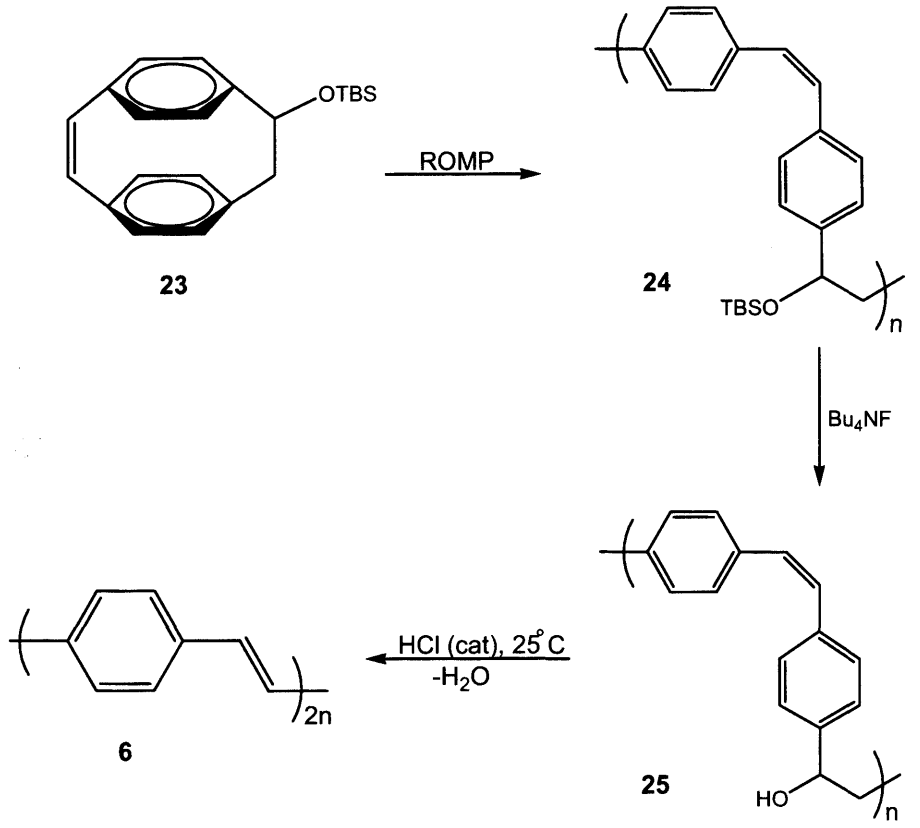
In contrast to the sulfonium precursor route described in previous paragraphs, the Grubbs' methodology introduces the conjugation to the final polymer through generation of the aromatic ring. This route achieves the synthesis of high molecular weight, low polydispersity PPV; however substitution at the aryl rings is not possible. Thus, the PPV obtained using this particular synthetic route cannot be 'tuned' to meet requirements of conductivity, solubility and emission wavelength.

In a related approach, Bazan and Miao have introduced another route to controlled molecular weight PPV, *via* ROMP of a single type of [2.2]-*para*-cyclophene derivative (**17**).[53] The necessary *para*-cyclophene monomer **23** can be synthesised, in a non-trivial fashion, in four steps from tetrabromo-*para*-cyclophene (**20**) (*Scheme 7*), then converted to precursor polymer **24** *via* ROMP using the Schrock initiator.

Precursor polymer **24** is produced in a *cis*-specific fashion, with a narrow polydispersity; the molecular weight being proportional to the amount of monomer used, as would be expected for a living ROMP process. Desilylation to give **25** followed by dehydration under mild conditions at 25°C (in the presence of a catalytic amount of HCl) is required to convert this precursor to *trans*-PPV (**6**). The overall route is shown in *Scheme 8*.



Scheme 7: Synthesis of 9-[(*tert*-butyl dimethylsilyl)oxy]-[2.2] *para*-cyclophan-1-ene (**23**)



Scheme 8: Bazan's route to PPV *via* ROMP of *para*-cyclophenes

Using *living* ROMP of [2.2] *para*-cyclophene (**26**), preparation of copolymers is possible, for example PPV-*block*-polynorbornene (**28**) (*Figure 15*).[54] However, as was outlined above, this particular method (namely, the monomer employed) suffers from the drawback that it does not allow substitution of the PPV at the aryl rings, hence tailoring of the emission properties or solubility is not possible. However, the copolymerisation of norbornene (**27**) with the PPV itself enhances the solubility of the polymer and, providing that the PPV blocks are of sufficient length, it does not affect the electronic properties of the resulting material.[54]

An alternative approach to copolymerisation of PPVs with nonconjugated, flexible linkers has been described by Hay and Klavetter, where a Wittig-type coupling is employed to incorporate hydrocarbon linkers (**30**) of various lengths into a PPV polymer backbone (**32**) (*Scheme 9*).[55] As these linkers interrupt the average conjugation length of the PPV, some degree of emission wavelength tuning is possible, as well as the more obvious benefits to solubility and processability presented using this approach.

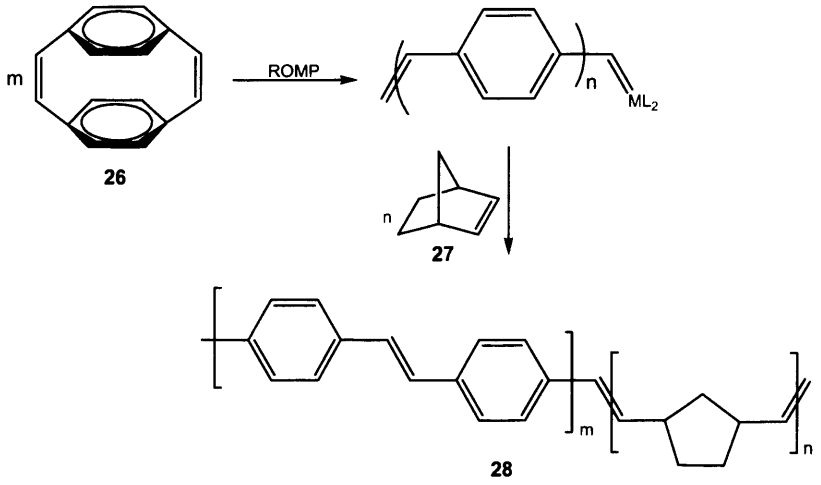
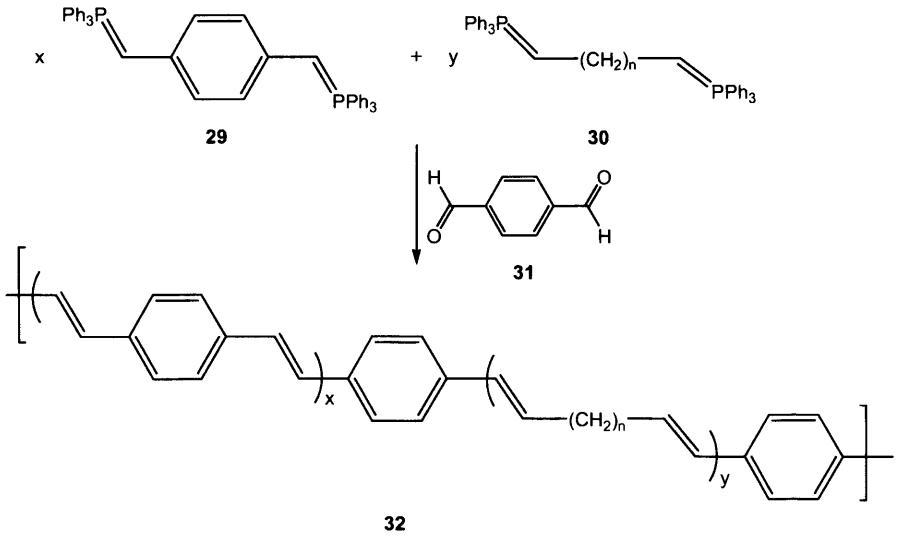
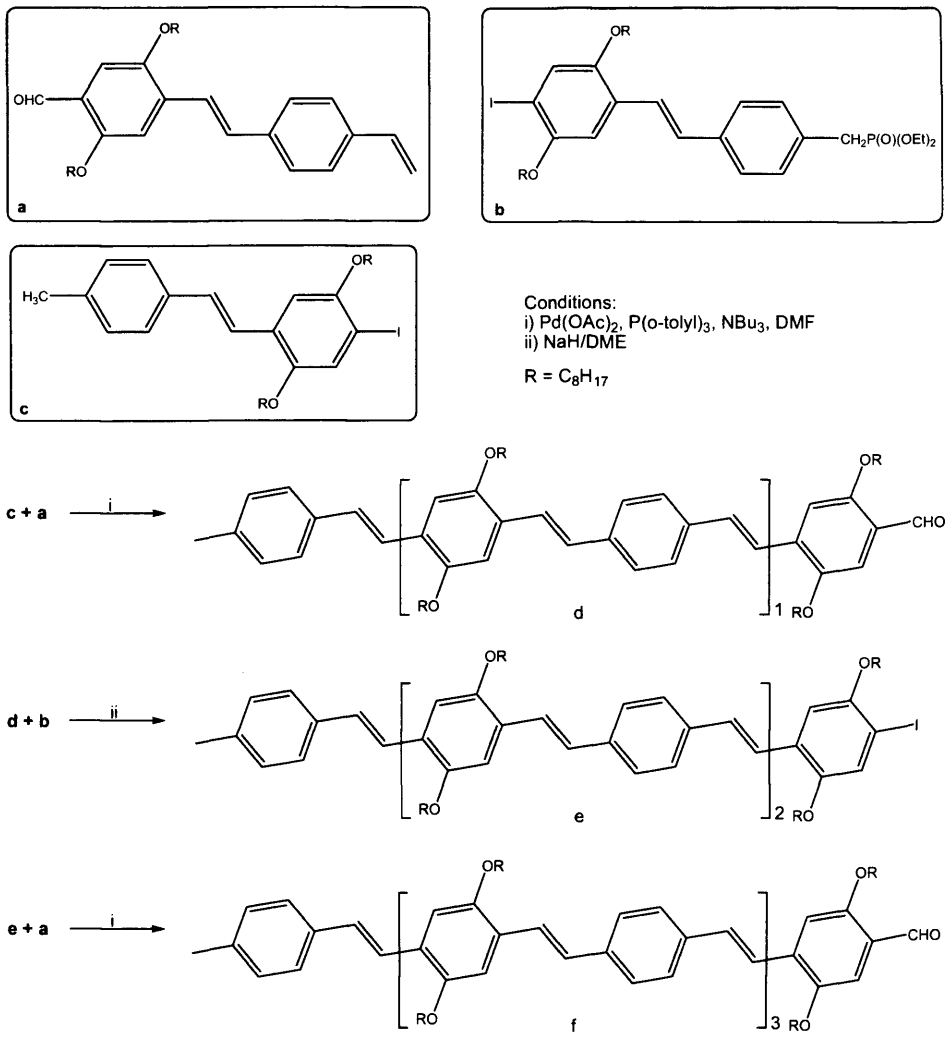


Figure 15: Preparation of PPV-block-Polynorbornene.



Scheme 9: PPV incorporating a flexible aliphatic linker in the polymer backbone.

Of the synthetic routes offering direct access to PPV, many are also employed to prepare oligomeric forms (between 4 and 12 aromatic rings) as opposed to the longer chain polymers. These shorter chain compounds offer advantages in characterisation and purification as they are generally more soluble than their polymeric counterparts, and are thus often studied as model compounds for PPV. However, there has also been interest in PPV oligomers as electroluminescent compounds in their own right, as they are inherently more processable and hence facilitate device fabrication.[56] The well-defined structure and conjugation path length of oligomeric PPVs allows for easy tuning of their electroluminescent properties. As well as using the oligomers themselves as the emissive layer in oLEDs, there has been a significant body of work carried out studying the incorporation of oligophenylenevinylenes into non-conjugated polymers as either side chains or part of the main chain, to form another class of interesting electroluminescent materials.[57] A particularly elegant example of the synthesis of oligo-(phenylenevinylene)s has been developed by Yu *et al.*,[58] using a tandem Heck/Horner-Wittig approach to progressively build oligomers containing from four to twelve aromatic units (see *Scheme 10*).



Scheme 10: Stepwise synthesis of oligo(phenylenevinylene).

Methods giving direct access to PPV are also often used to prepare copolymers of PPV with other monomers such as 2,8-dibenzothiophene-5,5-dioxide[59] and triazole (**33**),[60] these two examples having been synthesised by means of the Wittig reaction. Such copolymers are desirable as the incorporation of electron-transporting moieties, such as the triazole functionality in the PPV shown in *Figure 16,* improves the quantum efficiency of the polymer through balancing of the charge injection and transport.

Other reported direct routes to PPV include the Heck coupling between divinylbenzene and suitable aryl bromides,[61] metathesis polycondensation,[62] and Knoevenagel condensation,[63] this last being used to prepare oligomeric forms or cyano-substituted PPVs (**35**) (*Scheme 11*), the emission wavelength of which are strongly red-shifted due to the electronic effect of the cyano groups.

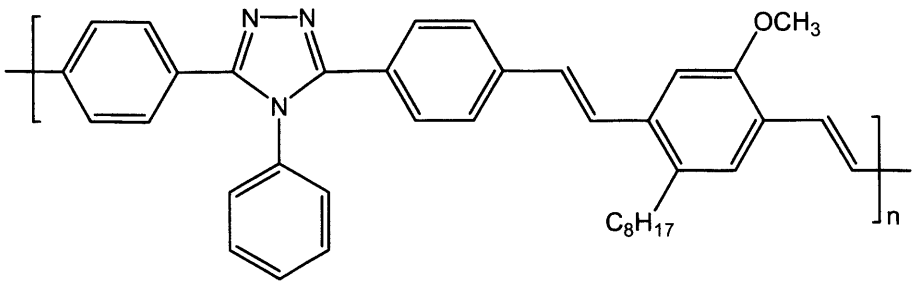


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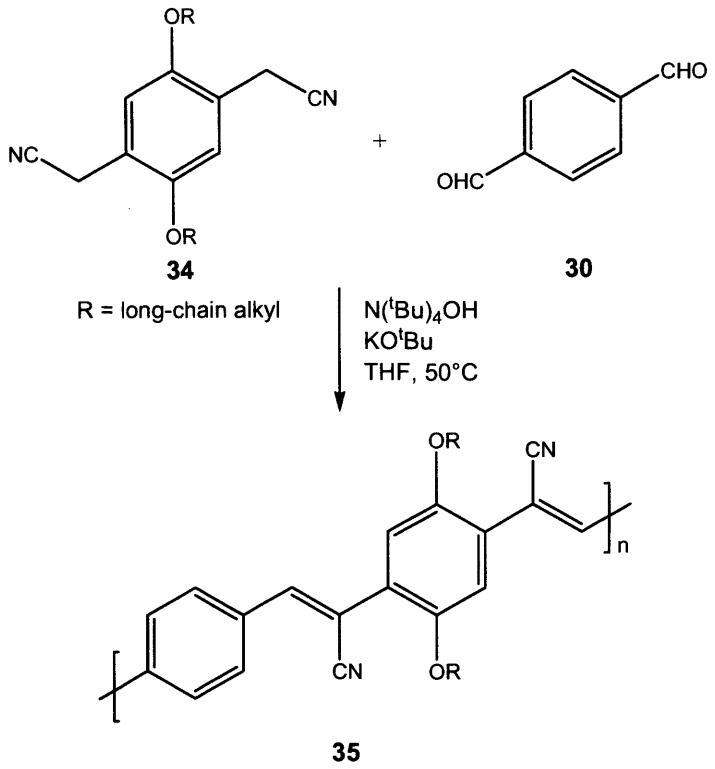
Figure 16: Copolymer of triazole with substituted PPV.



Scheme 11: Synthesis of a cyano-substituted PPV analogue *via* Knoevenagel condensation.[64]

A4: Poly(1,4-phenylene) (PP)

Typified by a wide band gap, hence emitting light in the blue region, poly(1,4-phenylene), or PP (**7**) (*Figure 17*), and derivatives comprise another variety of semiconducting, electroluminescent polymer that is of interest as a possible emissive layer in pLEDs. Achieving efficient blue emission has long remained a challenge to the field of electroluminescent polymer research, since the greater proportion of electroluminescent polymers, such as PPV, possessing a smaller band gap causing them to emit in the green / yellow region.

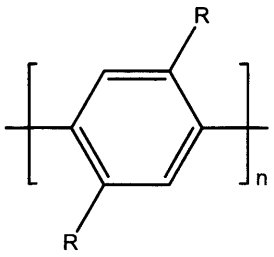


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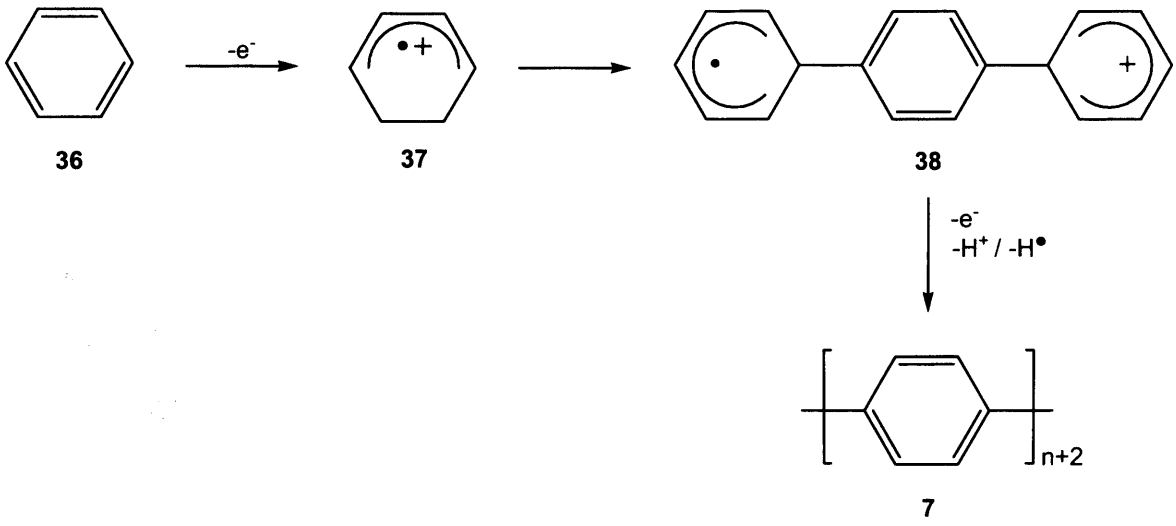
Figure 17: Poly(1,4-phenylene).

A4.1: Synthesis of Polyphenylenes

The most commonly employed 'direct' synthetic method for preparing polyphenylenes is *via* oxidative coupling of both substituted and unsubstituted benzenes using a Lewis acid catalyst/oxidant system. This reaction is believed to take place through a single electron oxidation of benzene (**36**) to form the radical cation **37**, followed by reaction of this intermediate with several benzene rings to yield an oligomeric radical cation **38**. Another single electron oxidation and loss of two protons, followed by oxidative re-aromatisation of the dihydro structures by $CuCl_2$ or a similar oxidant furnishes the desired PP (*Scheme 12*).[65]



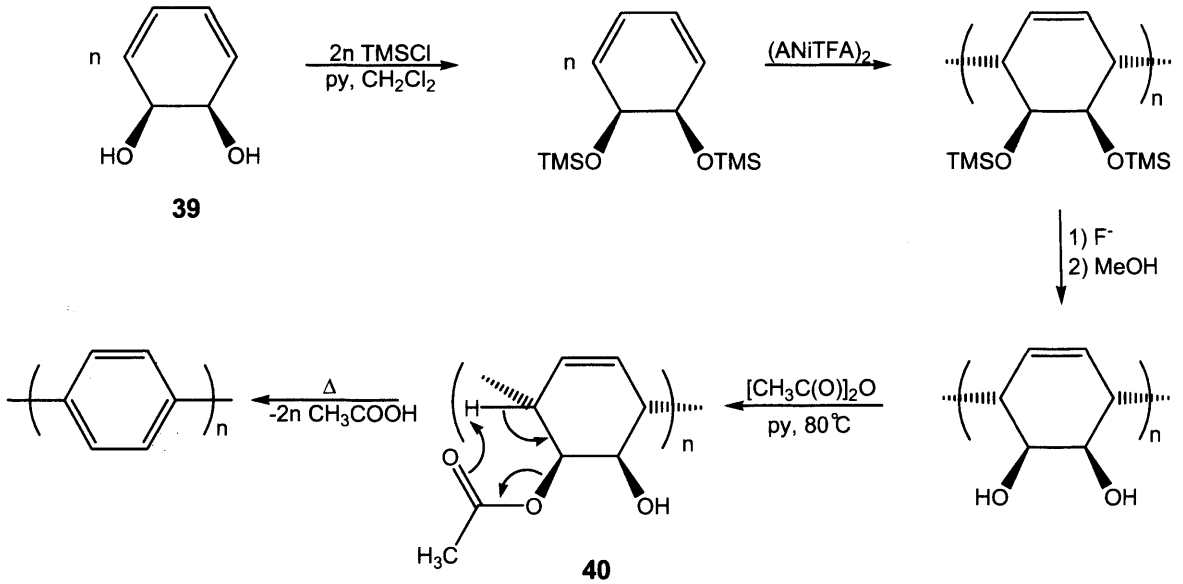
36 37 38 7

Scheme 12: Mechanism of coupling to form PP.

Alternative methods employed to synthesise PP include anodic electrochemical oxidation of benzene or biphenyl[66], organometallic coupling using Grignard reagents,[67] dehydrogenation of polycyclohexylenes[68], and cycloaddition reactions.[69] More recently, synthesis of substituted PPs has been deemed more attractive as, similarly to in PPV, the substituents can be employed to confer desirable solubility and wavelength tuning

characteristics upon the resulting polymer. Since the enhancement in solubility applies not only to the final polymer, but also to the monomer units themselves, this type of substituted PP can be prepared *via* more conventional chemistries such as the Suzuki coupling reaction. The increased solubility of these polymers has allowed high-quality films to be cast, and blue-emitting pLEDs have been developed that exhibit reasonable efficiencies.[70]

As with PPV, a range of 'precursor' routes to PP are available,[71] although these are as yet limited by problematic side reactions lowering the molecular weight of the precursor polymer. Also, the high temperatures necessary to effect conversion from the precursor polymer to PP has a tendency to adversely affect the quality of the polymer film and thus reduce its efficiency in light emissive devices.[72] The most developed of these precursor routes is that of Grubbs and coworkers involving transition metal-catalysed polymerisation of functionalised hexadienes **39**, yielding precursor polymer **40** with an average MW of 27000 and a PDI of 1.5-2.0, which can then be converted to PP by pyrolysis at 310-340°C (*Scheme 13*).[73]



Scheme 13: Preparation of PP *via* precursor route.

PPs are a highly valuable member of the family of conducting polymers, as described in the above section their wide band gap leads them to emit blue electroluminescence which is extremely difficult to obtain using any other electroluminescent polymer. There are

currently a range of routes available to give access to well-defined PP, in both its unsubstituted and functionalised forms.

Thus far, all the polymers discussed in this section have been similar in that they possess an all-carbon backbone, with tuning of their properties achieved by judicious choice of pendant substituents. Another method for the adjustment of the band gap in semiconducting polymers, thus altering their conductivity and emissive properties, is the inclusion of a heteroatom into the main polymer chain. Two examples, discussed below, aim to further illustrate the diverse range of conducting and electroluminescent polymers available, and the many methods used for tuning their properties.

A5: Polypyrrole.

The polymerisation of pyrrole (**41**) was first reported by Gardini in 1973,[74] and occurs extremely readily, even taking place on the surface of vessels left standing open to the atmosphere, to yield a black powdery substance. Although many different oxidizing agents can promote the polymerisation reaction, this type of chemical synthesis method has a significant drawback; namely that the polypyrroles obtained are usually intractable black powders. Films can however be formed at a solid or liquid interface, but they tend to be of a poor quality.[75] Thus, electrochemical methods are preferred for the synthesis of mechanically strong and good quality films of polypyrrole. In fact, continuous processes have been introduced to facilitate large-scale electrochemical preparation of the material (for example see *Figure 18*). The standard, laboratory electrochemical reaction is carried out in a one-compartment cell, comprising of a copper cathode and either platinum or ITO coated glass, with the electrolyte comprising of an aqueous solution of the pyrrole monomer and copper sulfate. The polymerization reaction proceeds *via* the radical cation as shown in *Scheme 14*.

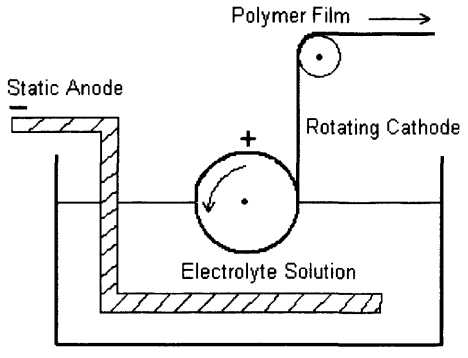
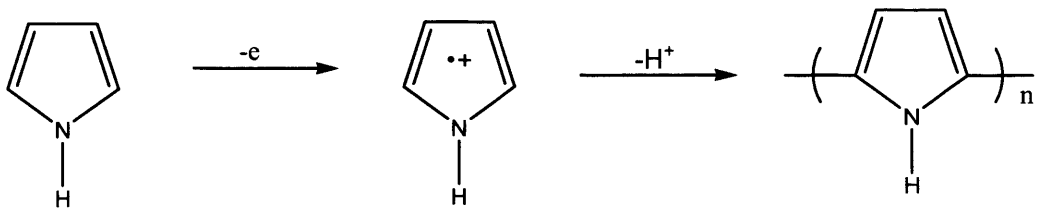


Figure 18: Continuous process for synthesis of polypyrrole using a rotating drum electrode.[76]



41 42

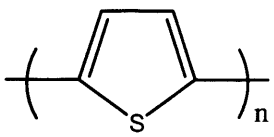
Scheme 14: Electrochemical Polymerization of Pyrrole.

Polypyrrole (**42**) is unusual amongst conducting polymers, in that it is typically prepared directly in its oxidised, conductive state. It can be reduced to the neutral polymer, but this is highly air-sensitive and must be handled in a dry box. Further reduction to the anionic form is extremely difficult; indeed calculations by Brédas *et al.* put the electrode potential of this form at -3.6 V with respect to the standard sodium calomel electrode,[77] giving a good indication as to why it is so inaccessible.

Polypyrrole exhibits remarkable stability, due in part to its low oxidation potential and also through the fact that O_2 can gain only limited access into the structure, which is always at least partly crystalline.[78] This versatile polymer finds applications in pLED's, chemical sensors,[79] and lightweight batteries, with the first commercially available batteries containing polypyrrole being released onto the market in 1992.

A6: Polythiophene.

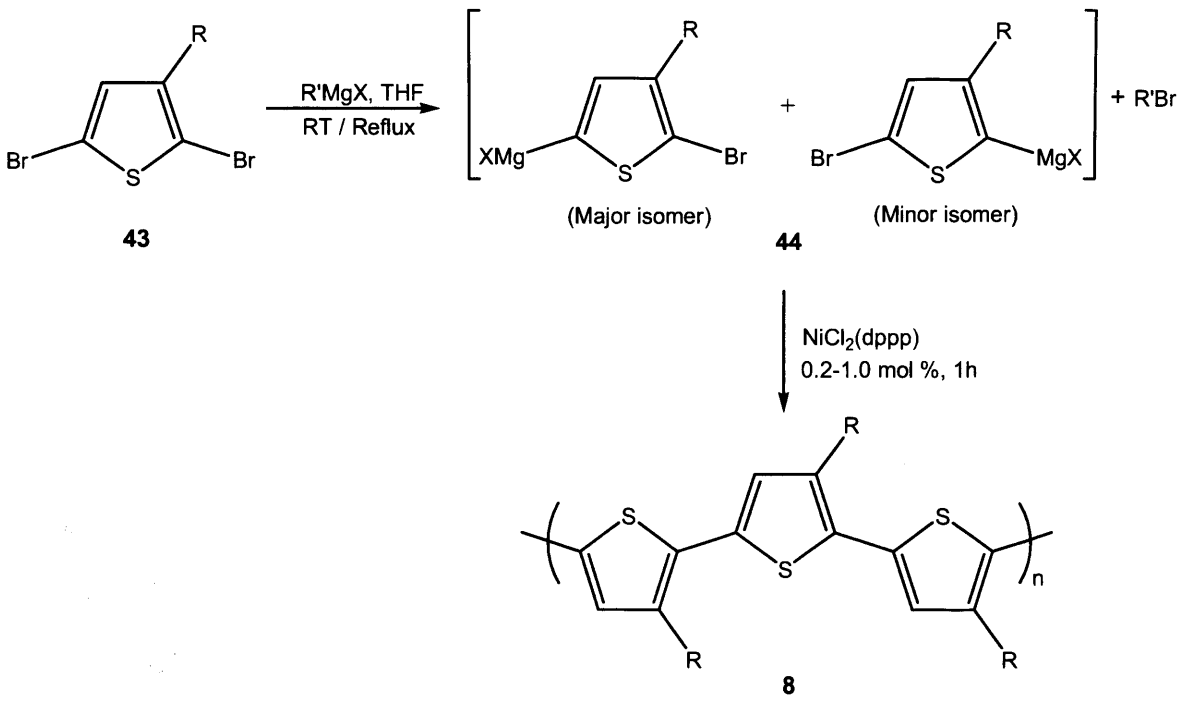
Polythiophene (**8**) (*Figure 19*) is a particularly desirable member of the family of conducting polymers, as it is stable to air and moisture in both the doped and pure forms. Structurally, polythiophene can be thought of as an analogue of polyacetylene where the diene is constrained in a five-membered ring by the addition of a sulfur atom.



8

Figure 19: Polythiophene.

Polythiophene can be synthesised from thiophene using a range of catalysts including sulfuric acid,[80] iron(III) chloride, and Ziegler-type initiators.[81] However, where an acidic promoter is used the resulting polymer has been shown to consist of alternating thiophene and tetrahydrothiophene units.[82] An alternative synthesis described by Yamamoto starts from a 2,5-dihalogenothiophene (**43**), which is converted to the corresponding Grignard reagent **44** and is subsequently cross-coupled on adding a catalyst (such as nickel acetylacetonate).[83] The resulting polythiophene polymer is purified by precipitation from methanol and can then be isolated. Further work by McCullough and coworkers on this type of polymerisation has shown that it is regioregular, resulting in over 95% 'head-to-tail' couplings.[84] This is thought to be due to a combination of kinetic and thermodynamic effects caused by steric and electronic effects in the catalytic reaction. The reaction scheme for this type of polymerisation is shown below in *Scheme 15*.



Scheme 15: Preparation of polythiophene using the Grignard metathesis approach.

Although the methods described above yield neutral polythiophene, the oxidised (doped) conducting form can be prepared directly *via* electrochemical methods. Electrochemical polymerisation of thiophene proceeds in the same manner as for pyrrole described in *Section A5*, and involves the loss of 2.25 to 2.50 electrons per unit monomer. The polymer thus produced is in the oxidised state, with 0.25-0.5 cationic centres per thiophene unit.[85] The best known electrochemical method used is the classical three-electrode approach in a

single compartment cell. The working electrode is most commonly platinum-, gold- or ITO-coated glass, with a saturated Calomel reference electrode and an auxiliary electrode of either platinum, nickel or carbon. The electrolyte is comprised of an organic solvent and a supporting electrolyte, examples of positive species used being $N(Bu)_4^+$ and Li^+, and anionic species including ClO_4^- and BF_4^-. The monomer, thiophene, is then added and a current applied. There has been a large amount of work carried out into the optimisation of the electrochemical conditions, leading to significant improvements in control of both the structural and electronic properties of the resulting polythiophene.[86] Conductivities of up to 2000 S cm^{-1} have been achieved.[87]

Polythiophenes exhibit strong electrochromism and are hence suited to applications in display technologies; the polymer can be switched reversibly between red (reduced) and dark blue (oxidised) forms. In addition, alkyl-substituted polythiophenes have been shown to exhibit *thermochromism,* meaning that the value of λ_{max} in their UV absorption spectrum is dependent upon temperature, shifting to shorter wavelengths at higher temperatures. This effect is attributed to a change in conformation at the aromatic backbone, arising from increased disorder in the alkyl substituents as the temperature is increased.[88]

A7: Summary

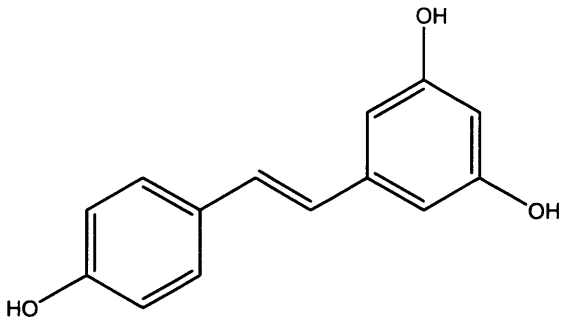
This section has illustrated the extremely diverse range of conducting polymers available to the modern chemist, describing both simply conducting polymers such as polyacetylene and those also exhibiting electroluminescent properties for example PPV. There has been significant progress in recent years toward the discovery of new routes towards the synthesis of these and similar polymers, with the emphasis being put upon reproducible, facile methods which produce well-defined, processable polymers. 'Precursor' routes, involving the preparation of a usually more soluble and tractable precursor polymer, then conversion to the desired conducting polymer in situ, have often been preferred for reasons of processability. Through the careful choice of polymerisation conditions, monomer employed, and functionalisation, the conductance and emissive properties of conducting and electroluminescent polymers can be 'tuned' to provide polymers suitable for a wide variety of applications including lightweight batteries, chemical sensors and polymer LEDs.

Section B: Stilbenes

B1: Introduction

Stilbene has been described as "the shortest possible oligomer of PPV",[89] and hence as such is of immediate interest in the study of conducting polymers. Unsurprisingly, stilbene and its derivatives have been extensively studied as both analogues of and precursors to PPV.

Stilbene (1,2-diphenylethene) itself can be isolated pure in both its *cis* and *trans* forms, and an extremely wide range of derivatives and analogues of stilbene are known, including naturally-occurring compounds such as resveratrol (**45**) (*Figure 20*), derived from grapes and shown to have beneficial properties in preventing heart disease. Many analogues of resveratrol, both naturally-occurring[90] and synthetic,[91] have been studied for their possible medicinal effects, including anticancer, antivirus and cytotoxic properties.



45

Figure 20: Structure of resveratrol.

Being highly conjugated species, stilbenes are also found frequently in fluorescent and electroluminescent molecules. For example, Yan has recently synthesised three new chromophores based on 4-Nitrobenzoic acid-2-({4-[(E)-2-(4-dimethylaminophenyl)vinyl] phenyl}ethylamino)ethyl ester (**46**) (*Figure 21*), in order to study the effect of different substituents on one- and two-electron-induced fluorescence.[92] It was shown that those compounds bearing *p*-nitrobenzoate groups at one aromatic ring of the stilbene showed no fluorescence due to fast intramolecular electron transfer, whereas those with hydroxyamino groups in place of the *p*-nitrobenzoate moiety exhibited strong two-photon-induced blue fluorescence.

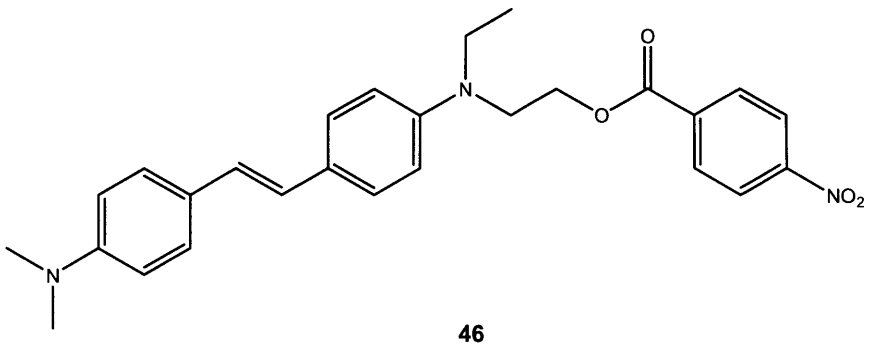


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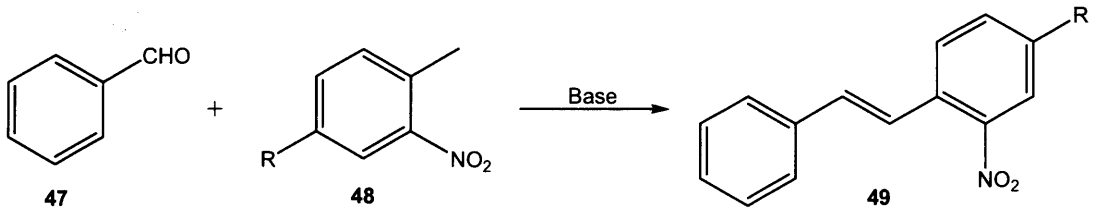
Figure 21: Structure of 4-Nitrobenzoic acid-2-({4-[(E)-2-(4-dimethylaminophenyl)vinyl] phenyl}ethylamino)ethyl ester.

B2: Stilbene Synthesis

B2.1: Classical methods

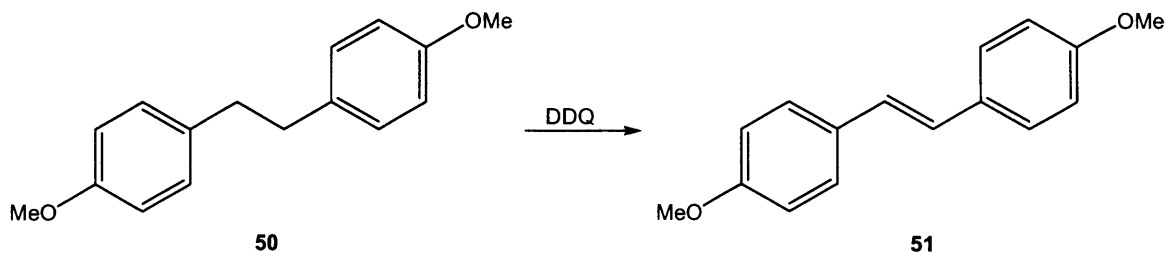
Classical synthetic approaches to stilbene include the base-catalysed condensation of aromatic aldehydes **47** with compounds of the type $ArCH_2X$ (**48**) (where X can be for example a carboxy, cyano or nitro group), the Wittig reaction, and the dehydrogenation of bibenzyls. The first of the above reactions proceeds *via* the addition of a carbanion to the carbonyl group of the aromatic aldehyde, with intermediate formation of a hydroxy compound. In the case where substituent X is a proton, the reaction will only be successful if this methyl group is activated by means of two or more nitro or cyano groups in the *ortho* and *para* positions, as shown in *Scheme 16.* Dehydration of bibenzyls **50** can easily be carried out using 2,3-dichloro-5,6-dicyanobenzo-1,4-quinone (DDQ) to furnish the corresponding stilbenes **51** (*Scheme 17*).



47 48 49

R = NO_2, CN

Scheme 16: Synthesis of stilbenes *via* base-catalysed condensation reaction.

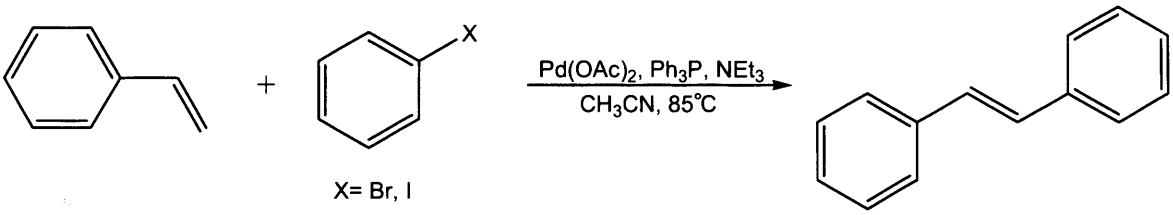


50 51

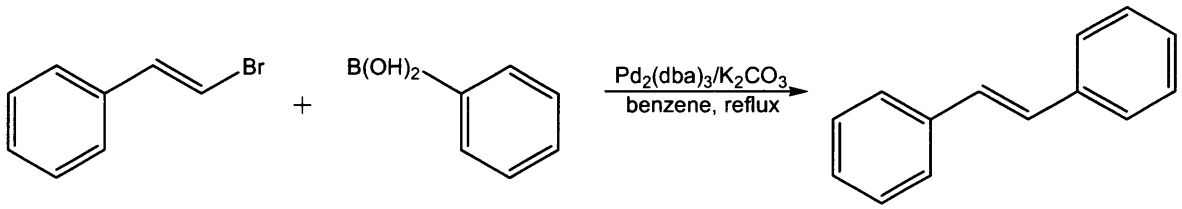
Scheme 17: Synthesis of a stilbene *via* dehydration of the corresponding bibenzyl.

B2.2: Modern methods

A wide range of synthetic strategies for the preparation of stilbenes are now recognized, with the emphasis in recent years having been placed generally upon metal-catalysed reactions. Amongst these, the Heck and Suzuki reactions are best known, offering extremely good efficiency and versatility and allowing the use of a large variety of starting materials due to their high functional group tolerance. General examples of these two reactions are shown in *Schemes 18 and 19*. The Heck reaction has been used in recent years to prepare an extremely diverse array of stilbenoid compounds including, for example, oligophenylenevinylenes[93] **(52)** (*Figure 22*) and dendrimeric molecules[94] **(53)** (*Figure 23*).



Scheme 18: An example of the Heck Reaction for stilbene synthesis.



Scheme 19: An example of the Suzuki Reaction for stilbene synthesis.

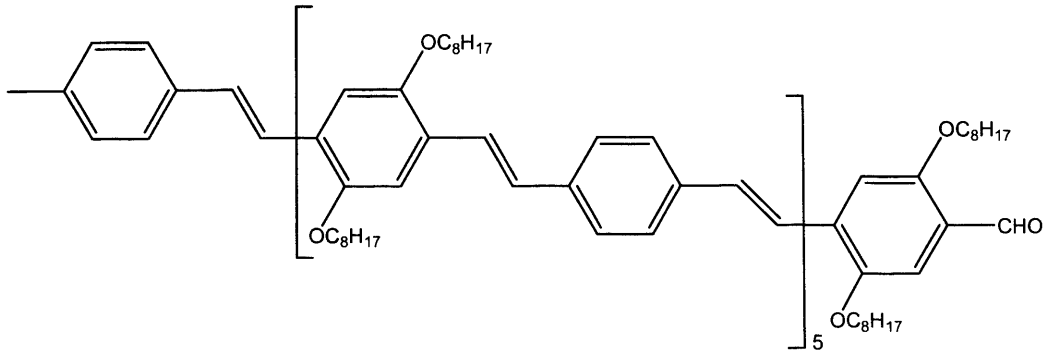


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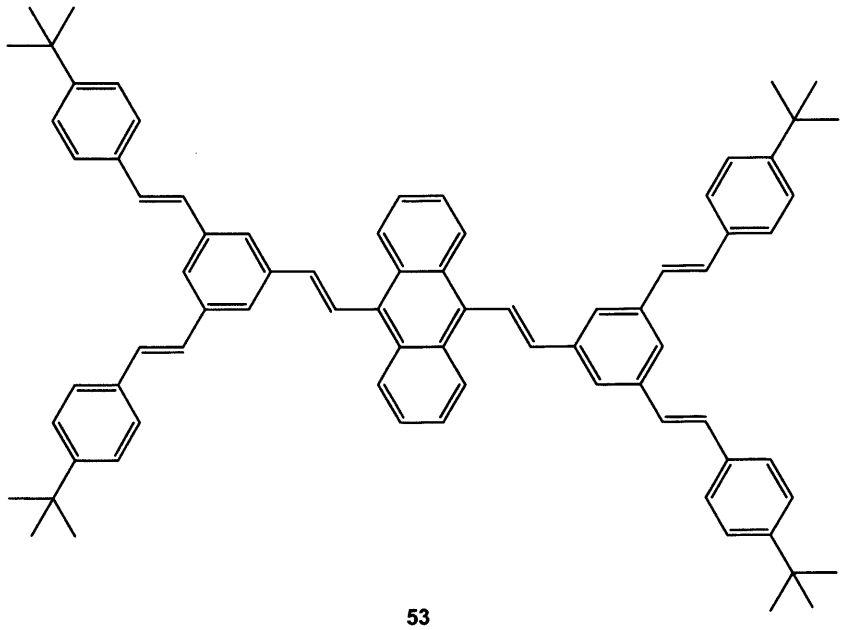
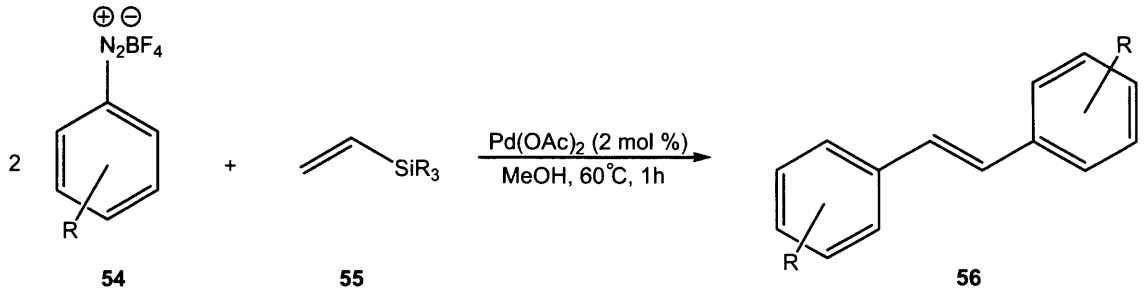
Figure 22: Oligomeric PPV synthesised using the Heck reaction.



53

Figure 23: Dendrimeric stilbenoid compound synthesised *via* the Heck reaction.

The Heck reaction is an extremely useful route into asymmetric stilbene compounds such as resveratrol and related analogues;[95] however, it can also be applied to the preparation of symmetrical stilbenes *via* the coupling of ethylene with two equivalents of the desired bromoarene.[96] As the success of the reaction depends strongly on precise control of the stoichiometry, it has been found practical to employ liquid 'ethylene equivalents' such as vinyltrialkyl or vinyltrialkoxy silanes (**55**) in place of ethylene gas itself, as exact measurements of gaseous reagents are both difficult and time-consuming. Using this method a range of symmetrical *trans*-stilbenes (**56**) has been effectively prepared by Sengupta *et al.* as shown in *Scheme 20*, starting from variously substituted diazonium salts (**54**).[97]

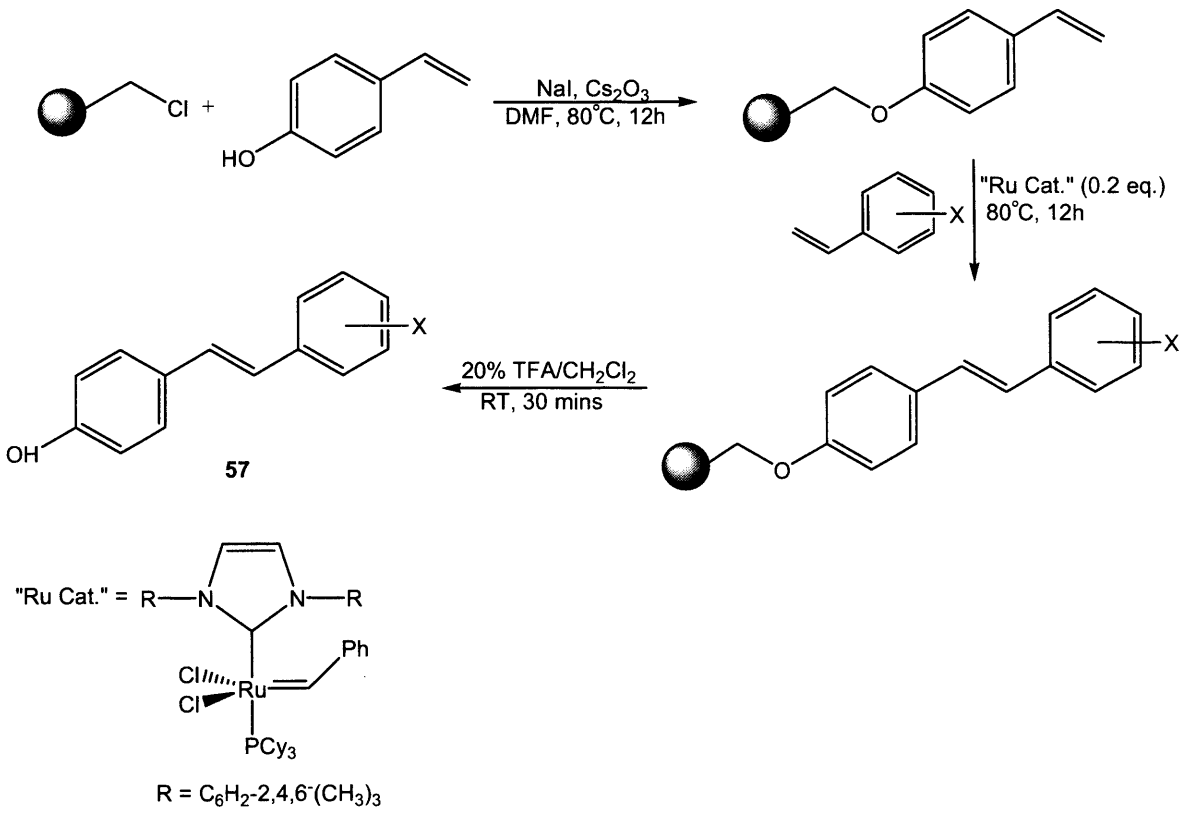


Scheme 20: Synthesis of symmetrical stilbenes using the Heck reaction.

Other transition metal-mediated C=C bond-forming reactions routinely employed in the synthesis of stilbene derivatives include the Suzuki coupling, the McMurry reaction, and alkene cross-metathesis. The McMurry reaction is an extremely well-known and versatile method of forming a C=C bond, involving the use of activated particles of titanium (0) to couple together two aldehyde moieties. Discussion of the McMurry reaction will be given in more detail in *Chapter 3*).

There are as yet only a handful of examples of the use of alkene cross-metathesis to form stilbenes. Schrock and coworkers[98] first investigated the possibility of reacting styrene with a molybdenum-based metathesis initiator to yield stilbene in 1994; however yields were not promising. More recently, work by Chang *et al.* has shown that, by using a highly active ruthenium-carbene initiator (second-generation Grubbs' initiator), yields in the cross metathesis of styrenyl ether with substituted styrenes to form stilbene derivatives can be increased; however there tended to be a mixture produced of both the homo- and cross-coupled products. By tethering the styrenyl ether reagent to a polymer support such as the Merrifield resin, the cross-coupling product (**57**) could be obtained in up to 95% yield with almost all *trans*-selectivity with regard to the stilbene double bond generated (*Scheme 21*).[99]

In addition to the methods detailed above, stilbenes can be prepared in good yield without the need for transition metal reagents *via* the Wittig and Horner-Wittig reactions. These methods entail the reaction of an aldehyde with a phosphorus ylide, to furnish the desired C=C bond through a 2+2 cycloaddition followed by elimination of a phosphorus oxide by-product. Similarly to the McMurry coupling reaction, the Wittig and Horner-Wittig reactions will be described in greater detail in *Chapter 3.*



Scheme 21: Polymer-supported alkene cross-metathesis to prepare stilbenes.

B2.3: Structure and Characterisation of Stilbenes

Upon comparing the energy-minimised molecular model representations of *cis* and *trans* stilbene, it can easily be observed that *trans*-stilbene (**B**) adopts a planar geometry whereas the two aromatic rings in *cis*-stilbene (**A**) are almost orthogonal to one another (see *Figure 24*). This is caused by steric repulsion between the two phenyl rings in the *cis* isomer, meaning that this form is higher in energy than the *trans* isomer; in the ground state, the energy difference being approximately 5 kcal mol^{-1}.[100]

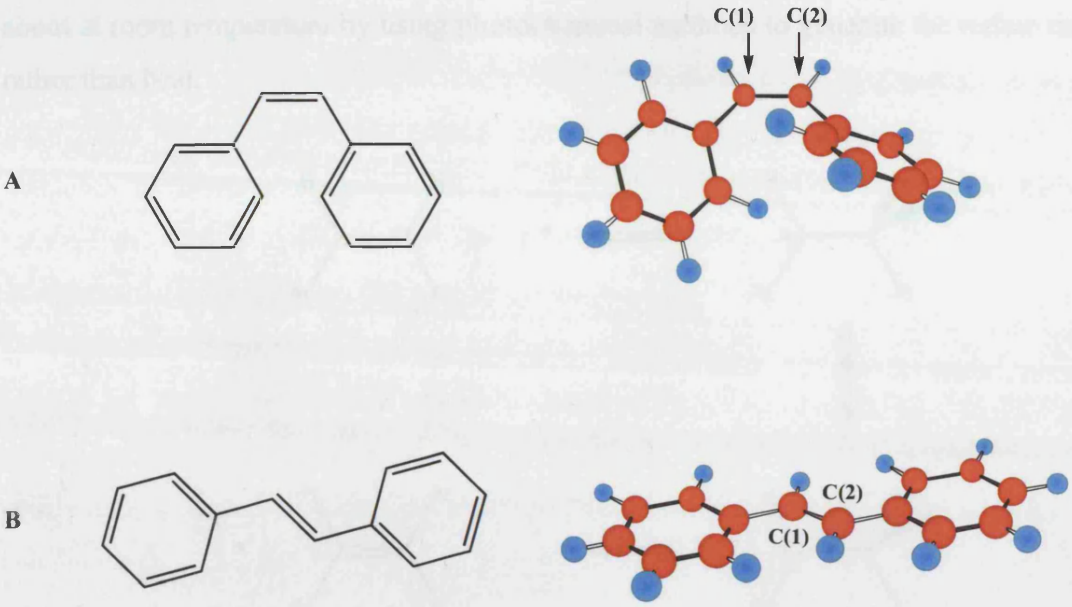


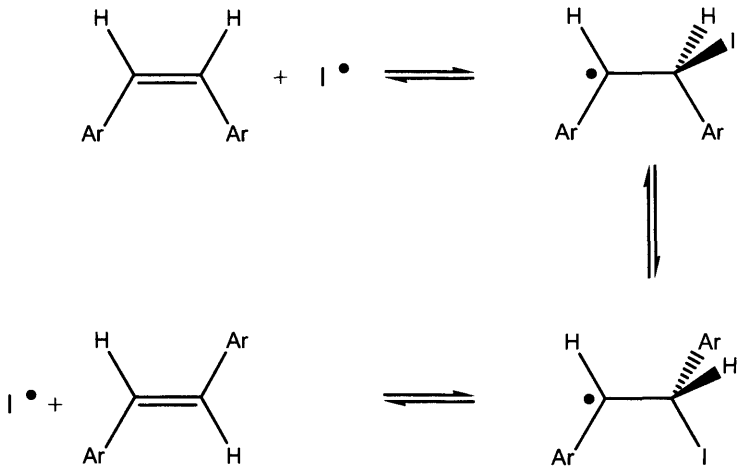
Figure 24: Three-dimensional representations of *cis*- and *trans*-stilbene.

The torsion in the *cis*-isomer causes the ethylene bond to be 'twisted' slightly, and also increases the C(1)-C(2)-C(3) angle from 126.4° in the *trans* form to 129.5° in the *cis* isomer.[101] The double bond C(1)-C(2) is slightly longer in the *cis* form as compared to the *trans*, probably also due to the higher strain in the *cis* isomer. Interestingly, reports of the actual length of the stilbene double bond determined *via* crystallographic methods have shown a marked tendency to estimate the length to be unusually short.[102] This anomalously short bond length is not confirmed by any other method, NMR,[103] UV spectroscopic studies, and theoretical calculation having all shown the bond length to be comparable with that of other ethylenes. Theoretical modelling of the *trans*-stilbene molecule has in fact suggested the unusually short bond length to be an artefact, caused by disorder in the crystal structure.[104] This disorder is due to a twisting motion of the aromatic rings, or more specifically, the torsional vibration of the C-Ph bonds.[105]

B2.4: *cis/trans* Isomerisation

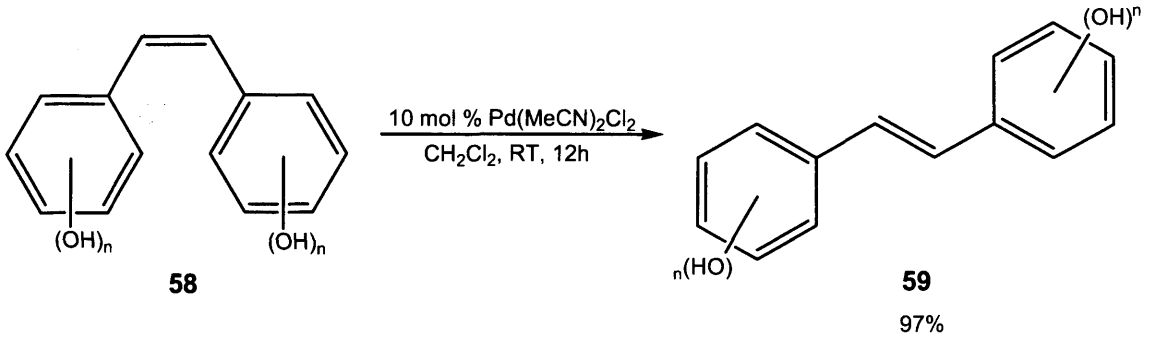
As described above, the *trans* form of stilbene and its derivatives are significantly more stable than the *cis* isomers. This being taken into account, it is evident that isomerisation observed in stilbenes is nearly always from the *cis* to the *trans* form and not *vice-versa.* The most facile approach to bringing about this isomerisation is simply to heat the stilbene in question with a trace of iodine. Heating brings about dissociation of the I_2 molecule to produce iodine radicals, which then interact with *cis*-stilbene *via* the mechanism shown in *Scheme 22* to effect the *cis/trans* isomerisation.[106] The same transformation can be brought

about at room temperature by using photochemical methods to generate the iodine radicals rather than heat.



Scheme 22: Iodine-catalysed isomerisation of *cis*-stilbene to *trans*-stilbene.

The isomerisation method detailed above involves somewhat harsh conditions, which can be detrimental to polyhydroxylated types of stilbene (**58**). The *trans* isomers of such compounds often have biological activity, so hence a method of converting a mixture of *cis* and *trans* isomers to the all-*trans* isomer is desired. Such methods are rare to date, with the only one of particular note being that of Spencer and coworkers, which employs $PdCl_2(MeCN)_2$ as a catalyst in 10 mol% loading and yielding the pure *trans* isomer in up to 97% yield (*Scheme 23*).[107]



Scheme 23: *cis / trans* Isomerisation of polyhydroxylated stilbenes using a palladium catalyst.

B2.5: Reactivity of the Stilbene Double Bond

Stilbenes are extremely useful precursors for the synthesis of PPV oligomers and related polymers. One of the most widely-used methods of preparing such polymers has been the synthesis of a non-conjugated, easily processable precursor polymer and subsequent thermal conversion of this to PPV *in situ*, after processing. Due to the success of this approach, not only stilbenes themselves are required as PPV precursors, but also of use are their non-conjugated analogues; *i.e.* stilbene derivatives from which the central ethylene linkage has been in some way 'removed' by conversion to a C-C single bond. This section aims to explore some of the most common reactions of the stilbene C=C unit, with a view to illustrating ways in which this reactivity can be exploited to effect the removal of the double bond.

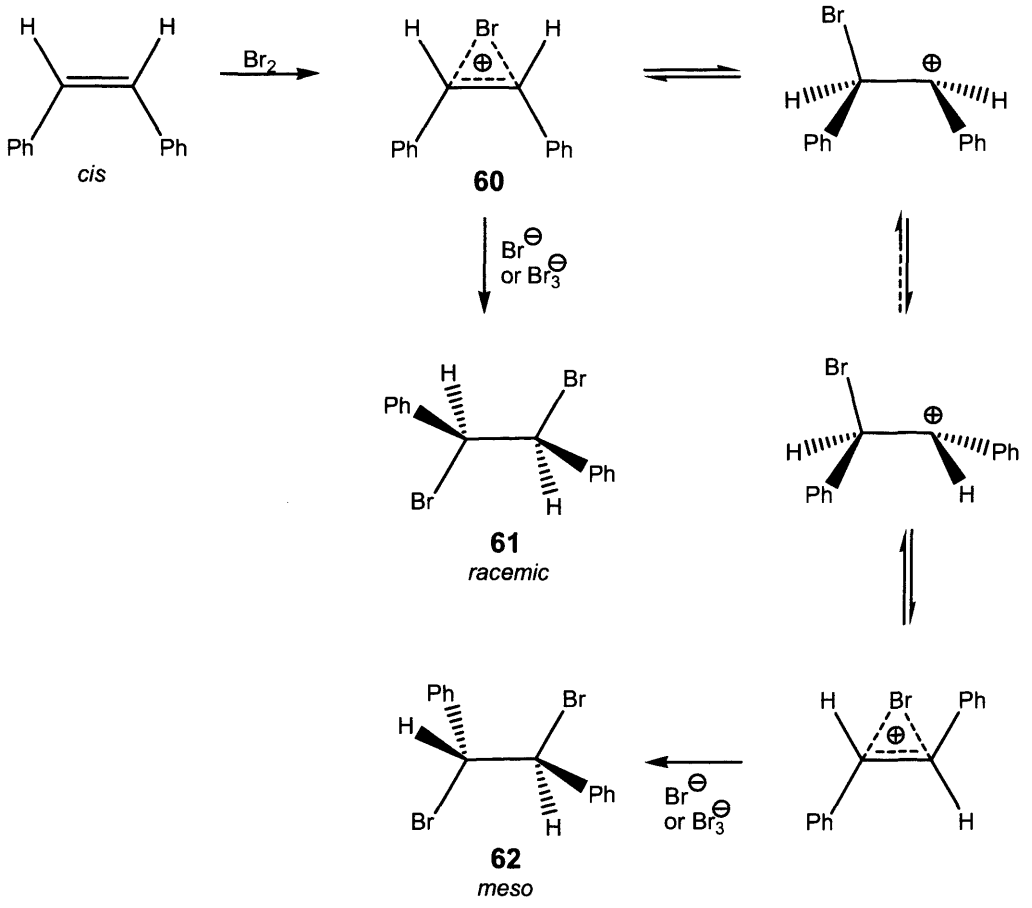
B2.5.1: Addition Reactions

Although the stilbene double bond does react with, for example, halogens, halogen acids, ozone, and peroxides, the rate of reaction is extremely slow compared to what might be predicted for a system comprising of an ethylenic moiety attached to two aromatic units. In the case of *trans*-stilbene, the rate of addition of elemental bromine is approximately one hundred times slower than the rate of the analogous reaction with styrene.[108]

Depending on reaction conditions, and hence on the mechanism, the addition of Br_2 to the stilbene double bond in *cis*-and *trans*-stilbene can yield either or both *meso* (**62**) and *racemic (***61**) 1,2-dibromo 1,2-diphenylethane, however the racemic form has a tendency to isomerise thermally to the *meso* compound. The stereochemistry of the reaction also depends strongly upon the polarity of the solvent. In solvents with a low dielectric constant such as carbon tetrachloride, the overall reaction proceeds in a *trans*-fashion, the reaction of bromine with *cis*-stilbene will hence yield the racemic dibromide. In solvents with a high dielectric constant, for example nitromethane, overall *cis*-addition becomes more favoured, with approximately 90% of the *meso* dibromo compound being formed.[109] In addition to the solvent effects described above, electron-withdrawing substituents at the aromatic rings give rise to overall *trans*-addition, whereas electron-donating substituents cause overall *cis*-addition.

The proposed mechanism of addition to the stilbene double bond is described in *Scheme 24,* again using the addition of elemental bromine as an example. It shows how the initial step involves *trans*-addition to the alkene, and the inversion of the intermediate

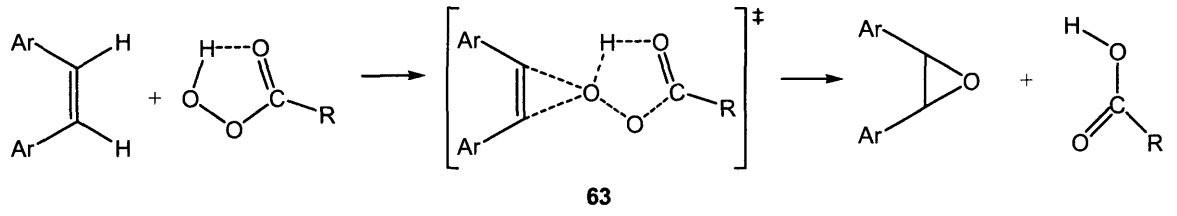
bromonium ion (**60**) can occur in nonpolar solvents.[110] Addition to *cis*-stilbene under free-radical conditions results in overall *cis*-addition leading to exclusively the *meso* dibromide.



Scheme 24: Mechanism of Br_2 addition to *cis*-stilbene.

B2.5.2: Epoxidation

Stilbenes, like any alkene, can be readily epoxidised using peroxy acids, the most widely used being *m*-chloroperoxybenzoic acid (mCPBA). The mechanism of epoxidation was proposed by Bartlett[111] in 1957 to be a concerted process involving a symmetrical transition state **63** (*Scheme 25*).



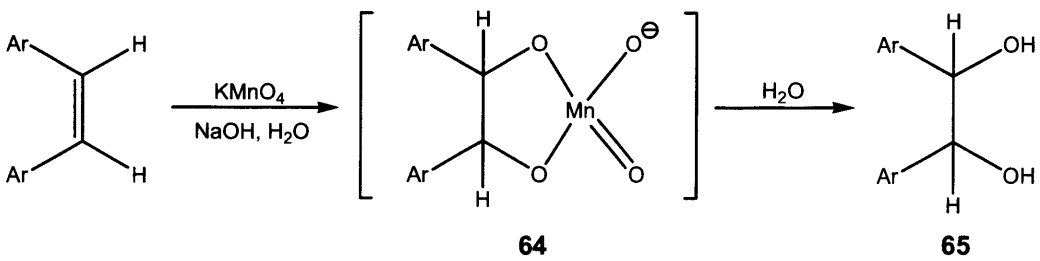
Scheme 25: Proposed mechanism of epoxidation.

This mechanism has been validated over the years by a number of studies, both experimental and theoretical. For example, through the investigation of kinetic isotope effects on the interaction between mCPBA and 1-pentene,[112] and spin-restricted DFT calculations on the reaction between peroxyformic acid and ethylene.[113] However, some researchers dispute this mechanism, a theoretical investigation by Leszczynski and coworkers showing the transition state to be highly unsymmetrical. There has been evidence put forward by Ortuno *et al.* for a biradical mechanism, through an ESR spin trapping study of the diels-alder reaction of 5-methylene 2(5H)-furanes.[114]

Epoxidation can also be achieved *via* the use of a transition metal catalyst in conjunction with molecular oxygen or an alkyl peroxide. Probably the most famous example of this approach is the *Sharpless Asymmetric Epoxidation*, where allylic alcohols are converted to epoxides in over 90% ee using catalytic amounts of titanium tetraisopropoxide and optically active diethyl tartrate.[115] However, this approach cannot be applied to stilbenes as the –OH functionality of the allylic alcohol is necessary in order to achieve complexation of the substrate to the titanium catalyst.

B2.5.3: Dihydroxylation

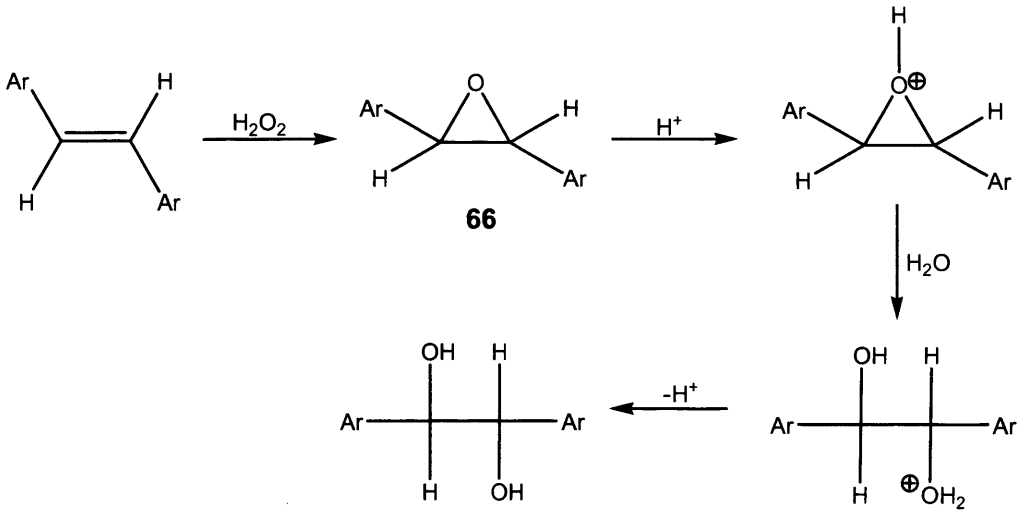
The double bond in both stilbene itself and substituted analogues has been demonstrated to be a suitable substrate for dihydroxylation. This can be carried out using a range of reagents, the best known of which are potassium permanganate and osmium tetroxide. Both of these reagents give *syn* addition as they attack from the least hindered side of the alkene and proceed *via* a cyclic manganate or osmate intermediate (**64**), the mechanism for dihydroxylation using potassium permanganate being shown in *Scheme 26.* As osmium tetroxide is highly toxic and extremely expensive, it is more commonly employed in a catalytic role, in conjunction with hydrogen peroxide as oxidant.[116]



64 **65**

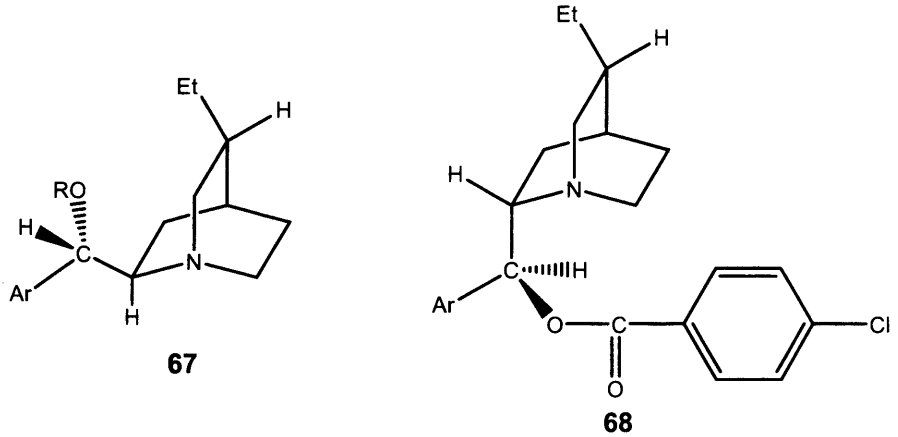
Scheme 26: Mechanism of dihydroxylation using potassium permanganate.[117]

In order to achieve *anti*-dihydroxylation, the double bond can be treated with hydrogen peroxide and formic acid; in this case the mechanism proceeds *via* an epoxide (**66**), followed by subsequent S_N2 reaction, as shown in *Scheme 27.*



Scheme 27: *Anti*-dihydroxylation using hydrogen peroxide and formic acid.

The dihydroxylation of alkenes such as stilbenes has been made both enantio- [118] and diastereo-[119] selective, through the use of optically active amines as chiral ligands binding to osmium tetroxide. Examples of such ligands include naturally-occurring derivatives of quinine and quinidine as shown in *Figure 25.*



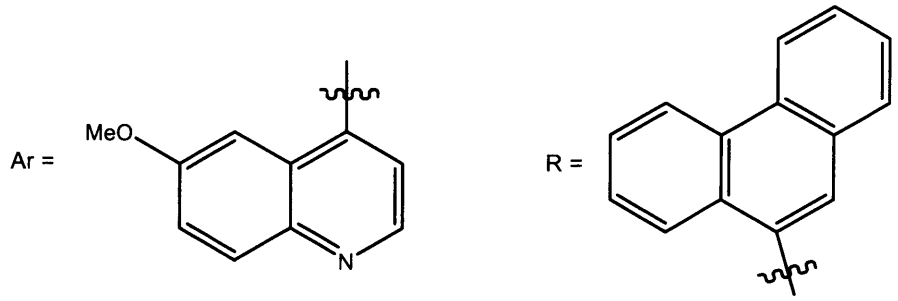
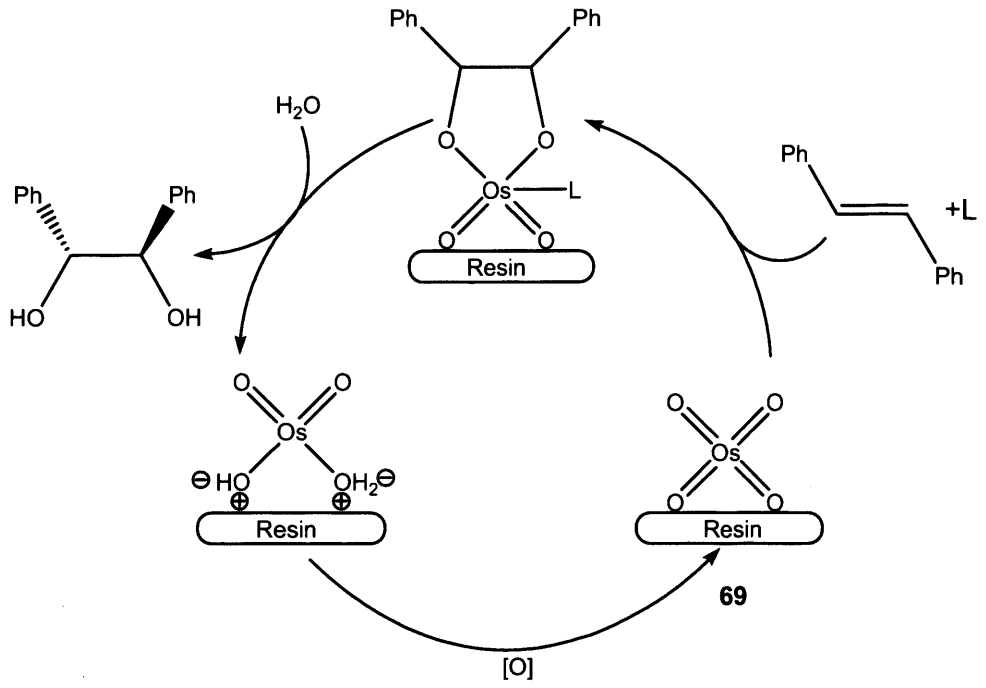


Figure 25: Optically active ligands (**67** and **68**) used in asymmetric dihydroxylation.

In recent years, asymmetric dihydroxylation has frequently been carried out using a pre-formed mix of reagents such as AD-Mixes α and β, which are commercially available. These consist of potassium osmate, a chiral ligand such as those shown above, potassium carbonate as base, and potassium hexacyanoferrate as a co-oxidant. Using these readily available dihydroxylation mixes avoids the use of highly toxic osmium tetroxide, and provides researchers with a facile route into a wide range of chiral dihydroxylated compounds. In addition to the use of reagents such as AD-Mix, research has also been conducted into using solid-supported osmium tetroxide to catalyse the dihydroxylation of alkenes; *trans*-stilbene is in fact often used as a 'model' substrate in the study of such reactions. For example, Choudary *et al.* have demonstrated that osmium tetroxide immobilised on both silica and ion-exchange resin beads (**69**) dihydroxylates *trans*-stilbene in up to 95% yield with an ee of 99% (*Scheme 28*).[120]



Scheme 28: Catalytic cycle of dihydroxylation of stilbene, using ion-exchange resin tethered osmium tetroxide.

B3: Summary

Stilbene has been shown to be a compound which is of interest for two main reasons; both in its own right, usually in functionalised form, for applications as wide ranging as anticancer treatments and fluorescent dyes, and also as a model for the behaviour of other, more complex systems, for example in catalytic studies. The synthesis and reactivity of stilbene and derivatives has been explored, with emphasis on the formation of, and further reactions involving, the C=C double bond.

Section C: Cyclophanes and Cyclophenes

C1: Introduction to Cyclophanes

The term 'cyclophane' is employed to describe any molecule of the type shown in *Figure 26*, where a benzene ring is bridged by an aliphatic chain of varying length. The prefix 'cyclo' itself stands for the benzene ring, parallel classes of compounds exist in which this is replaced by another aromatic unit, for example anthracene, in this case the compounds are termed *anthracenophanes*. The lengths of the aliphatic bridges in a cyclophane are denoted by numbers in square brackets placed before the compound name. For example [2.2] *para*-cyclophane (**70**) (*Figure 27*) contains two bridges each of two carbons in length. The position of these bridges on the benzene ring (*ortho*, *meta* or *para*) is also placed in front of the name of the compound. The first cyclophane was discovered by Pellegrin as early as 1899 with his synthesis of [2.2] *meta*-cyclophane,[121] however the field as a whole did not find popularity until 1949 when Brown and Farthing published the synthesis of [2.2] *para*-cyclophane in *Nature*.[122]

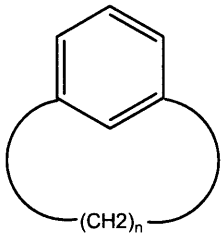
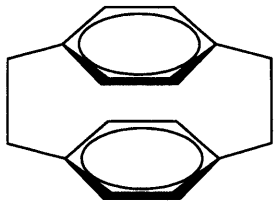


Figure 26: Generic structure of a *meta*-cyclophane.



70

Figure 27: [2.2] *para*-Cyclophane.

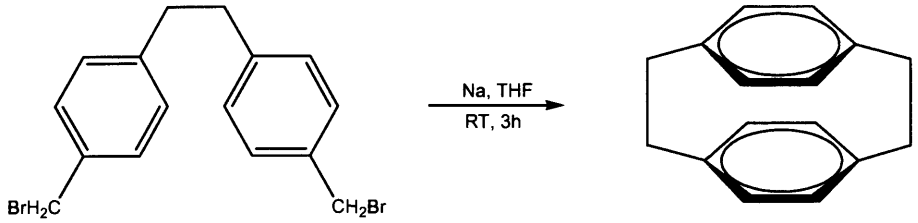
Cyclophanes are examples of highly strained molecules, especially those examples where the aliphatic bridge is short such as [6] *para*-cyclophane. The strain is such that often the benzene ring is not planar, but 'bent' out of shape into *boat-*, *chair-* or even *twist-* forms by the constraining action of the aliphatic bridge. Those cyclophanes containing two or more

benzene rings, for example [2.2] *para*-cyclophane, have the added interest of transannular ring interactions, a topic which will be discussed in detail later in this chapter.

Although cyclophanes are an exceptionally diverse range of compounds, there is not sufficient scope within this thesis to consider all the various forms in detail. [2.2] *para*-Cyclophanes can be considered the key members of the cyclophane family, as their reactivity and structural properties can be applied to almost all the cyclophanes, hence only these compounds will be discussed at greater length in this chapter.

C2: Synthesis of [2.2] *para*-Cyclophanes

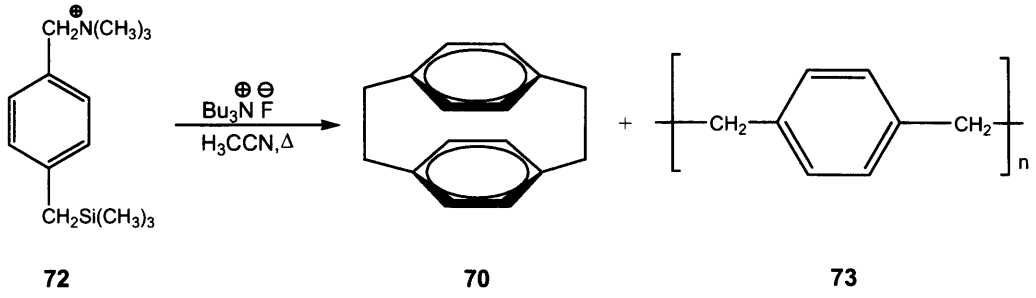
The first deliberate, directed synthesis of a cyclophane was carried out by Cram and Steinberg, who prepared [2.2] *para*-cyclophane *via* an intramolecular Wurtz coupling reaction of 4,4'-bis(bromomethyl)bibenzyl (**71**) (*Scheme 29*).[123] This reaction was later expanded upon and optimised by Mandolini *et al.*, who used a high-dilution variant to ensure cyclisation was favoured.[124]



71 **70**

Scheme 29: Synthesis of [2.2] *para*cyclophane *via* Wurtz coupling.

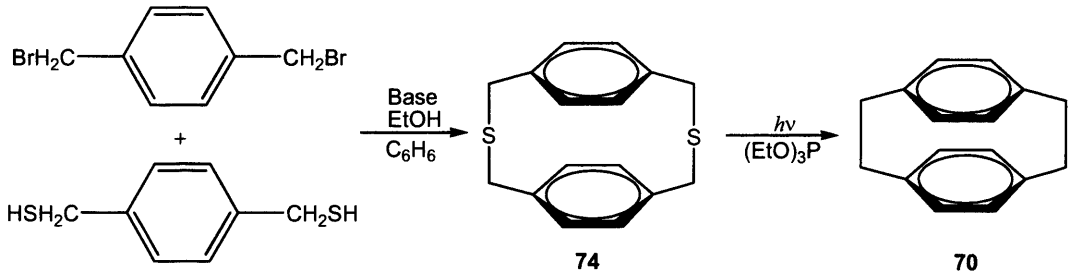
A 1,6-Hofmann elimination with *para*-methylbenzylammonium chloride (**72**) has been successfully employed to synthesise [2.2] *para*-cyclophane, although low-yielding this approach is often applied to the preparation of multi-layer cyclophanes.[125] The preparation of [2.2] *para*-cyclophane *via* this method has been somewhat optimised to afford yields of up to 56% in some cases (For example, see *Scheme 30*). Further optimisation and increase of yields in this reaction is hindered by the ever-present problem of polymerisation occurring, rather than cyclisation.



72 70 73

Scheme 30: [2.2] *para*-Cyclophane synthesis *via* modified Hofmann elimination.

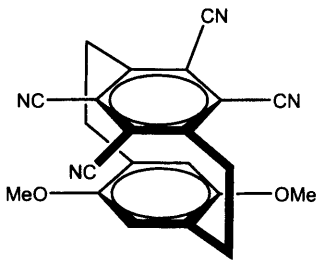
A higher-yielding approach for the synthesis of [2.2] *para*-cyclophanes was introduced in 1969 by Vögtle and coworkers, which involved the ring-contraction of large-ring dithiaphanes (**38**) *via* sulfur extrusion,[126] reaction is achieved either photochemically or through pyrolysis (*Scheme 31*).



74 70

Scheme 31: Preparation of [2.2] *para*-cyclophenes *via* a dithiacyclophane precursor.

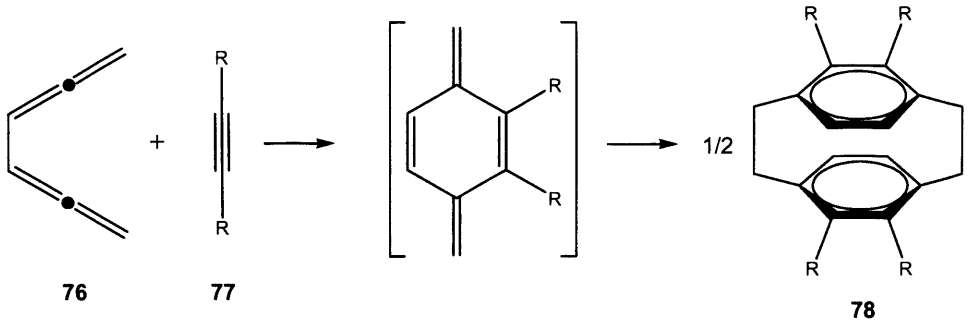
The dithiacyclophane route of Vögtle has been employed to synthesise substituted *para*-cyclophanes as well as the unsubstituted variant. For example it was usedd by Staab and coworkers to prepare cyano-substituted analogues (**75**) of the type illustrated in *Figure 28*.



75

Figure 28: Cyano-substituted [2.2] *para*-cyclophane.

Another approach towards substituted [2.2] *para*-cyclophanes, first developed by Hopf in the 1970s, involves a Diels-Alder reaction between 1,2,4,5-hexatetraene (**76**) and acetylenes (**77**) to furnish substituted [2.2] *para*-cyclophanes (**78**) as shown in *Scheme 32*.[127] The reaction has been demonstrated to be amenable to scale-up, with up to 60 g of *para*-cyclophane product able to be synthesised in one batch.[128]



R = CO_2CH_3, $CO_2C(CH_3)_3$, CN, CF_3

Scheme 32: Preparation of substituted [2.2] *para*-cyclophanes *via* Diels-Alder reaction.

C3: Structure and Characterisation of [2.2] *para*-cyclophanes

Probably the most well-documented feature of the structure of [2.2] *para*-cyclophanes is the distortion of the benzene rings away from planarity. This effect, along with the π-π interactions between the two aromatic units, controls much of the unique reactivity observed for these species. The structure of [2.2] *para*-cyclophane is shown in *Figure 29*, and illustrates how the benzene rings take up a shallow 'boat' conformation with a strain energy of 129.6 kJ mol^{-1}.[129] Due to the close proximity of the aromatic units to one another, the π orbitals of the two rings penetrate one another and essentially form one overall 3-dimensional π-electron system, which has been compared to that of C_{60}.[130] This combined system has a HOMO that is of higher energy, and a LUMO that is lower in energy, than those of the corresponding alkyl-substituted benzenes, thus resulting in a smaller HOMO-LUMO gap as compared to benzene.[131]

In contrast to 'normal' van der Waals separation between parallel benzene rings, which has minimum value of 3.40 Å, the centres of the benzene rings in [2.2] *para*-cyclophane are separated by only 3.08-3.09 Å.[132] This effect is attributed to the transannular π-π overlap narrowing the separation between the bridgehead carbons to 2.75-2.77 Å, the 'boat' conformation of the aromatic ring increasing this separation in the centre of the ring to

around 3.08 Å. This 'boat' conformation is found to be more common than the alternative 'chair' conformation in [2_n] cyclophanes, due to its being a minimum of 16.7 kJ mol^{-1} more stable. This is presumed to be because deformation of a benzene ring to a boat conformation retains more π-orbital overlap than does deformation to a chair conformation.

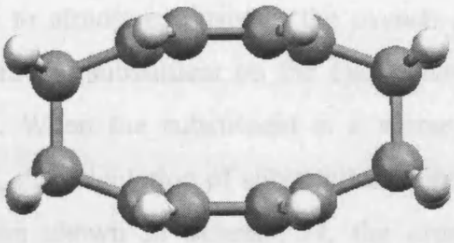


Figure 29: Ball and stick representation of [2.2] *para*-cyclophane (**70**), showing the shallow 'boat' conformation of the aromatic rings (modelled using the CAChe molecular modelling package).

The reduced separation between the cyclophane 'decks' and the deformation of the benzene rings mentioned above gives rise to an interesting feature in the UV-vis spectrum of [2_n] *para*-cyclophanes, generally termed the 'cyclophane band'. This is an absorption band at far longer wavelength than anything observed in the spectra of alkylbenzenes. The exact value of this absorption varies between 275 and 312 nm, with the cyclophane band of [2.2] *para*-cyclophane appearing at 302 nm.[133]

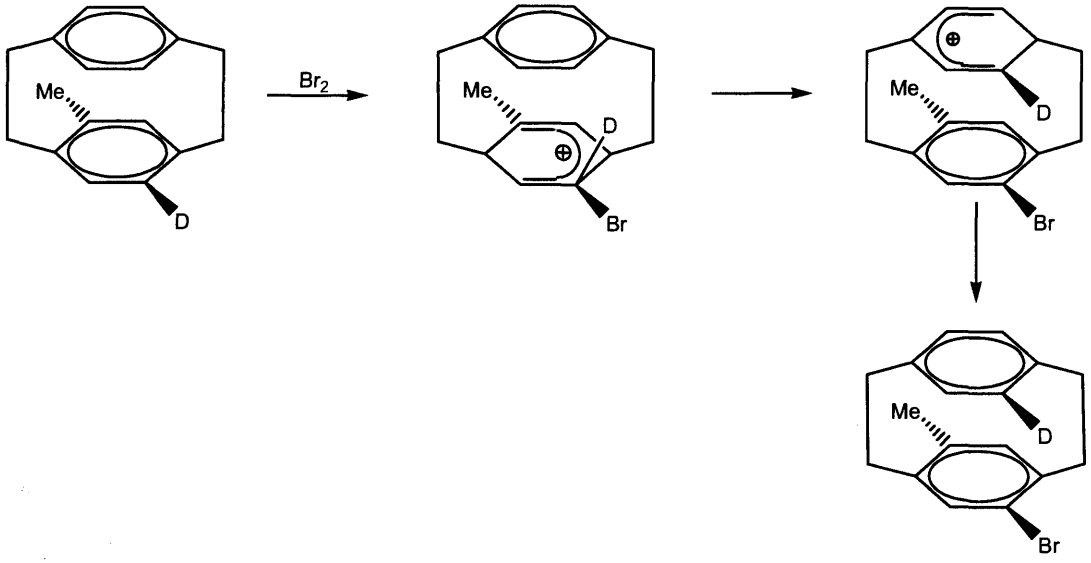
C4: Reactivity of Cyclophanes.

C4.1: Reactions at the Aromatic Rings

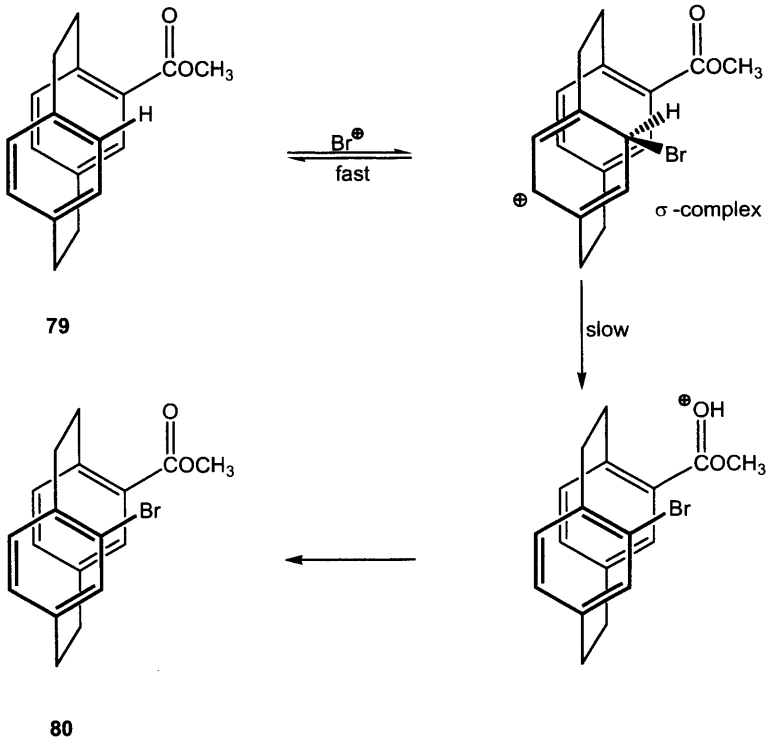
The reactivity of the aromatic rings in [2.2] *para*-cyclophane is characterised by what is known as the 'transannular direction effect' – the steric or electronic effect exerted by one aromatic ring upon the other during the course of a reaction.[134] This effect has been extensively studied by Cram *et al.,* using the electrophilic substitution reactions of a monosubstituted [2.2] *para*-cyclophane as a model.[135] In contrast with 'normal' electrophilic substitution of arenes, where formation of the σ-intermediate is the slow step, in electrophilic substitution of [2.2] *para*-cyclophanes the loss of a proton from this σ-intermediate is the rate-limiting step. This difference has been attributed to the ability of the aromatic π-electron cloud of the opposite ring to act as an intramolecular base and assist proton transfer. This has been proven through the use of isotope labelling

experiments, in which a deuterium present on the aromatic ring at which substitution takes place is found to have shifted to the opposite ring after the reaction (*Scheme 33*).[136]

An example of the unusual directing effects exhibited by [2_n] *para*-cyclophanes is shown in *Scheme 34*, where the bromination of [2.2] *para*-cyclophanes bearing an O-basic substituent (**79**) gives rise to almost exclusively the *pseudo*-geminal product (**80**). This direction occurs only where the substituent on the cyclophane is a better base than the aromatic π-electron cloud. When the substituent is a worse base, or simply when no substituent is present at all, the orientation of substitution is generally random. In addition to the bromination reaction shown in *Scheme 34*, the aromatic rings in [2.2] *para*-cyclophene have been shown to undergo all common electrophilic substitution reactions of arenes, including nitration and Friedel-Crafts acylation.



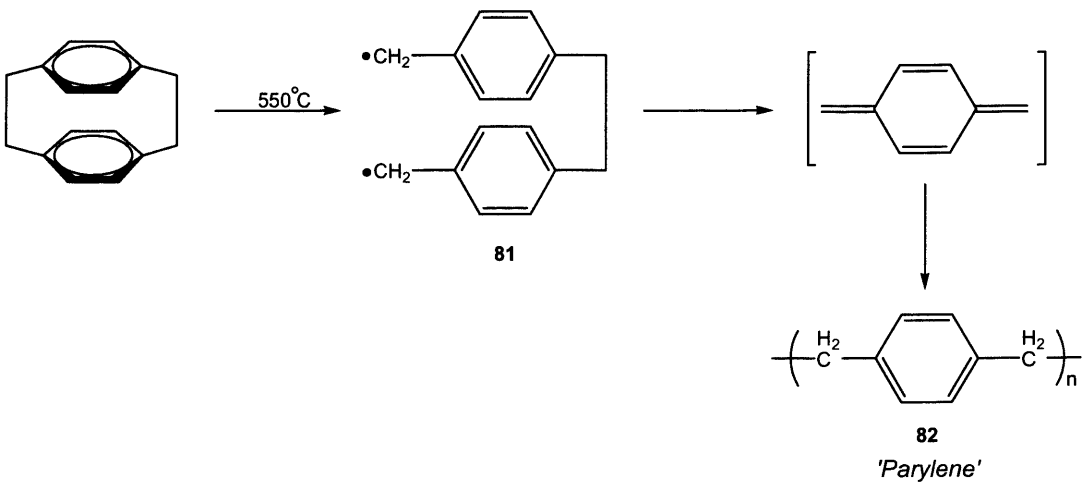
Scheme 33: Deuterium transfer illustrating transannular interaction.



Scheme 34: Bromination of a substituted [2.2] *para*-cyclophane, illustrating the transannular directing effect.

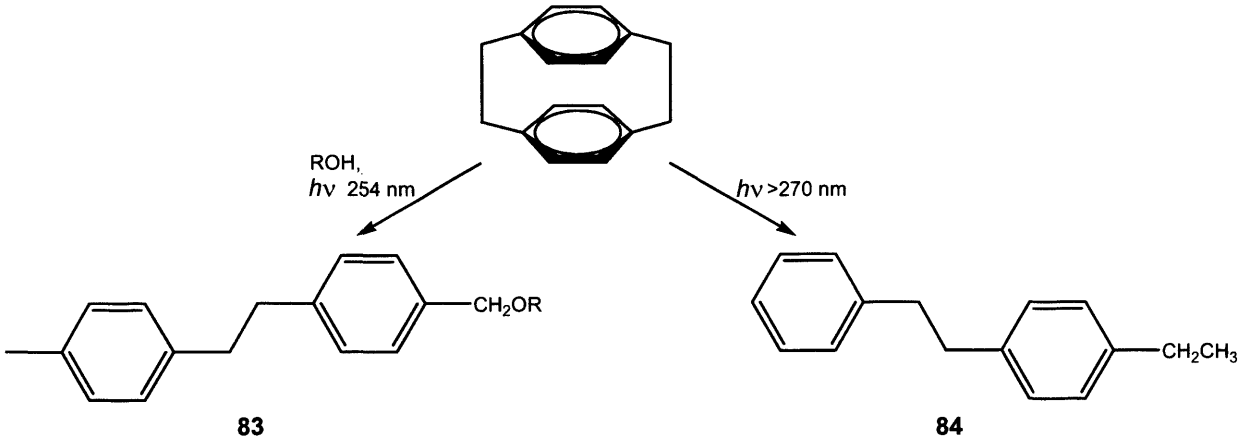
C4.2: Ring-Opening Reactions

Due to the inherent ring-strain present in [2.2] *para*-cyclophane, it is perhaps unsurprising that opening of the cyclophane ring can take place to yield an open-chain species. The best known example of this reaction is the thermal ring-opening of [2.2] *para*-cyclophane in the gas phase to yield, on condensation upon a cooled surface, a coating of a hard wearing polymer known commercially as 'Parylene' (**82**).[137] This reaction proceeds via a *para*-xylyl diradicaloid intermediate (**81**), as shown in *Scheme 35.*



Scheme 35: Thermal ring-opening of [2.2] *para*-cyclophene.

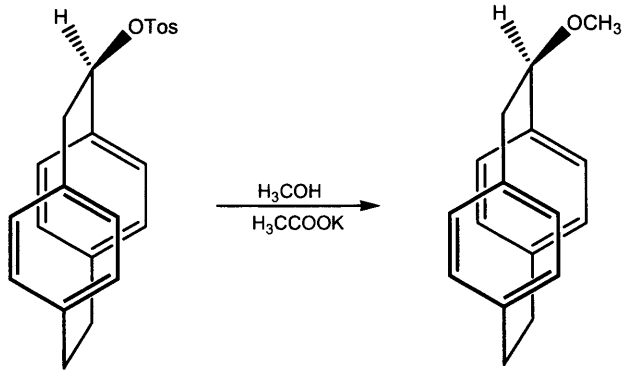
The ring-opening of [2.2] *para*-cyclophane can also be performed photochemically. For example Kaup *et al.* irradiated a sample in a glassy matrix of 2-methyltetrahydrofuran at 77K. Study of the products using UV and fluorescence spectroscopy showed them to be the diradical intermediate **81** shown above in *Scheme 35,* and *para*-xylylene.[138] Irradiation of [2.2] *para*-cyclophane in different solvents at room temperature has been shown to produce different ring-opening products. In alcohol, irradiation at 254 nm yields the corresponding ring-opened ethers **83**, whilst irradiation in acetone with light of wavelength exceeding 270 nm leads to ring-opening at the bridgehead carbon to give bibenzyl **84** (*Scheme 36*).[139]



Scheme 36: Photochemical ring-opening reactions of [2.2] *para*-cyclophane.

C4.3: Reactions at the Bridging Carbons

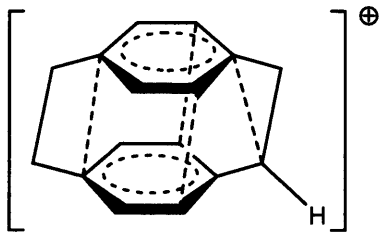
The reactivity of the bridging carbons in [2.2] *para*-cyclophanes has been extensively studied by Cram, using the optically active compounds 1-hydroxy [2.2] *para*-cyclophane (**85**) and 1-tosyloxy [2.2]-*para*-cyclophane (**86**) as model substrates. As would be predicted, reactions of **85** such as methylation with methyl iodide and acetylation using acetic anhydride and pyridine proceed with full retention of configuration. More surprisingly, the solvolysis (methanolysis, acetolysis and trifluoroacetolysis) of **86** also take place with retention of configuration (for example see *Scheme 37*).



86

Scheme 37: Methanolysis of 1-tosyloxy [2.2] *para*-cyclophane.

Cram postulated that to obtain the stereochemistry observed in the above solvolysis reactions, the aromatic ring β to the reaction site must become involved in the formation of a highly strained bridged carbonium ion **87**, shown in *Figure 30.* This allows distribution of the positive charge in the ion across both of the aromatic rings, and also, due to the slightly twisted structure of **87**, some of the π-π repulsions between the aromatic rings are decreased. Both the formation of ion X, and its subsequent ring-opening during solvolysis, proceed with full inversion of configuration leading to the overall retention of configuration observed during the solvolysis of 1-tosyloxy [2.2] *para*-cyclophane.[140]



87

Figure 30: Highly strained carbonium ion intermediate

C4.4: Transition Metal Chemistry of [2.2] *para*-Cyclophanes

The aromatic rings in [2.2.] *para*-cyclophane can, like their simple alkyl benzene counterparts, be complexed to transition metals such as chromium, ruthenium and iron. These compounds are not only fascinating from a structural viewpoint, but also the complexation of a metal with a *para*-cyclophane ligand changes the electronic properties of the *para*-cyclophane. This affects the reactivity of the aromatic rings within the ligand, just as for simple arene complexes. As early as the 1960s study into the complexes of

chromium with unsubstituted [2.2] *para*-cyclophane was being carried out. Work by Cram and Wilkinson,[141] Misumi,[142] and Elsenbroich[143] yielded the complexes **88-91** shown in *Figure 31*, which illustrate the four possible binding modes of [2.2] *para*-cyclophane. The field of *para*-cyclophane transition metal chemistry has continued to attract attention, and complexes are now known containing the metals Cr, Mo, W, Fe, Ru, Os, Co, Rh, Ir, Ni, Cu, Ag, and U.[144] The preparation of a range of both known and novel iron cyclophane complexes using room-temperature ionic liquids as solvent has been described by Dyson and coworkers, providing an alternative route to this type of complex.[145] Maekawa *et al.* have reported the preparation of a range of *para*-cyclophane complexes incorporating rhodium and iridium in both their +1 and +3 oxidation states, these have been characterised crystallographically and have demonstrated that complexation to a transition metal decreases the interannular distances between the aromatic 'decks' due to a reduction in the π-π repulsive forces.[146]

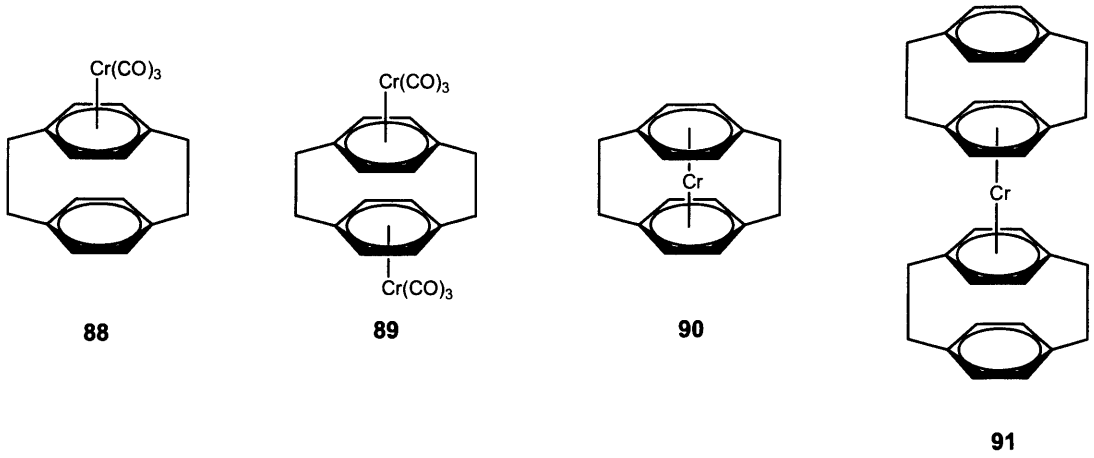
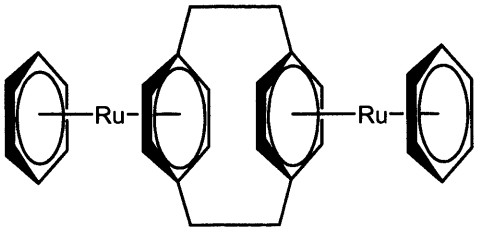


Figure 31: Examples of chromium (0)-[2.2] *para*-cyclophane complexes demonstrating the four possible binding modes.

One of the eventual goals of transition metal – *para*-cyclophane chemistry is to construct a polymer consisting of alternating transition metal fragments and paracyclophane molecules. Such a polymer, having essentially a backbone made up of face-to-face benzene rings, would have extremely exciting electronic and chemical properties. To date, the synthesis of such a polymer has not been achieved, although complexes containing up to four face-to-face units have been synthesised (**92**) (see *Figure 32*).[147]

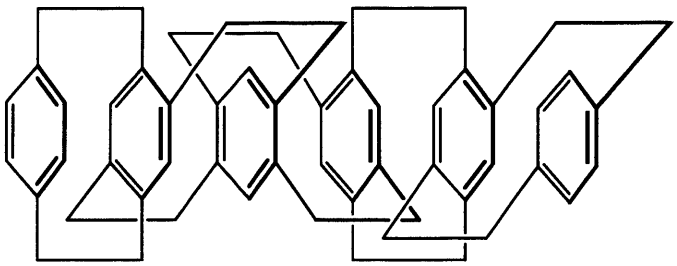


92

Figure 32: Ruthenium [2.2] *para*-cyclophane complex (**92**) containing four face-to-face benzene rings.

3.5: Polymers containing [2.2] *para*-cyclophane

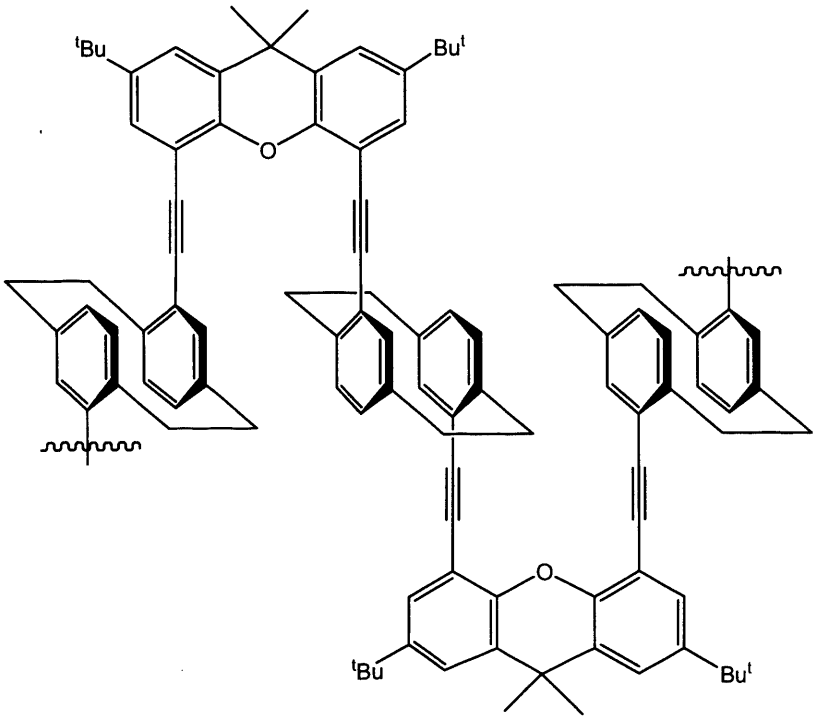
Due to their novel electronic properties, there has been much research into the preparation of *para*-cyclophane-containing polymers. Although work by Misumi and coworkers has yielded multilayered *para*-cyclophanes with up to six 'decks' (**93**) (*Figure 33*), [148] extension of this framework to yield a polymeric form has not, to date, been achieved.



93

Figure 33: Stacked *para*-cyclophane with six aromatic decks.

Although 'true' poly-*para*-cyclophanes have not yet been prepared, polymers do exist in which the [2.2] *para*-cyclophane unit is incorporated into the polymer chain. An interesting example is that prepared recently by Morisaki and Chujo, where an alternating *para*-cyclophane-xanthene polymer (**94**), the structure of which holds the *para*-cyclophane units in a face-to-face arrangement as shown in *Figure 34*.[149] This novel polymer is hoped to find application as a molecular wire, as the stacked benzene rings are expected to allow for efficient through-space charge transfer.



94

Figure 34: Fragment of unusual *para*-cyclophane containing polymer **94**, in which the paracyclophane units are held face-to-face.

Morisaki and Chujo have also prepared and studied the more 'conventional' type of *para*-cyclophane-containing polymers shown below in *Figure 35,* where the *para*-cyclophane is incorporated into poly phenylene-ethynylene (PPE) (**95**), PPV (**96**) or polyfluorene (**97**) based structures. Although these polymers do not exhibit the type of aromatic ring stacking behaviour as shown in *Figure 34,* they still possess novel photophysical and charge-transfer behaviour and may find application as the emissive layer in pLEDs due to their strong electroluminescence.

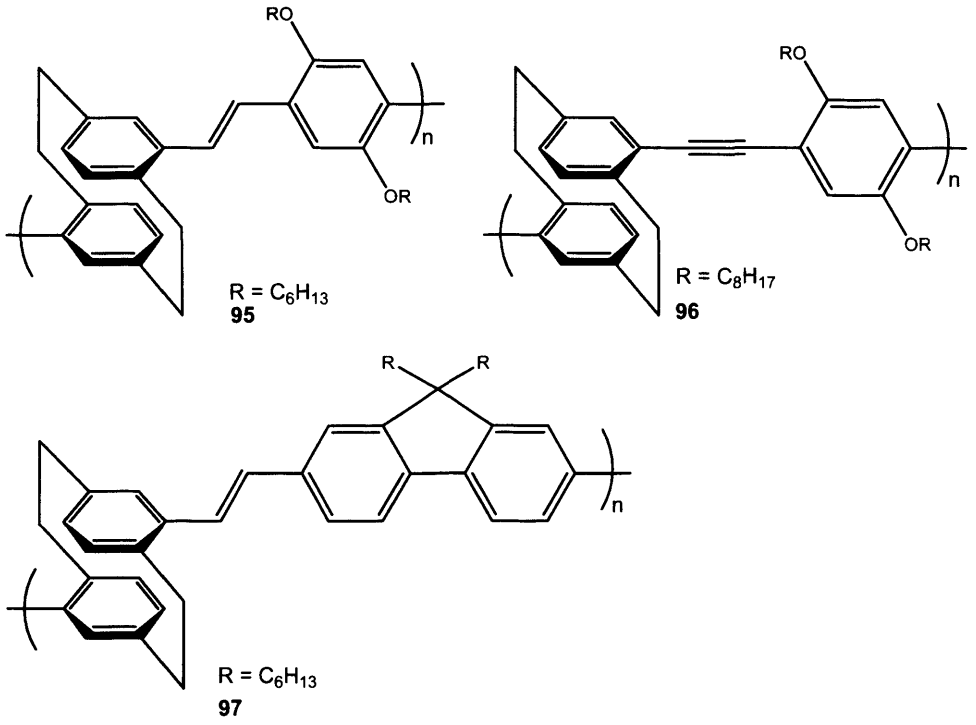
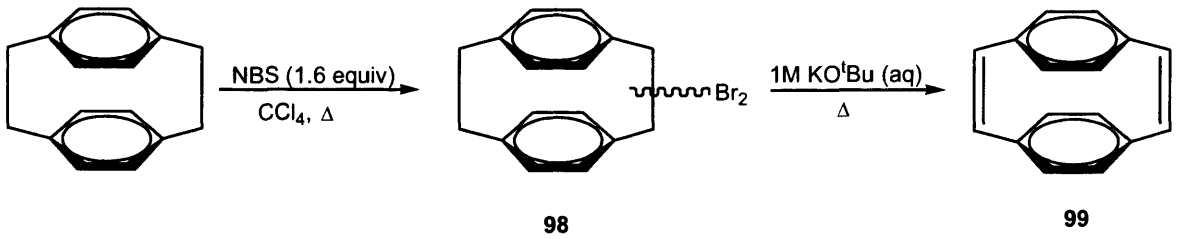


Figure 35: Paracyclophane containing polymers based upon PPV, PPE and polyfluorene structures.

C6: Dehydrogenation of [2.2] *para*-Cyclophanes: Synthesis of [2.2] *para*-Cyclophenes

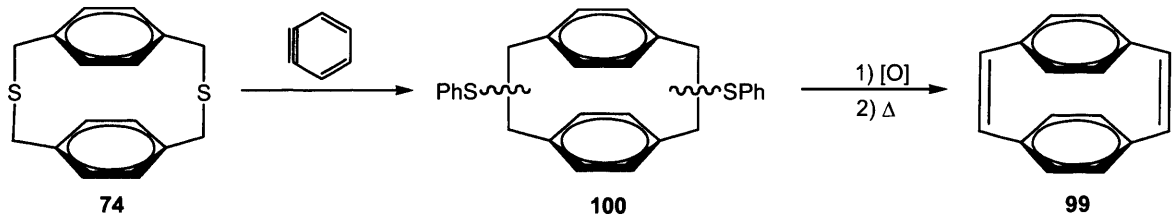
The first dehydrogenation of [2.2] *para*-cyclophane was carried out by Dewhirst and Cram in 1958.[150] Their attempts to carry out this reaction directly, either catalytically or using 2,3-dicyano-5,6-dichlorobenzoquinone were unsuccessful, however treatment of [2.2] *para*-cyclophane with *N*-bromosuccinimide yielded the dibromide (**98**), which could subsequently be transformed into 1,4-*para*-cyclophane-1,9-diene ([2.2.] *para*-cyclophene, **99**) using potassium *t*-butoxide (*Scheme 38*). The final product was obtained in a yield of only 4%, due to the low-yielding nature of the first step of the synthesis, where a mixture of the desired dibromide plus starting *para*-cyclophane, monobromide and polybromides was obtained.



Scheme 38: The first dehydrogenation of [2.2] paracyclophane to yield [2.2] *para*-cyclophene.

The dehydrogenation of [2.2] *para*-cyclophane to yield [2.2] *para*-cyclophene gave access to another fascinating molecule with similar, but not identical, properties to [2.2] *para*-cyclophane. Due to the introduction of unsaturation into the system, new reactivity could be exploited and new applications found for this class of molecules, the synthesis, structure and reactivity of which will be discussed in the subsequent section.

To date, the preparation of [2.2] *para*-cyclophene remains non-trivial. The method of Dewhirst and Cram described above is still occasionally employed; however the preferred route involves ring-contraction of a dithia-*para*-cyclophane precursor (**100**) *via* either a Stevens,[151] Stevens-benzyne,[152] or Wittig rearrangement.[153] This is followed by either a Hofmann elimination or sulfoxide pyrolysis to yield the unsaturated *para*-cyclophene (For example see *Scheme 39*).



Scheme 39: Preparation of [2.2] *para*-cyclophene *via* Stevens-benzyne rearrangement followed by sulfoxide pyrolysis.

C6.1: Structure of [2.2] *para*-cyclophenes

The solid-state structure of [2.2] *para*-cyclophene is very similar to that of its parent compound [2.2] p*ara*-cyclophane (*Figure 36*). Due to the shorter distance between the carbon atoms in the bridges caused by their containing a C=C double bond, the interannular distance is slightly decreased when compared to [2.2] *para*-cyclophane, and the benzene rings are also show a little more tendency to distort into a boat conformation. These factors serve to increase the strain of the molecule. Indeed, calculations by de Meijere and coworkers based upon combustion calorimetry analyses quote the strain energy of [2.2] *para*-cyclophene as 42 kcal mol^{-1}.[154] This increased strain energy correlates well with both the observed reactivity of [2.2] *para*-cyclophene as compared to [2.2] *para*-cyclophane, and also with the difficulties encountered in preparing the compound.

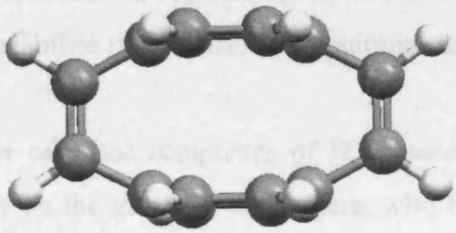
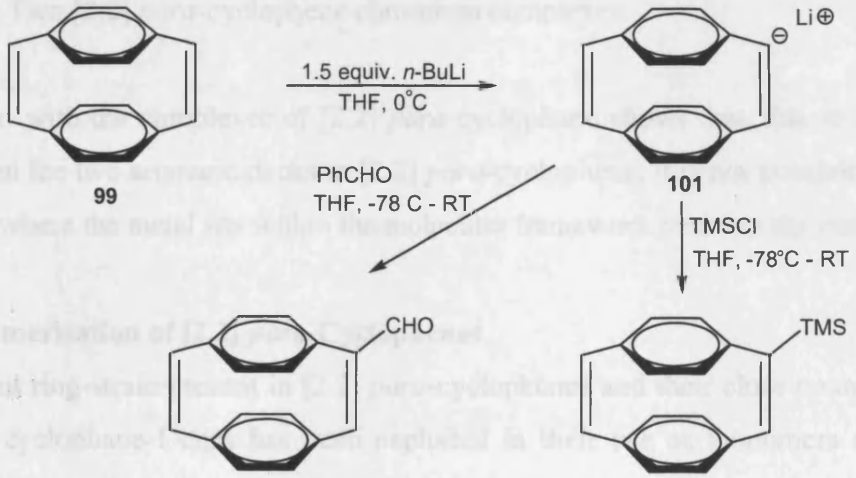


Figure 36: Ball and stick representation of [2.2] *para*-cyclophene, showing the 'boat' conformation of the aromatic rings (modelled using the CAChe molecular modelling package).

C6.2: Reactivity of [2.2] *para*-Cyclophenes

The majority of the studies carried out on the reactivity of [2.2] *para*-cyclophene involve reaction at the two C=C bridging bonds. de Meijere *et al.* have showed that deprotonation at the ethylene bridges proceeds easily and cleanly at 0°C using *n*-butyl lithium in THF, to yield the lithiated species **101**, which can then go on to react with a range of electrophiles such as trimethylsilylchloride and benzaldehyde (for example see *Scheme 40*).[155]

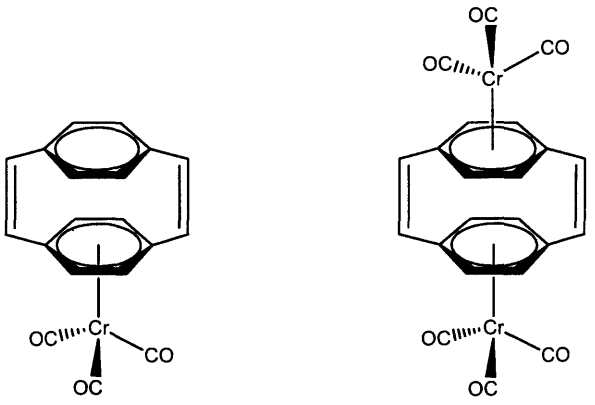


Scheme 40: Lithiation of [2.2] *para*-cyclophene followed by reaction with an electrophile.

It has also been shown possible to generate dilithiated species using excess *n*-BuLi and TMEDA, which affords a mixture of the 1,9- and 1,10- lithiated species. Upon trapping these intermediates with electrophiles, it was observed that the 1,9-disubstituted derivative was formed preferentially. Interestingly, if the [2.2] *para*-cyclophene was complexed to tricarbonylchromium prior to lithiation and trapping, the 1,10- disubstituted compound was

the major product. This difference in regiochemistry has been attributed to the ability of the chromium fragment to stabilise two adjacent carbanionic sites.[156]

There have been a number of metal complexes of [2.2] *para*-cyclophenes prepared and characterised, most notably by the group of de Meijere, who have prepared complexes of [2.2] *para*-cyclophene and derivatives with both chromium and iron.[157] Two chromium complexes **102** and **103** are shown below in *Figure 37,* illustrating the only two metal binding modes observed for [2.2] *para*-cyclophenes.



102 **103**

Figure 37: Two [2.2] *para*-cyclophene chromium complexes.

Comparison with the complexes of [2.2] *para*-cyclophane shows that, due to the smaller gap between the two aromatic decks in [2.2] *para*-cyclophene, it is not possible to prepare a complex where the metal sits within the molecular framework between the benzene rings.

C6.3: Polymerisation of [2.2] *para*-Cyclophenes

The inherent ring-strain present in [2.2] *para*-cyclophenes and their close counterparts the [2.2] *para*-cyclophane-1-enes has been exploited in their use as monomers for ROMP. Referring back to *Section A4.2*, it has been demonstrated that the co-polymerisation *via* ROMP of [2.2] *para*-cyclophene and norbornene gives rise to a block copolymer which possesses both reasonable solubility and electroluminescent properties.[54] The work of Bazan *et al.* has also been discussed earlier in this chapter, using the [2.2] *para*-cyclophene monomer 9-(*t*-Butyldimethylsilyl)oxy[2.2] *para*-cyclophane-1-ene the group was able to prepare a soluble precursor polymer, which could then be converted to PPV *in situ* by heating with HCl gas.

C7: Summary

The [2.2] *para*-cyclophane framework is a highly attractive and versatile molecule which has been extensively researched and developed since its discovery in 1949. Both its organic and organometallic reactivity has been explored, finding application in areas as wide-ranging as asymmetric catalysis and molecular wires. Dehydrogenation of the [2.2] *para*-cyclophane framework gives access to yet another desirable class of molecule, the [2.2] *para*-cyclophenes. These, being more highly strained than their parent [2.2] *para*-cyclophanes, have a more limited reactivity and have hence been less widely studied, however in more recent years their utility as monomers in the preparation of PPV has begun to be exploited.

Section D: Aims and Objectives.

As has been illustrated in *Section A* of this chapter, there are currently a number of successful approaches for the synthesis of conducting and electroluminescent polymers, specifically of PPV and related analogues. This thesis aims to build on these foundations by combining and optimising a number of the best features of the routes discussed, to explore a potential new synthetic route to alkoxy-functionalised PPVs. Specifically, the aim is to expand upon the work of Bazan *et al.*,[52] through the synthesis of functionalised [2.2] *para*-cyclophene derivatives **104** and **105** (*Figure 38*), which could then be converted to either PPV or a precursor polymer using ROMP. In order to further enable the ease of purification and processing of PPV and its related polymers, research has also been directed into several non-conjugated 'precursor polymer' routes, as were discussed in *Chapter 1.*[41,42,45,51] This thesis seeks to combine the two approaches, extending the work in this field by preparing a way for the synthesis of a well-defined, alkoxy-functionalised precursor to PPV from suitably modified [2.2] *para*-cyclophane-1-enes.

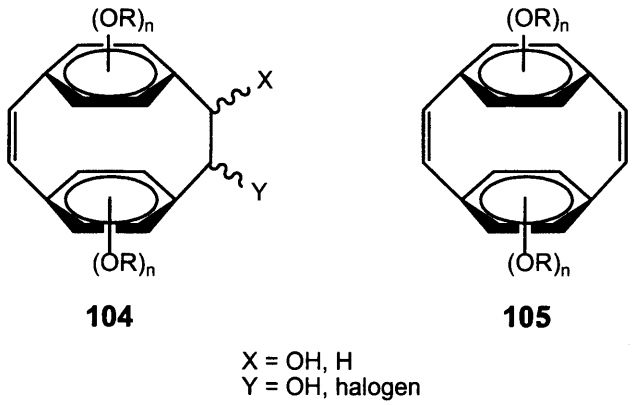


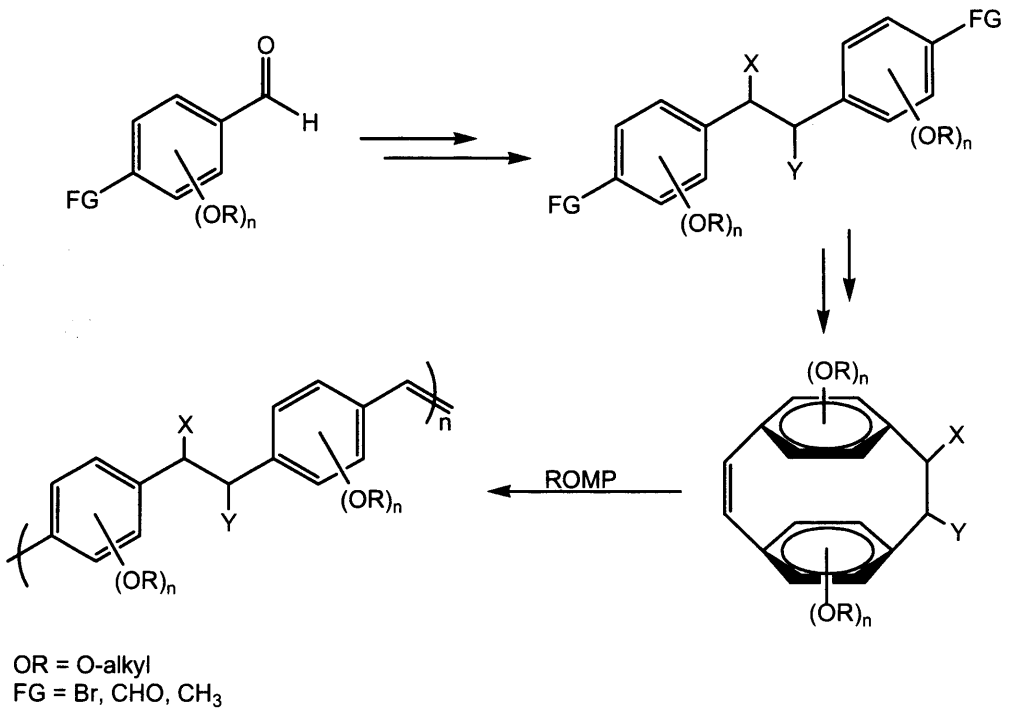
Figure 38: Potential [2.2] *para*-cyclophene and [2.2] *para*-cyclophane-1-ene monomers for conversion to PPV or a PPV precursor *via* ROMP.

Previously the use of *para*-cyclophene monomers has been restricted to the synthesis of un-substituted PPVs, as functionalisation at the aromatic rings has not been investigated. As described in *Section A* of this chapter, by adding alkoxy functionalisation at the aromatic rings in the PPV backbone the solubility of the final polymer can be enhanced and the wavelength of light emitted tuned. Although routes already exist that allow these modifications, the polymerisation methods employed in such approaches are not as effective as ROMP for controlling the properties of the final polymer, e.g. molecular weight and polydispersity. Hence, by combining the functionalisation approaches of routes

such as that of Yu and the Knoevenagel method and the easily controllable polymerisation afforded by applying ROMP to [2.2] *para*-cyclophenes (*Section A3.2.2*), it is hoped that a straightforward, versatile approach to the synthesis of well-defined functionalised PPV and PPV precursor polymers can be achieved.

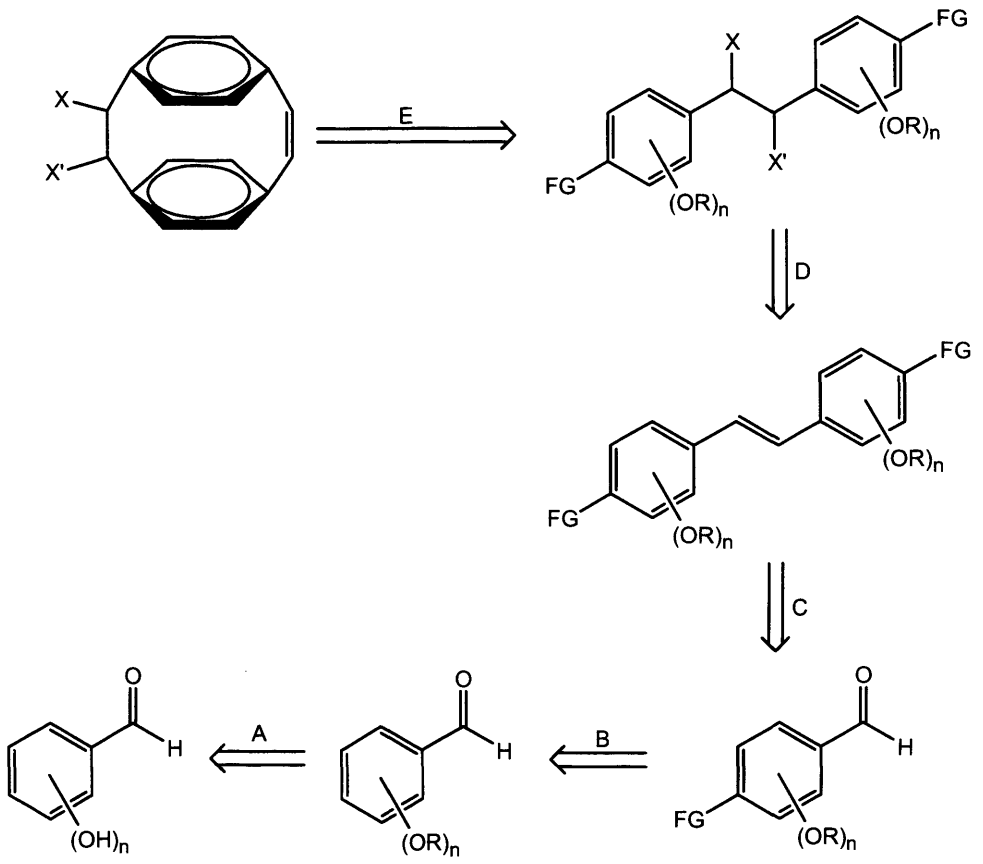
The synthesis of [2.2] *para*-cyclophenes and their derivatives has been outlined in *Section C* of this chapter, and is in general a non-trivial, often low-yielding process, affording little opportunity for functionalisation at the aromatic rings. Thus, the main aim of this work was to develop a new, facile route towards functionalised [2.2] *para*-cyclophenes, starting from alkoxy-substituted stilbene precursors. As was discussed in *Section B*, a wide range of approaches are already available for the preparation of such stilbenes, hence a reproducible route allowing straightforward variation of substituents at the aromatic rings should be accessible.

In conclusion, the overall aim of this project was to synthesise and fully characterise a range of alkoxy-substituted [2.2] *para*-cyclophane-1,9-dienes ([2.2] *para*-cyclophenes) and [2.2] *para*-cyclophane-1-enes (*Figure 39*) as potential monomers for the preparation of PPV *via* ROMP (See *Scheme 41*).



OR = O-alkyl
FG = Br, CHO, CH_3

Scheme 41: Generalised overview of proposed PPV precursor synthesis.



Scheme 42: Retro-synthetic analysis of [2.2] *para*-cyclophane-1-enes *via* stilbene intermediates.

One possible retrosynthetic analysis of [2.2] *para*-cyclophane-1-enes is outlined above in *Scheme 42*. From these five disconnections, a number of potential synthetic strategies were developed, all relying on the same basic reaction framework, namely alkoxy-substituted benzaldehydes, as a starting point. These versatile molecules have the advantage of being relatively simple to prepare (step A, *Scheme 42*), and allow facile variation of the alkoxy substituents. Subsequent transformation of these benzaldehydes to the corresponding alkoxy-substituted stilbenes (step C), followed by introduction of suitable leaving groups across the stilbene double bond (step D), provides a prospective route into the desired [2.2] *para*-cyclophane-1-enes *via* an appropriate ring-closing reaction (step E). This ring-closing can be brought about through further functionalisation of either the stilbenes or their parent alkoxy benzaldehydes to introduce reactive groups at the *para* position relative to the stilbene C=C bond (for example step B). This additional functionality, for example an aldehyde, can then go on to react intramolecularly, yielding the desired ring-closed product.

The research carried out into the above synthetic strategy will be discussed in subsequent chapters. *Chapter Two* explores the preparation and characterisation of the alkoxy-substituted benzaldehyde precursors, while *Chapter Three* extends the discussion into the preparation and of alkoxy-functionalised stilbenes. *Chapter Four* deals with the further functionalisation and characterisation of these stilbenes, and *Chapter Five* introduces an alternative strategy towards the synthesis of [2.2] *para*-cyclophenes, using the Ramberg-Bäcklund reaction.

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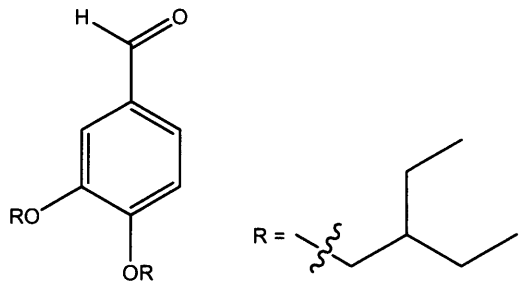
CHAPTER TWO

Synthesis and Characterisation of Alkoxy-Substituted Benzaldehydes

2.1: Introduction

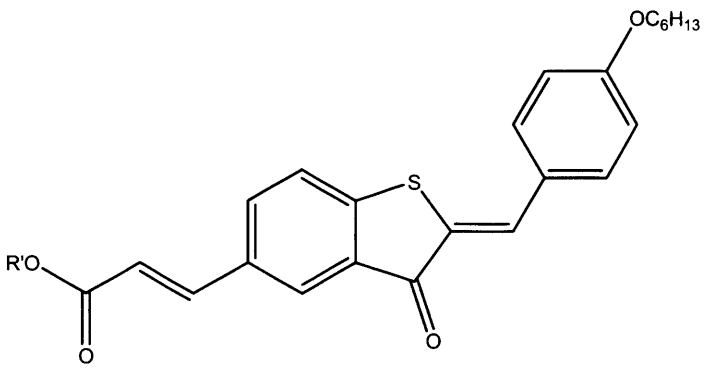
Alkoxy-substituted benzaldehydes constitute the primary precursors employed in almost all the synthetic work carried out in this thesis. Conceptually, they are highly versatile and straightforward to prepare and, without significant adjustment to the reaction methodology, a diverse range of analogues may be generated. During this work only the straight-chain alkoxyderivatives were considered, mainly to facilitate the spectroscopic analysis of the alkoxy-substituted benzaldehydes and their subsequent derivatives. There are, however, many examples to be found in the literature of analogues bearing branched-chain alkyl groups. For instance Richardson *et al.* prepared the derivative **106** illustrated in *Figure 39* as a precursor to tetrasubstituted porphyrin dyes for use as nitrogen dioxide sensors.[1] Extending the field to include aromatic and heteroatom-containing side chains provides further examples including bromoalkyl-,[2] phenyl-,[3] naphthyl-[4] and polyether-[5] substituted benzaldehydes.



106

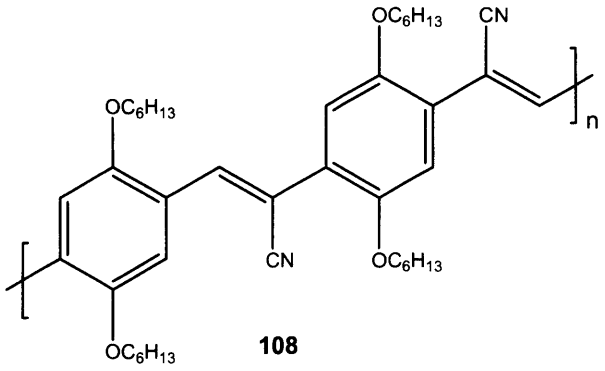
Figure 39: Example of a branched-chain alkoxy benzaldehyde.

Both mono- and di-alkoxy benzaldehydes have found uses in a wide variety of chemical syntheses, ranging from biological applications through to the preparation of conducting polymers. For example, mono-alkoxy benzaldehydes have been used extensively as precursors in syntheses of biologically-active compounds such as that described by Li, Dietrich, and Hansch; where 3-pentyloxy benzaldehyde is involved in the preparation of 5-(substituted benzyl)-diaminopyrimidines, which inhibit bovine liver and *E. coli* dihydrofolate reductase (DHFR).[6] Mono-alkoxy benzaldehydes are also used in the synthesis of dyes such as those based on indigo (**107**) (*Figure 40*).[7] Di-alkoxy benzaldehydes are more commonly found in the preparation of PPV and related analogues (*Figure 41*),[8] since the second alkoxy group confers increased solubility to the final polymer when compared to their mono-alkoxy analogues.



107

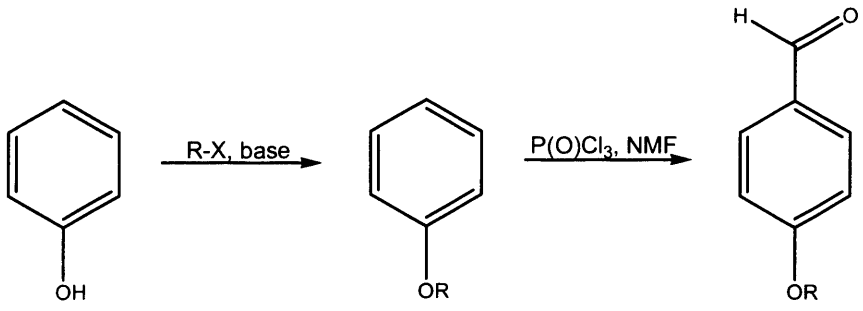
Figure 40: Hemithioindigo derivative dye.



108

Figure 41: Cyano-substituted alkoxy PPV analogue.

The most common synthetic route used to prepare alkoxy-substituted benzaldehydes is *via* a simple base-induced S_N2 reaction between a hydroxy-substituted benzaldehyde and the corresponding haloalkane. A related, but similar, route also frequently used is to alkylate an aromatic substrate such as a phenol, then subsequently introduce the aldehyde functionality to the aromatic ring (for an example of this latter method using the Vilsmeier formylation, see *Scheme 43*).

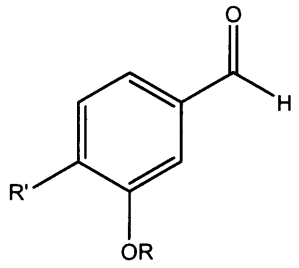


R = alkyl

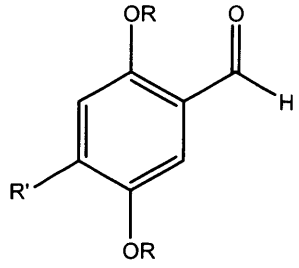
Scheme 43: An example of an alkoxy benzaldehyde synthesis where the formyl moiety is added after the alkylation step *via* a Vilsmeier formylation.

Variations in the base and the halide leaving group (Cl, Br, or I) used in the alkylation step are widespread, with the most popular base being potassium carbonate due to its ready availability, low toxicity and efficient reactivity. The addition of a catalytic amount of caesium carbonate is said to increase yields in otherwise slow and low-yielding transformations,[9] due to its increased solubility in organic solvents in comparison to potassium carbonate. However, the high cost of this reagent outweighs the benefits of its use in all but the most difficult reactions.

During the course of experimental work for this thesis, a range of alkoxy-substituted benzaldehydes has been prepared and fully characterised; these are detailed below in *Figure 42*. The particular benzaldehydes chosen were selected as they contain a series of relatively short-chain alkyl substituents making NMR analysis of the benzaldehydes themselves and subsequent derivatives reasonably straightforward, whilst still conferring the desired increase in solubility to future higher MW derivatives.



109a-c
111a-c



114a, 114b
115a, 115b

Compound	R	R'	Yield
109a	1-Propyl	H	46%
109b	1-Pentyl	H	93%
109c	1-Hexyl	H	29%
111a	1-Propyl	Me	95%
111b	1-Hexyl	Me	73%
111c	$(CH_2)_3Ph$	Me	72%

Compound	R	R'	Yield
114a	1-Butyl	H	57%
114b	1-Pentyl	H	74%
115a	1-Propyl	Me	59%
115b	1-Butyl	Me	79%

Figure 42: Alkoxy benzaldehyde derivatives.

As is evident above, these molecules fall into two distinct categories of mono- and di-alkoxy substituted. Each category can be further divided into two sections, those compounds possessing a methyl group *para* to the aldehyde moiety, and those without.

Although by nature these compounds are closely related, the two distinct groups of molecules are synthesised in a slightly different way, thus each will be discussed separately.

2.2: Synthesis of 3-Alkoxybenzaldehydes.

3-Alkoxybenzaldehydes **109a-c** were synthesised *via* the O-alkylation of 3-hydroxy benzaldehyde with the desired haloalkane in either acetone or acetonitrile at reflux, using excess potassium carbonate as base. All three compounds **109a-c** are very similar in both their appearance and characteristics. They were all isolated in the pure form as pale yellow oils, and are readily soluble in a variety of common organic solvents. Due to the low yields of **109a** and **109c** obtained while using acetone as solvent, this was changed to acetonitrile for the preparation of **109b**, and subsequent yields were much improved.

From a study of selected ^{1}H and ^{13}C NMR data (summarised in *Table 1*) it is possible to see that the aldehyde fragment in these compounds is sufficiently far removed from the alkoxy substituent that the exact nature of the alkyl chain present does not in any way affect the chemical shift of the aldehyde moiety. The observed data compare well with that in the literature, for example Fyles *et al.* quote the ^{1}H chemical shift of the aldehyde moiety in 3-hexyloxy benzaldehyde as 9.94 ppm, and the ^{13}C chemical shift as 192.2 ppm.[7]

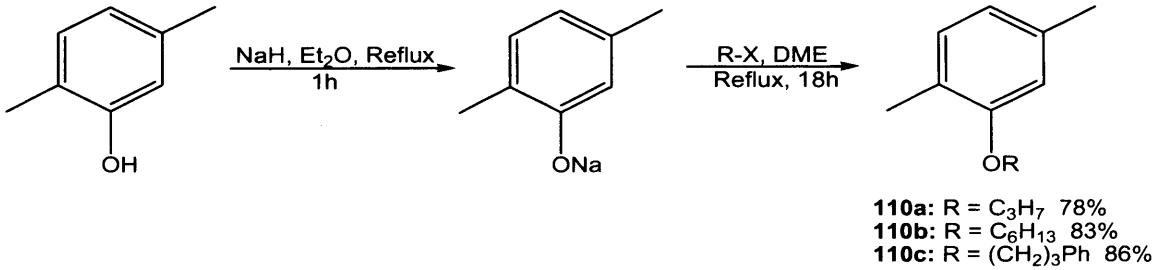
Compound	Alkylating Agent	$\delta^{1}H$ CHO (ppm)	$\delta^{13}C$ CHO (ppm)
109a	1-Bromopropane	9.90	192.2
109b	1-Bromopentane	9.95	192.1
109c	1-Iodohexane	9.95	192.3

Table 1: Representative examples of reagents, and selected NMR data for compounds **109a-c.**

2.3: Synthesis of 3-Alkoxy-4-Methyl Benzaldehydes.

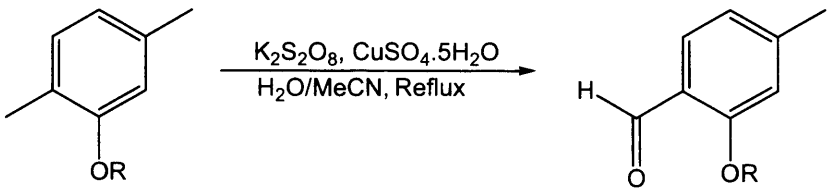
An alternative method was necessary to prepare the 3-alkoxy-4-methylbenzaldehydes, as alkylation using potassium carbonate as base as used to synthesise compounds **109a-c** proved unsuccessful, returning only starting materials after the reaction. Compounds **111a-c** were hence prepared *via* a two-step method starting from 2,5-dimethylphenol and an appropriate alkylating agent (see *Scheme 44*). The first step involves the deprotonation of 2,5-dimethylphenol with sodium hydride in dry diethyl ether under an inert atmosphere.

Using sodium hydride as an alternative base surmounted the solubility problem encountered when using potassium carbonate, as it is far more soluble in diethyl ether. However, the introduction of a two-step methodology was required, as the sodium salt of 2,5-dimethylphenol generated through deprotonation is insoluble in diethyl ether resulting in the need for a change of solvent. The sodium salt was thus isolated as a white air-sensitive powder, which was then re-dissolved in dry DME and the alkylating agent added. After heating at reflux for 18h, subsequent filtration and aqueous work-up, the resulting 1,4-dimethyl-2-alkoxybenzenes (**110**) were isolated and purified *via* Kügelrohr distillation under reduced pressure, and were obtained in high yields as pale yellow oils (78-86%).



Scheme 44: Preparation of 1,4-dimethyl-2-alkoxybenzenes *via* a two-step method.

In order to prepare the desired 3-alkoxy-4-methylbenzaldehydes, *i.e* to introduce the aldehyde fragment, alkoxy 2,5-dimethyl compounds **110a-c** were added to a mixture of one molar equivalent copper sulfate pentahydrate and three molar equivalents potassium persulfate in 1:1 acetonitrile:water as solvent, following a method of oxidation first suggested by Bhatt and Perumal (*Scheme 45).* [10] The reaction was heated at a vigorous reflux for 1h and, after cooling and aqueous work-up, the desired 3-alkoxy-4-methylbenzaldehydes **3** were isolated in good yields as viscous red-orange oils. Three analogues were prepared *via* this method, compounds **111a-c**, bearing 1-propyloxy, 1-hexyloxy and 1-(3-phenyl)propyloxy groups, respectively. The intermediate 2,5-dimethyl alkyloxy benzenes **110a-c** were also isolated and fully characterised.



110a: R = C_3H_7
110b: R = C_6H_{13}
110c: R = $(CH_2)_3Ph$

111a: R = C_3H_7 95%
111b: R = C_6H_{13} 73%
111c: R = $CH_2)_3Ph$ 72%

Scheme 45: Synthesis of 1,4-dimethyl-2-alkoxy benzaldehydes.

2.3.1: The Single-Electron Oxidation Reaction.

The oxidation reaction employed to effect the transformation from **110** into **111** is of interest in its own right, being a single-electron oxidation proceeding *via* a radical mechanism. Although many such reactions using a wide assortment of substrates and reagents have been documented,[11] the method described above is by far the simplest and most synthetically useful in this situation, giving the desired product cleanly and in good yield.

It is evident that during the course of the reaction, either one or both of the methyl groups present in the 2,5-dimethylalkoxybenzene could be attacked and oxidised. However, after repeating the reaction several times using alkyloxy benzenes **110a-c** it became apparent that only one methyl group was oxidised in every case, despite attempts to oxidise both through the use of two equivalents of oxidising agent. This result is thought to be due to the inherent deactivation of the aromatic ring by an aldehyde functionality. Once there is one aldehyde present on the ring, the molecule is sufficiently deactivated to further oxidation such that no reaction can take place at the remaining methyl group.

The oxidation reaction has been reported to be regiospecific,[12] oxidising only the methyl groups *ortho* to the alkoxy substituent. This was shown in the case of the analogues synthesised here by the use of nOe experiments, where irradiation of the aldehyde proton led to collapse of the signals for the alkoxy group. The results of the nOe experiments are illustrated below in *Figure 43*. If the methyl *meta* to the alkoxy group had been the one oxidised, the alkoxy functionality would have shown no response to the nOe experiment as the separation between the two moieties is too great. Thus, the nOe results show that the reaction is indeed regioselective, having yielded only the product where the aldehyde moiety is in the *ortho* position to the alkoxy group.

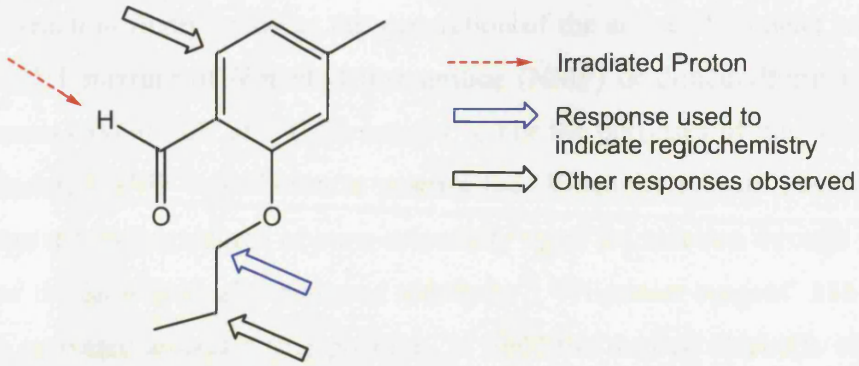
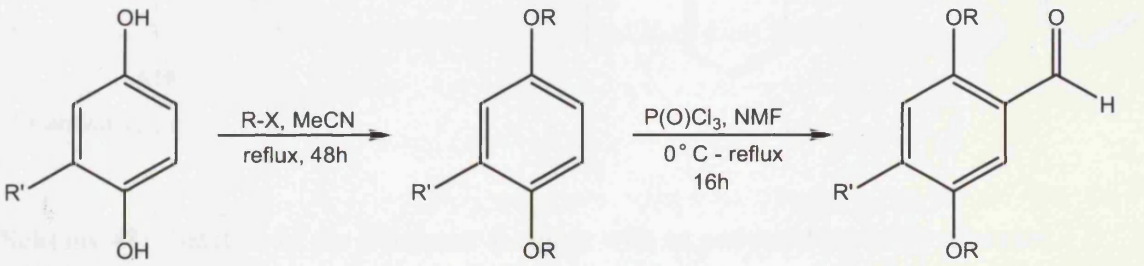


Figure 43: Response of compounds **110a-c** to nOe irradiation at the aldehyde position.

2.4: Synthesis of 2,5-Dialkoxy-Substituted Benzaldehydes.

The significant advantage in synthesis of using dialkoxy-substituted benzaldehydes as precursors to PPV-like compounds is one of solubility; compared to the monoalkoxy substituted analogues this property is significantly enhanced. At the most extreme scale, polymers such as PPV require some degree of alkyl substitution to give them any reasonable level of solubility at all. Towards this end, a range of 2,5-dialkoxybenzaldehydes (**114** and **115**) were synthesised according to the reactions shown in *Scheme 46*.



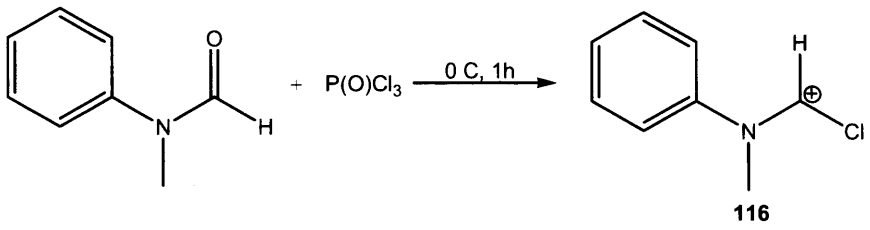
112a: - R' = H, R = C_4H_9 75 %
112b: - R' = H, R = C_5H_{11} 63%
113a: - R' = CH_3, R = C_4H_9 68%
113b: - R' = CH_3, R = C_4H_9 86%

114a: - R' = H, R = C_4H_9 57%
114b: - R' = H, R = C_5H_{11} 74%
115a: - R' = CH_3, R = C_3H_7 59%
115b: - R' = CH_3, R = C_4H_9 79%

Scheme 46: Synthesis of 2,5-dialkoxybenzaldehydes.

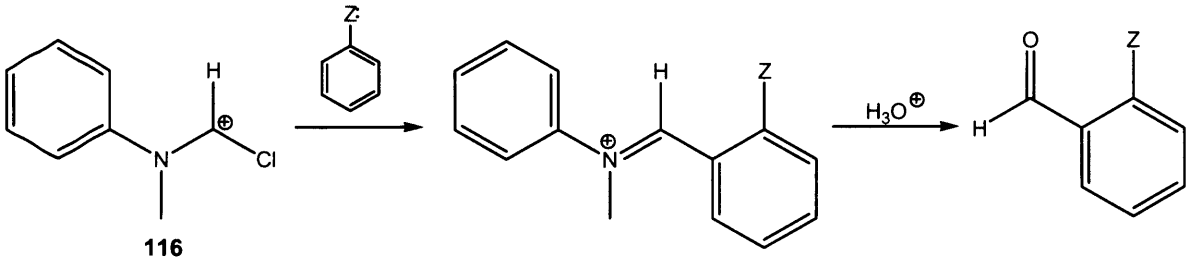
The first step of the above transformation, as with all syntheses of alkoxybenzaldehydes undertaken in this work, is simply an S_N2 reaction between either hydroquinone or methyl hydroquinone and two equivalents of a corresponding bromoalkane to yield dialkoxy-substituted benzene compounds **112** and **113.** Subsequent Vilsmeier formylation of **112** and **113** furnishes the desired 2,5-dialkoxybenzaldehydes **114** and **115**. The Vilsmeier

formylation reaction firstly involves the generation of the active 'Vilsmeier reagent' **116**, by stirring a 1:1 mixture of *N*-methyl formanilide (NMF) or dimethylformamide (DMF) and phosphorus oxychloride at 0°C (*Scheme 47*). For the purposes of this work, the more sterically hindered NMF was chosen to prepare the 'Vilsmeier reagent', as this has been shown to confer a higher degree of *para*-selectivity upon the reaction through preferential formation of the least sterically hindered aldehyde.[13] 'Vilsmeier reagent' **116** goes on to attack at an activated aromatic ring position, to yield the desired aldehyde after aqueous work-up (*Scheme 48*).



116

Scheme 47: Formation of the 'Vilsmeier Reagent' using NMF.

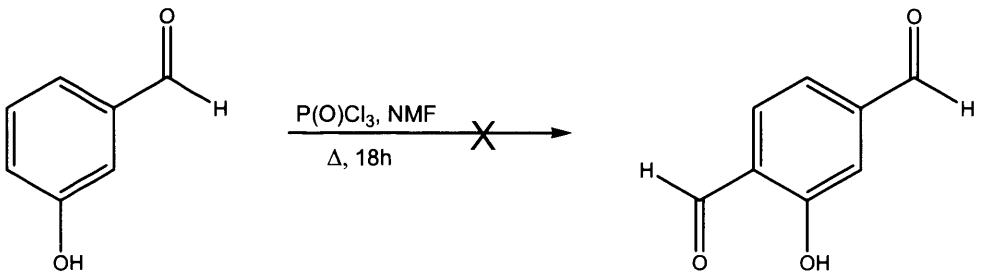


116

Z = activating group

Scheme 48: Reaction of the Vilsmeier Reagent with an activated aromatic substrate.

As the Vilsmeier reaction will only work when applied to suitably activated substrates,[14] formylation will not occur when there is already a deactivating aldehyde functionality present on the aromatic ring. This latter deactivation effect also proved problematic when attempting to further formylate 3-hydroxy benzaldehyde to yield the *para*-dialdehyde – no reaction occurred and the starting material was returned unchanged (*Scheme 49*). No synthesis of 3-hydroxy benzene 1,4-dicarbaldehyde **117** has been reported previously in the literature, and this was seen as a highly desirable compound, as coupling of two equivalents of **117** *via* the aldehyde functionalities using a McMurry reaction could give direct access to a substituted [2.2] *para*-cyclophene.



117

Scheme 49: Attempted Vilsmeier formylation of 3-hydroxy benzaldehyde.

As a consequence of the plane of symmetry in the 1,4-dialkoxy benzene starting material **112**, coupled with the fact that Vilsmeier formylation has been proven to occur only once per aromatic ring, reacting **112** under the conditions given in *Scheme 46* gives rise to one product only, the 2,5-dialkoxybenzaldehydes **114**. The same products **114** are formed no matter which position on the ring is formylated, with the ^{1}H NMR spectrum of the aromatic region showing a singlet integrating to one proton, and an AB system integrating to two protons. In contrast, applying identical reaction conditions to 1,4-dialkoxy-2-methylbenzene (**113**), although again giving rise to only one product, produces only the regioisomer **115**, where the aldehyde functionality is formed *para* to the methyl group. This is again evident from ^{1}H NMR spectroscopic studies, where the aromatic ring gives rise to two singlet peaks each integrating to one proton. As discussed earlier in this section, this *para* regioselectivity can be attributed to the use of the more sterically demanding N-methyl formanilide (NMF) rather than dimethylformamide (DMF) in formation of the Vilsmeier reagent, as this has previously been shown to favour formation of the least hindered aldehyde.[13]

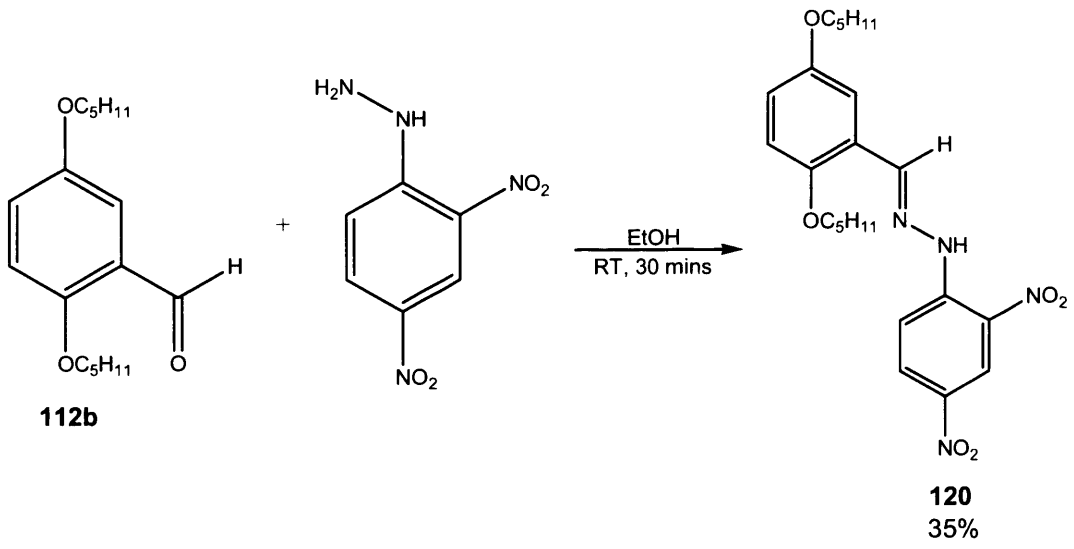
2.5: Synthesis of *para*-Bromo-Dialkoxybenzaldehydes.

In order to easily introduce functionality at the para-position to the aldehyde moiety in dialkoxy benzaldehydes, for example through a Stille coupling to yield the corresponding alkene, the synthesis of *para*-bromo-dialkoxybenzaldehydes was necessary. These compounds are closely related in structure to those described in the previous section; however the method of preparation was changed due to the need for a bromine atom in the *para* position. Two methods were postulated; dibromination of a symmetrical alkoxy compound followed by lithium-halogen exchange at one brominated site, yielding the formylated compound **119** upon quenching with DMF or, alternatively, the direct bromination of a protected dialkoxy benzaldehyde. Protection of the aldehyde moiety was

necessary as the reaction conditions needed to brominate aromatic rings, for example AIBN and *N*-bromosuccinimide in refluxing carbon tetrachloride will react with and destroy an unprotected aldehyde moiety.

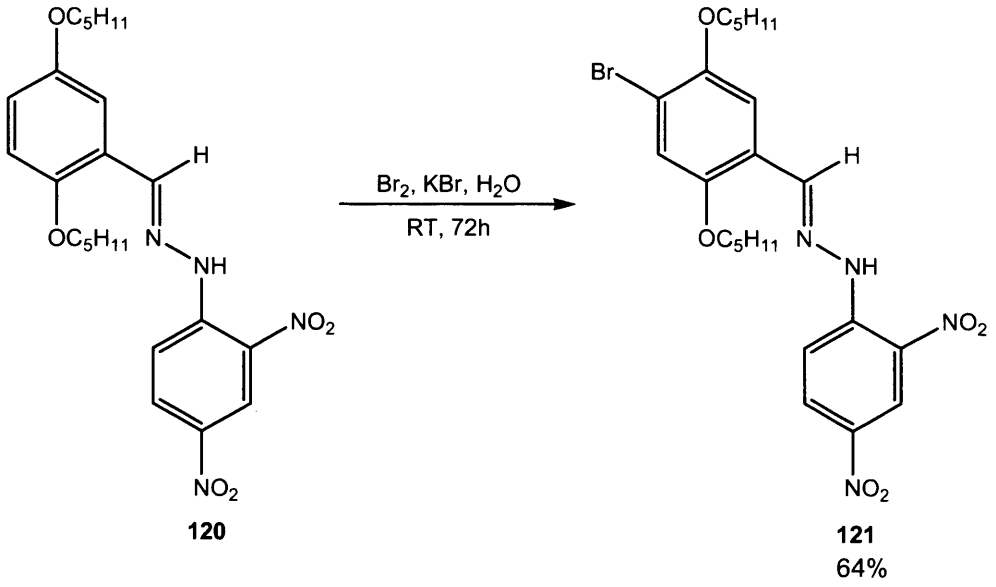
2.5.1: Protection of Dialkoxy Benzaldehydes.

The protecting group of choice for the dialkoxy aldehydes was a 2,4-dinitrophenyl hydrazine (2,4-DNP), as not only are these groups stable to NBS and CCl_4, but they are also resistant to elemental bromine.[15] Thus the testing of a number of different bromination methods, if necessary, would be possible using the 2,4-DNP-protected alkoxy aldehydes. The protection was carried out as shown below in *Scheme 50*, using similar conditions to those first proposed by McMurry,[16] with 2,5-pentyloxybenzaldehyde **112b** being chosen as a test substrate. After a short reaction time of 30 minutes, the reaction mixture was filtered *via* suction filtration to yield a red solid. Subsequent recrystallisation of this solid from hot methanol gave the desired *N*-(2,5-dipentyloxybenzylidene)-*N'*-(2,4-dinitrophenyl) hydrazine **120** in 35% yield. This relatively low yield after purification is thought to be due to the limited solubility of dinitrophenylhydrazine in organic solvents; a reasonable proportion of the starting materials remained after completion of the reaction, which were removed during the recrystallisation process.



Scheme 50: Preparation of *N*-(2,5-dipentyloxybenzylidene)-*N'*-(2,4-dinitrophenyl) hydrazine **120.**

Bromination of **120** proved straightforward: using a method first described by Guillaumel and coworkers,[17] namely a combination of potassium bromide and elemental bromine in water yielded *N*-(4-bromo-2,5-dibutyloxybenzylidene)-*N'*-(2,4-dinitrophenyl)hydrazine **121** in 64% yield (*Scheme 51*).



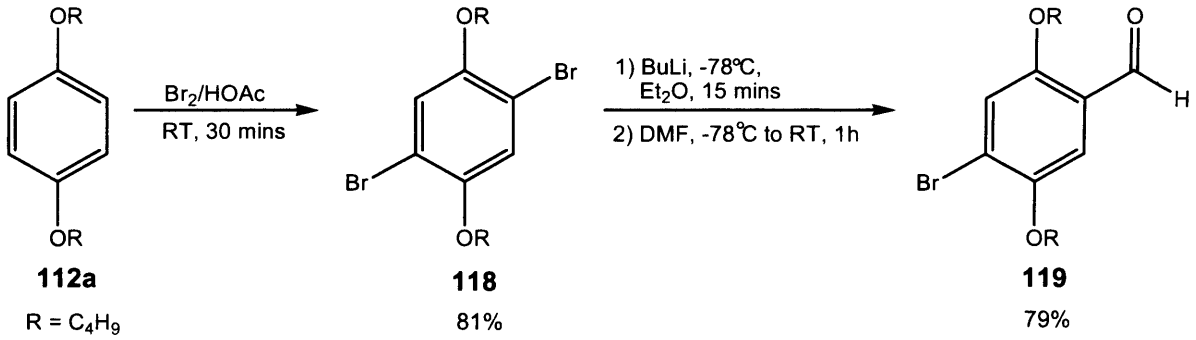
Scheme 51: Bromination of *N*-(2,5-dipentyloxybenzylidene)-*N'*-(2,4-dinitrophenyl)-hydrazine **120.**

Unfortunately, deprotection of **121** proved extremely difficult. Literature methods involved the use of hazardous procedures, such as bubbling ozone through a solution of the dinitrophenyl hydrazine to be deprotected.[16] As for the purposes of this work the deprotections were to be carried out on a reasonably large scale, such procedures were not deemed safe and an alternative method of deprotection was sought.

Heating to reflux in absolute ethanol for 18 hours followed by vacuum filtration yielded an orange solid, shown by ^{1}H NMR analysis to be the starting 2,4-DNP-protected species **120**. Upon removal of the solvent from the yellow-coloured filtrate a yellow/orange solid was obtained, which by ^{1}H NMR analysis was proven to be a mixture of largely starting material and a very small amount of the desired deprotected product. An attempt was made to deprotect **121** in absolute ethanol *via* microwave irradiation using a single-mode automated "CEM Explorer" microwave reactor at 300 W for two minutes; however this returned only the starting protected species.

2.5.2: An Alternative Route Towards *para*-Bromo-Dialkoxybenzaldehydes

As the deprotection of brominated 2,4-DNP derivatives had proved impossible, attention was focussed upon the alternative method of synthesising dibromodialkoxy benzenes **118** shown below in *Scheme 52.* Bromination of related substrates using elemental bromine and acetic acid upon a symmetrical alkoxy benzene substrate has previously been demonstrated to be successful by Pelter and coworkers in 1997,[18] and application of this methodology upon 1,4-dibutoxy benzene **112a** furnished the desired dibromodialkoxy benzene **118** cleanly in good yield (81%). Compound **118** was then formylated using a method adapted from that of Egbe *et al.*,[19] and Maier and Aust[20] using addition of exactly one equivalent of butyl lithium to effect lithium-halogen exchange at only one brominated site, and subsequent quenching of the lithiated intermediate with DMF to furnish the desired aldehyde **119** in 79% yield.



112a
$R = C_4H_9$

118
81%

119
79%

Scheme 52: Synthesis of *para*-bromo-dialkoxybenzaldehydes.

2.6: Conclusions

Efficient, high-yielding syntheses of a range of alkoxybenzaldehydes were pivotal to the research for this thesis, as these compounds constitute the starting point for almost all further synthetic work undertaken. This section has illustrated that the goal was achieved, as a range of syntheses of alkoxybenzaldehydes have been described, demonstrating not only straightforward, reproducible chemistry, but also that these syntheses are flexible, allowing a choice of substituents and functionalisation to be employed. This flexibility of the reaction methodology is vital, as subsequent reactions which will be described in the next sections of this chapter require, for their success, a range of different functional groups to be introduced onto the benzaldehyde starting material backbone. Although the syntheses developed here allow for the use of a range of differing alkoxy substituents, subsequent work described in this thesis concentrates mainly upon the butyloxy substituted

derivative only. This is to allow for easy comparison of both reaction methodologies and the products obtained through further reaction of these benzaldehydes.

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CHAPTER THREE

Synthesis of Substituted Stilbenes as Precursors to [2.2] *para*-Cyclophenes and [2.2] *para*-Cyclophane-1-enes

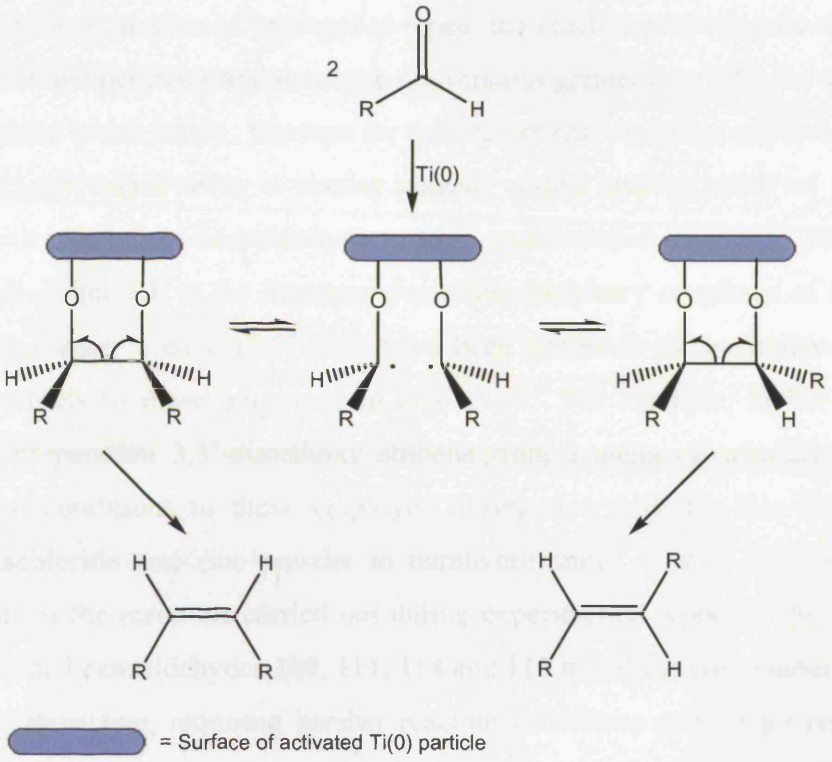
3.1: Introduction.

To generate alkoxy-substituted stilbenes from the alkoxy benzaldehydes described in *Chapter 2* for use as precursors to [2.2] *para*-cyclophenes, three reactions could possibly be employed; the McMurry coupling, the Horner-Wittig reaction, and the Siegrist reaction. While the Siegrist reaction involves one further step, and the Horner-Wittig approach requires a number of further transformations to be carried out in order to synthesise the necessary phosphonate ester reagent from the parent aldehyde, the McMurry coupling can be carried out on the aldehydes themselves. Thus, at the outset the McMurry reaction appeared to be the most attractive route from a synthetic viewpoint, as it achieves the desired transformation from the aldehydes to the stilbenes in only one step, avoiding lengthy synthetic work and loss of material in purification steps.

3.2: The McMurry Reaction.

Coupling of two carbonyl compounds to form an olefin can only be carried out by low-valent titanium species.[1] Named the McMurry coupling after its discoverer, John McMurry, this reaction is a two-step process, the first step being simply a pinacol coupling and the second, a deoxygenation to yield the olefin. The mechanism of the McMurry coupling is shown in *Scheme 53*. The scope of the reaction is wide, tolerating many functional groups, and it is applicable to both aldehydes and ketones. The McMurry reaction is a heterogeneous process, with electron spin resonance (ESR) studies showing that the active species in the reaction are very finely divided particles of titanium(0).[2]

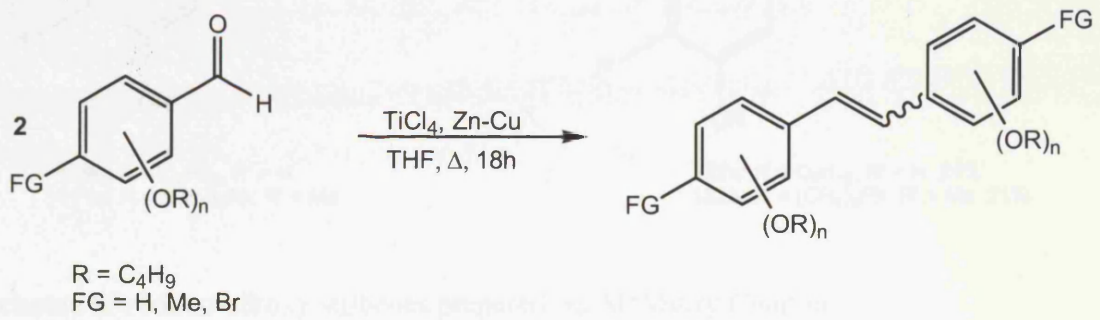
The desired low-valent titanium reagent can be prepared by reducing titanium(III) or titanium(IV) (usually as the titanium tri- or tetra-chlorides) with a number of reducing agents, including lithium aluminium hydride, potassium, magnesium or zinc. More recently, a zinc-copper couple, formed from the reaction of copper sulfate and zinc powder in water, has been shown to be an efficient reducing agent, which when reacted with titanium trichloride-DME gives an extremely active titanium(0) species.[3] This combination of reagents exhibits enhanced reactivity compared to older systems, giving high yields of olefins from couplings that have previously been difficult and low yielding. For example, the preparation of tetraisopropylene was reported by Morton to occur in only 12% yield using $TiCl_3/LiAlH_4$,[4] but when the new $TiCl_3$-DME/Zn-Cu reagent was employed this increased to 94%.[1]



Scheme 53: Mechanism of the McMurry coupling.

3.2.1: Preparation of Alkoxy-Substituted Stilbenes *via* the McMurry Reaction.

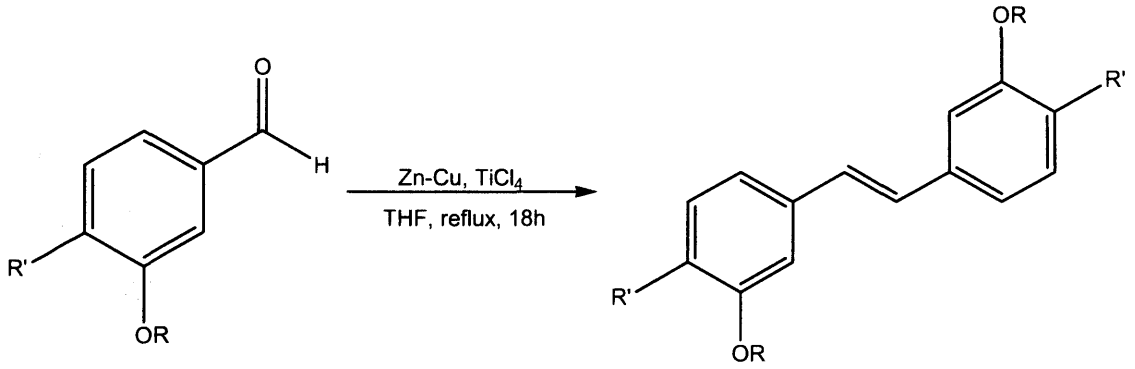
Throughout the course of this work, the reaction conditions employed to bring about the desired McMurry coupling were $TiCl_4$ and a zinc-copper couple (prepared from zinc powder and copper sulfate), under an inert atmosphere using THF or DME as solvent (*Scheme 54*). [5] This choice of reagents was principally made due to the increased ease of handling and availability of $TiCl_4$ compared to $TiCl_3$.



Scheme 54: Generalised stilbene synthesis *via* McMurry coupling.

Disappointingly low yields were obtained for all the McMurry couplings attempted on the alkoxy-functionalised aldehydes **109** and **111**, with each being in the region of 20-30%.

Despite a significant number of attempts to repeat the reaction and optimise the yields by altering reaction temperatures and times, no conversions greater than 30% for any substrate could be obtained in our hands. Reasons for this are not entirely clear, as previous work by McMurry and coworkers using a similar reagent system quotes yields of 97% in the coupling reaction of parent benzaldehyde to form unsubstituted stilbene.[31] There are also references, albeit limited, in the literature describing McMurry couplings of *meta*-alkoxy benzaldehydes, where yields of 57-88% have been achieved using similar or identical reaction conditions to those employed in this thesis.[6] For example, Dyker *et al.* have reported the preparation 3,3'-dimethoxy stilbene from 3-methoxybenzaldehyde in 88% yield identical conditions to those employed during the work for this thesis, namely titanium tetrachloride and zinc powder in tetrahydrofuran.[7] It was, however, observed throughout all of the reactions carried out during experimental work for this thesis using alkoxy-substituted benzaldehydes **109, 111, 114** and **115** that these compounds appeared to be unusually unreactive, requiring harsher reaction conditions and longer reaction times than would perhaps be predicted from their structure. A test reaction was carried out using the optimised $TiCl_3$-DME / zinc-copper couple conditions to ascertain whether this would increase these previously low yields observed when using $TiCl_4$/Zn-Cu. However, this was proved not to be the case and yields remained unpromising (approx. 30%). Nonetheless, two stilbenes were prepared and characterised using this method; they are shown below in *Scheme 55*.



109c: R = C_6H_{13}, R' = H
111c: R = $(CH_2)_3Ph$, R' = Me

122a: R = C_6H_{13}, R' = H 24%
122b: R = $(CH_2)_3Ph$, R' = Me 21%

Scheme 55: Mono-alkoxy stilbenes prepared *via* McMurry Coupling.

3.2.2: Structure and Characterisation of Alkoxy-Substituted Stilbenes Prepared *via* the McMurry Coupling.

As discussed above, stereochemical control is not possible in the McMurry reaction due to the reversible nature of the radical dimerisation step.[6] As the stilbenes described here are

symmetrical, determination of the *cis/trans* geometry is not easily possible using NMR spectroscopy at this resolution. It would be necessary to compare the small ^{13}C satellite peaks to perform this type of analysis, and although they are always present in ^{1}H NMR spectra, they are rarely visible except at very high resolution. The ^{1}H NMR spectrum of stilbene **122a** is shown for reference in *Figure 44*, showing the singlet resonance corresponding to the two alkene protons and illustrating that the ^{13}C satellites are not readily visible. Through X-ray crystallographic studies of **122b** (undertaken by Dr. J. Fawcett at the University of Leicester, see *Appendix 2* for details), it has been shown that in accordance with predictions made regarding the steric demands of the molecule, the stilbene **122b** is formed with *trans* geometry (see *Figure 45*). It is therefore reasonable to suggest that **122a** also forms as the *trans* isomer.

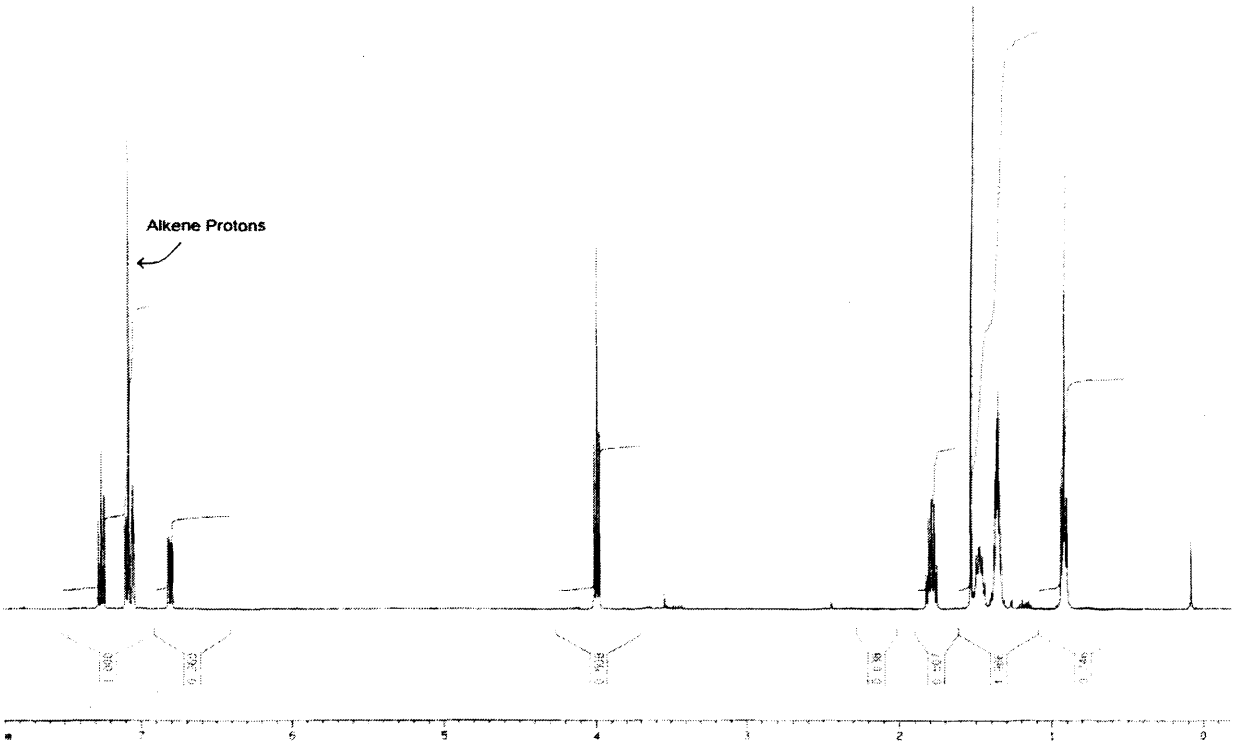


Figure 44: ^{1}H NMR spectrum (300 MHz, $CDCl_3$) of **122a**, di-hexoxy-*trans*-stilbene, showing the singlet resonance for the alkene protons.

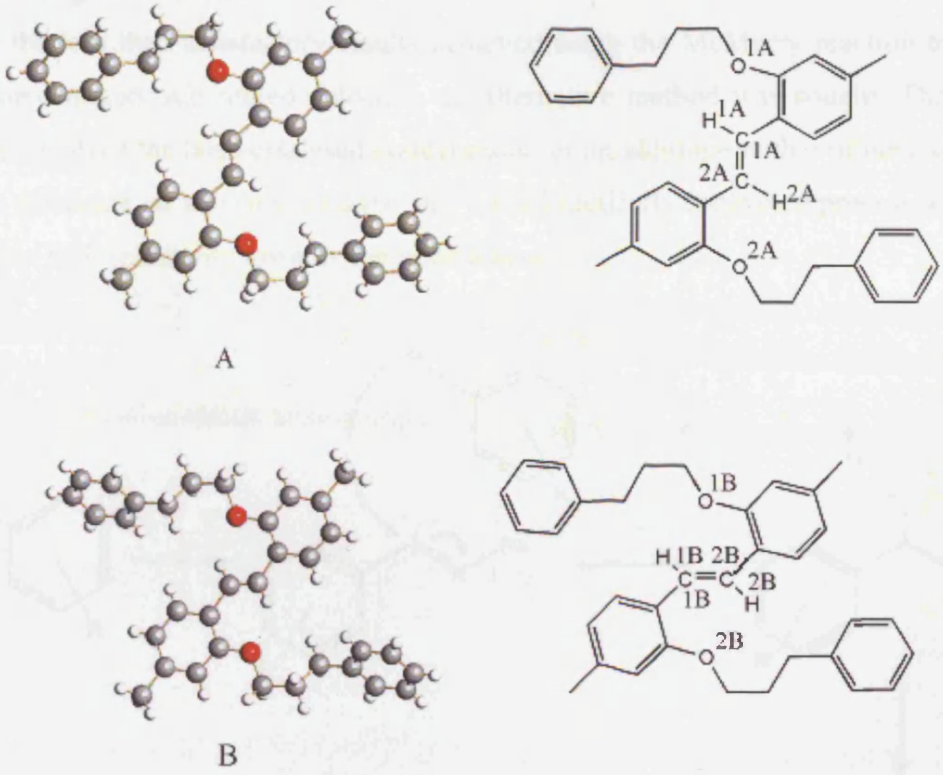
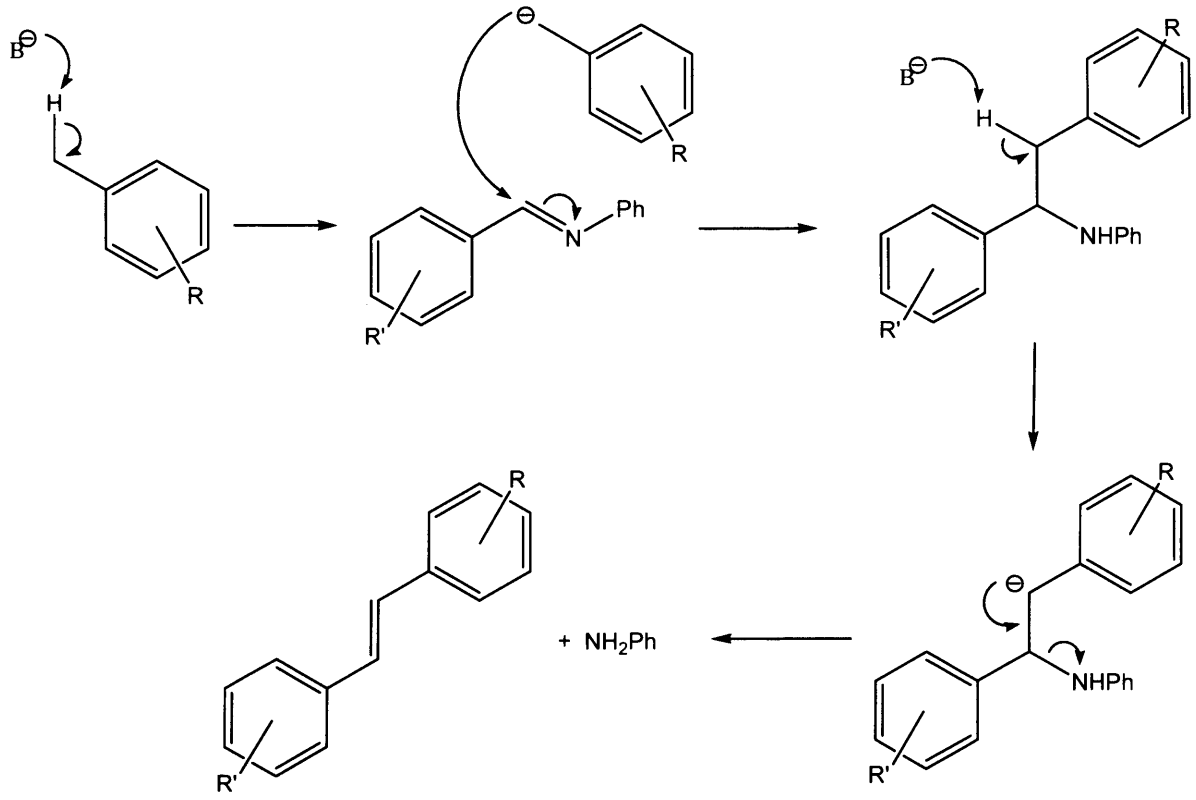


Figure 45: Ball and stick representation of the molecular structure of **122b**, di-(3-phenylpropoxy)-*trans*-stilbene, as determined by X-ray crystallography (*See Appendix 2*).

Two distinct, but similar, molecules (**A** and **B**) are present in the unit cell. Both molecules **A** and **B** adopt a *trans*-geometry about the double bond, the ether oxygens lying in the plane of the C=C unit in each case. The two crystallographically independent molecules differ from one another as a result of the orientation of the ether oxygens. In molecule **A** the atoms O(1A) and O(2A) lie adjacent to the stilbene protons located on the '*trans* carbon' {C(1A) and C(2A), respectively} relative to their parent substituted ring. For form **B**, the ether oxygens O(1B) and O(2B) lie closest to the H atoms {H(1B) and H(2B), respectively} located on the same carbon as the parent aromatic ring. In molecule **A,** the phenyl rings of the alkyl substituents lie almost in the plane of the C=C double bond, whereas in molecule **B** these phenyl rings are rotated parallel to the plane of the C=C bond. A detailed discussion of the metric parameters associated with **A** and **B** is precluded by the low quality of the data (Final $R_1 = 0.1254$). The poor data are believed to be a consequence of the poor diffraction of the crystals, something that has been attributed to the rather waxy nature of this material.

3.3: The Siegrist Reaction.

Due to the less than satisfactory results achieved using the McMurry reaction to prepare the desired alkoxy-substituted stilbenes, an alternative method was sought. The Siegrist reaction involves the base-catalysed condensation of an aldimine with a toluene derivative to form an alkene, as shown in *Scheme 56*.[8] It is a kinetically controlled process, exhibiting extremely high selectivity towards the *trans* alkene.[9]

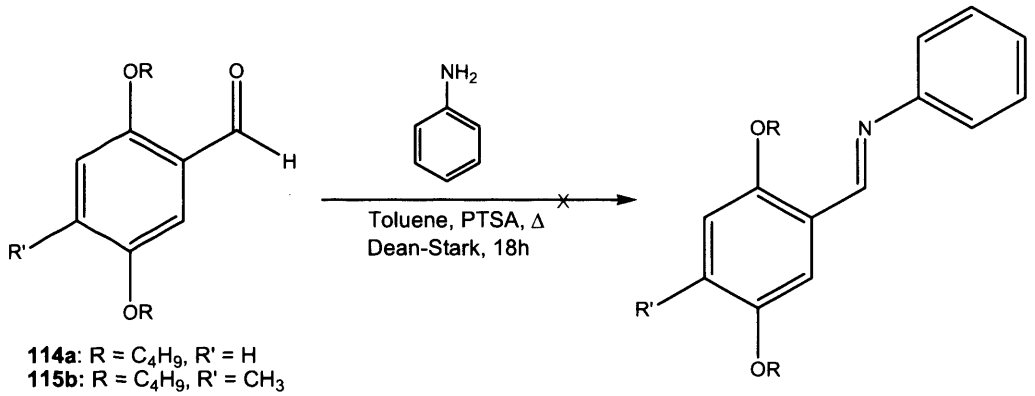


Scheme 56: Generalised overview of stilbene synthesis using the Siegrist reaction.

3.3.1: Attempted Preparation of Alkoxy-Substituted Stilbenes *via* the Siegrist Reaction.

In order to make use of this 'Siegrist' approach for the preparation of the alkoxy-substituted stilbenes required in this work, it was first necessary to synthesise an aldimine precursor from a suitable alkoxy benzaldehyde. Alkoxy-substituted benzaldehydes **114a** and **115b** were chosen as test substrates for this reaction. Initial strategies examined straightforward condensation reactions between the desired aldehyde and aniline under Dean-Stark conditions in toluene, using an acid catalyst (PTSA), as shown in *Scheme 57*.

Although the basic imine condensation reaction is an extremely well-known procedure, there has been comparatively little work reported using alkoxy substituted aldehydes as substrates, and then generally only the methoxy derivative is used.[10] For example, Olivieri *et al.* have prepared *meta*-methoxybenzylideneaniline from *meta*-methoxy benzaldehyde and aniline in refluxing methanol.[11] The choice of a higher-boiling solvent, namely toluene, and use of an acid catalyst for the purposes of the work for this thesis was governed by the expected lower reactivity of the dialkoxy benzaldehydes employed when compared to the methoxy derivatives discussed in the literature, hence a higher temperature was expected to be required.



114a: R = C_4H_9, R' = H
115b: R = C_4H_9, R' = CH_3

Scheme 57: Attempted synthesis of aldimines as precursors for the synthesis of alkoxy-substituted stilbenes *via* the Siegrist Reaction.

All of the attempted aldimine syntheses yielded a sticky brown oil upon removal of the solvent, which when analysed by ^{1}H NMR spectroscopy was found to contain a reasonable percentage (approx. 40%) of the desired aldimine, but was contaminated with both the starting aldehyde and excess aniline. All attempts to purify these mixtures met with no success, as the aldimines appeared to be extremely prone to decomposition upon either distillation or column chromatography on silica gel. Both ^{1}H NMR spectroscopy and GC-MS analysis after these purification attempts had been undertaken revealed a mixture of products had been obtained, however none of the components could be identified. In an endeavour to enhance the conversion and hence remove the need for purification of the product, a variety of different reaction conditions were employed (*e.g.* changing the solvent, reflux temperature, reaction time and acid catalyst etc.), but with no beneficial effect. A different methodology, involving stirring the reaction mixture at room temperature over activated 4Å molecular sieves to remove the water generated and drive the reaction to completion, was also unsuccessful.

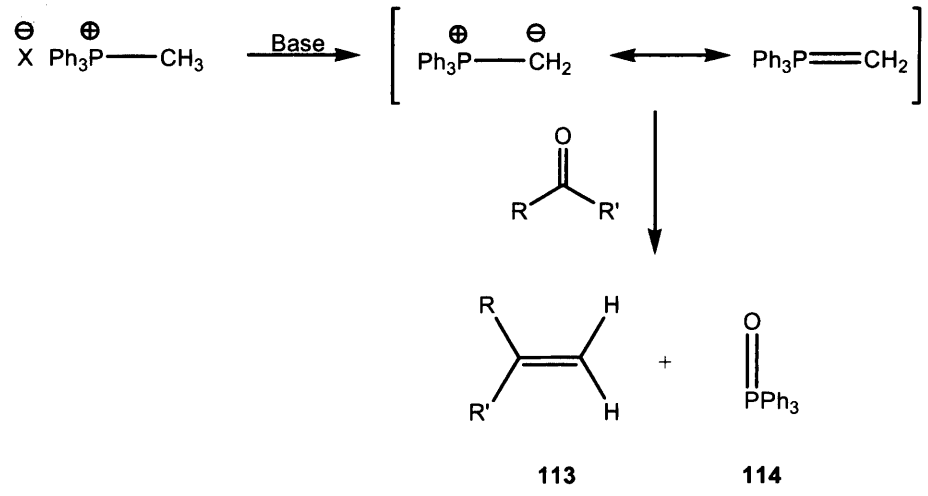
Conventional heating methods did not appear to be achieving a satisfactory result when applied to the problem of the desired aldimine synthesis. Hence the same reaction, between an alkoxy substituted aldehyde and aniline in toluene using PTSA as an acid catalyst, was tested under microwave heating conditions in a single-mode automated "CEM Explorer" microwave reactor system. Unfortunately, this alternative approach also proved ineffective, the same mixture of product and starting materials being obtained as with the conventional Dean-Stark methods. Variation of the reaction protocol by altering the pressure, temperature, reaction time and microwave power employed gave little variation in the product distribution except for when a high microwave power (300 W) was used, in which case pyrolysis of the reaction mixture resulted yielding an intractable black solid.

As is evident from the above discussion, the failure to prepare successfully the necessary substituted aldimine substrates meant that it was thus not possible to prepare the desired alkoxy stilbenes through a Siegrist reaction. Hence, attention was concentrated upon the Wittig / Horner-Witting routes which will be discussed in subsequent sections.

3.4: The Wittig Reaction and Variants.

3.4.1: The Wittig Reaction.

The Wittig reaction allows for the preparation of asymmetric olefins, is chemoselective and regioselective,[12] and is one of the most widely used methods for the synthesis of olefins. A phosphorus ylide is generated through the action of base upon a phosphonium salt, which is then reacted with a suitable aldehyde to afford the desired alkene **113**, and a phosphine oxide by-product, the example shown below being triphenylphosphine oxide **(114)** (*Scheme 58*).



113 **114**

Scheme 58: The Wittig Reaction.

3.4.2: The Horner-Wittig Reaction.

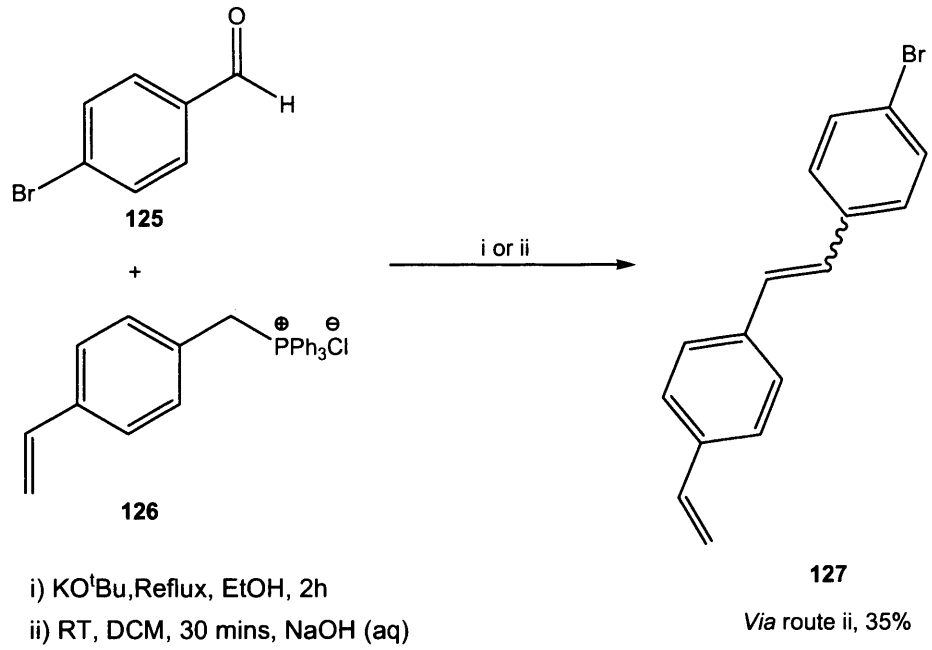
In 1958, Horner and co-workers were the first group to react phosphoryl-stabilised carbanions with aldehydes and ketones to produce olefins,[13] but the reaction did not gain significant popularity until 1961 with the publication of a paper by Wadsworth and Emmons.[14] Although the conventional Wittig reaction still finds many applications in modern synthesis,[15] this alternative known variously as the Horner-Emmons, Wadsworth-Emmons or Horner-Wittig reaction (herein referred to as the Horner-Wittig reaction) holds several advantages over the more traditional route. The Horner-Wittig reaction is very similar to the Wittig reaction, however the phosphorus-containing reagent employed is nearly always stabilised *via* an electron-donating moiety, although notable exceptions to this rule are known which will be discussed later in this section. Examples of commonly used phosphoryl-stabilised carbanions include phosphonate, phosphine oxide, phosphonamide and thiophosphonate species. The action of base upon these species generates highly reactive ylides, permitting their use even in transformations involving relatively unreactive carbonyl compounds.

From a practical standpoint, the most attractive feature of the Horner-Wittig reaction when compared to the Wittig reaction is the formation of water-soluble phosphorus-containing by-products. This facilitates work-up and purification of the desired alkenes without the need for complex column chromatography or crystallisation techniques such as are needed to remove phosphine oxides. These favourable features, combined with the considerable level of stereocontrol that is now possible using the Horner-Wittig reaction, make the use this versatile method of synthesis extremely widespread. Recent examples of its application include natural product synthesis such as that of the polyketide herboxidiene by Banwell *et al.*;[16] assorted functional group transformations including homologation of ketones to carboxylic acids,[17] and the synthesis of methyl esters from alkyl iodides;[18] and the preparation of allyl phosphine oxides, common intermediates in the synthesis of polyenes.[19]

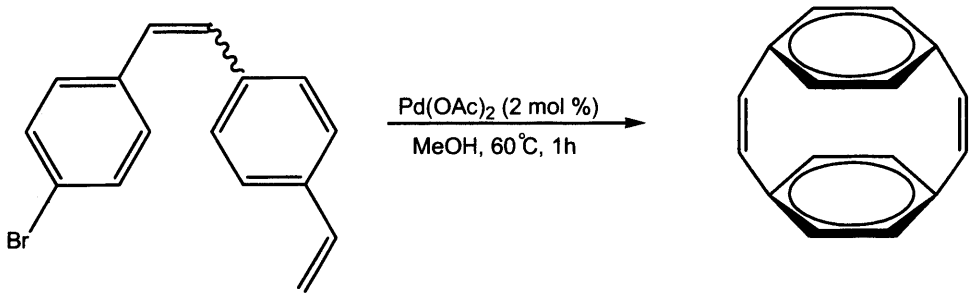
3.4.1: Preparation of Stilbenes *via* the Wittig Reaction.

Synthesis of stilbene **127** was attempted using two differing sets of reaction conditions for the Wittig reaction, as shown in *Scheme 59.* The premise behind the preparation of **127** was to use it as a model to test the viability of *para*-cyclophene synthesis using a Heck-type ring-closure such as that shown in *Scheme 60.* The unsubstituted form was favoured at this stage mainly due to the commercial availability of 4-bromo benzaldehyde **125,** and 4-

vinyl benzyl chloride, from which phosphonium salt **126** could be easily synthesised in good yield (74%) by stirring with triphenylphosphine in refluxing dichloromethane. Derivative **77** has previously been reported by Detert and Sugiono using a two-fold Heck reaction between 1,4-dibromobenzene and ethylene under high pressure.[20] Due to the harsh reaction conditions necessary to prepare stilbene **127** according to the literature procedure, an alternative novel strategy was attempted here.



Scheme 59: Two routes towards stilbene synthesis *via* Wittig reaction.



Scheme 60: Proposed *para*-cyclophene synthesis *via* Heck reaction.

Synthesis of **127** *via* a Wittig reaction (*Scheme 59*) was originally attempted using potassium *t*-butoxide as base to generate the ylide from phosphonium salt **126** in ethanol at reflux (Route i, *Scheme 59*). Monitoring the course of the reaction by ^{31}P NMR spectroscopy indicated, through the presence of a singlet at δ+ 31 ppm (C_6D_6 external lock), that triphenylphosphine oxide had been formed, suggesting the formation of the desired Wittig product had indeed occurred, although the ^{31}P spectrum was reasonably

complex. Upon evaporation of the solvent from the reaction mixture a brown oil was obtained, which proved to be extremely impure by both ^{31}P and ^{1}H NMR spectroscopy. Rather than attempting purification of this complex mixture, an alternative method was sought which was hoped would yield the desired stilbene more cleanly.

The phase-transfer method detailed above in *Scheme 59* (route ii) has been previously reported in the literature, for example a similar method using aqueous sodium hydroxide and chloroform was employed by Gilheaney and coworkers to prepare a family of *ortho*-halo-substituted stilbenes,[21] and was easily adapted to suit the synthesis of stilbene **127.** This type of reaction methodology proceeds well due to the phosphonium salt reagent itself acting as a phase-transfer catalyst. Using a reaction time of 30 minutes followed by a straightforward aqueous/organic work up, a white solid was isolated; this was shown by ^{1}H and ^{31}P NMR spectroscopy to be a mixture of the desired stilbene product **127** and triphenylphosphine oxide. Simple washing of this mixture with hexane was insufficient to remove the triphenylphosphine oxide leaving the purified product. Purification was eventually achieved *via* column chromatography using neat diethyl ether as eluent on silica gel, with triphenylphosphine oxide eluting first having an R_F value of 0.21, and the stilbene product eluting in 35% yield, with an R_F value of 0.86.

3.4.1.1: Structure and Characterisation of 4-Vinyl Triphenylphosphonium Chloride 126.

Precursor phosphonium salt **126** has been previously prepared, using a similar method to that employed in work for this thesis, in a study by Bazan and coworkers in 1998, where it was synthesised as a precursor to *trans*-4,4'-*tert*-butylvinylstilbene. The ^{1}H NMR spectroscopic data obtained for this compound during work for this thesis correlates well with that obtained by Bazan *et al.* [22] On acquisition and analysis of the previously unreported ^{13}C $\{^{1}H\}$ NMR spectroscopic data of **126**, long range P-C coupling could be readily observed, almost all the signals appearing as doublets rather than the expected singlets. This phenomenon is very rare in saturated systems, but can occasionally be detected in π-conjugated systems such as naphthalene derivatives (For example, see *Figure 46*).[23] A summary of the observed P-C couplings is presented below in *Figure 47.*

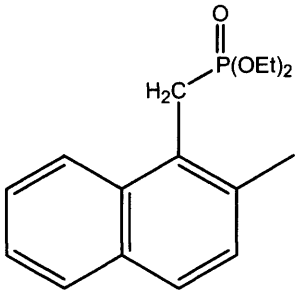
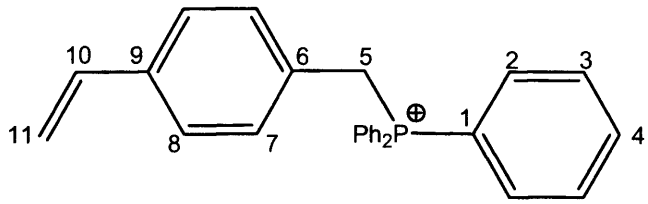


Figure 46: Naphthalene derivative prepared by Verkade *et al.* which exhibits long range phosphorus-carbon couplings.



Assignment	δ (ppm)	$^{x}J_{P-C}$ (Hz)	x
C1	117.8	85.6	1
C2	130.1	12.4	2
C3	134.3	9.6	3
C4	131.7	5.9	4
C5	30.4	46.2	1
C6	126.7	8.8	2
C7	126.4	2.9	3
C8	134.9	2.9	4
C9	137.4	4.4	5
C10	135.9	2.9	6
C11	114.7	0	-

Figure 47: Carbon-phosphorus coupling constants observed for phosphonium salt **126** (100 MHz, $CDCl_3$).

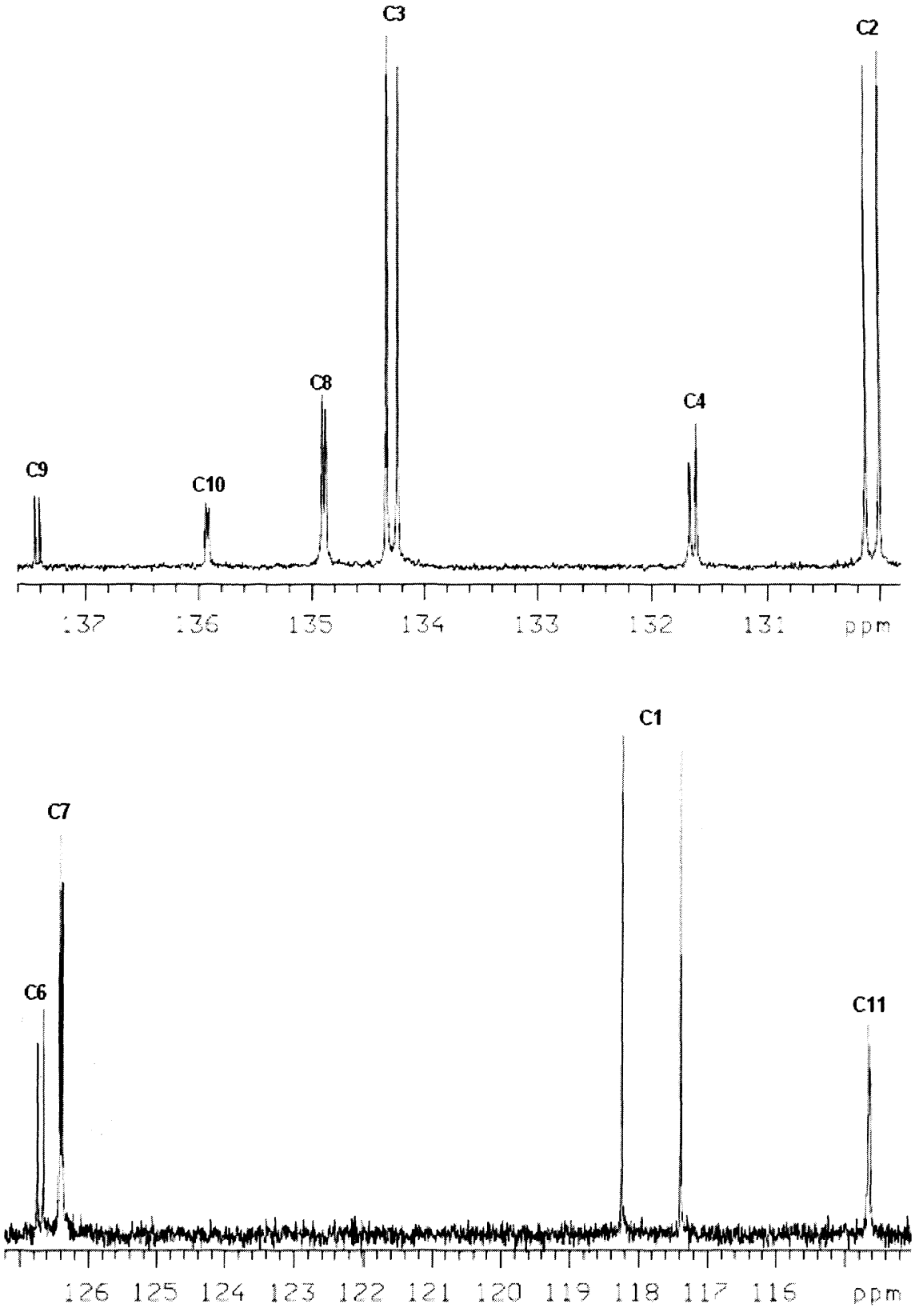
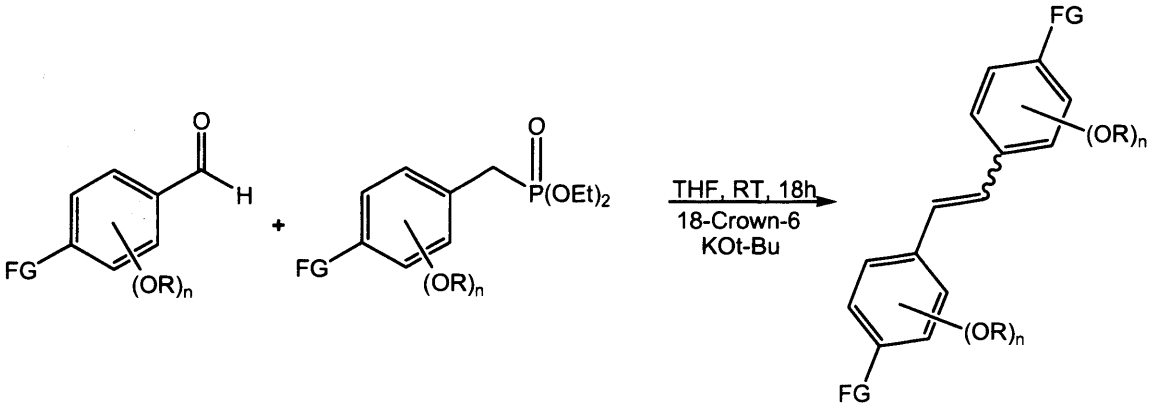


Figure 48: Expansions of the ^{13}C NMR spectrum (100.6 MHz, $CDCl_3$) of phosphonium salt **126**, showing P-C couplings.

As can be seen from the spectroscopic data presented in *Figure 47*, the coupling constants tend to decrease with increasing distance from phosphorus, as expected, until finally for C11 (which is seven bonds away from the phosphorus centre), the value for J_{P-C} is too small to be reliably calculated. Expansions of the ^{13}C NMR spectrum from 114 to 138 ppm are shown in *Figure 48;* these illustrate all the peaks tabulated above apart from that for carbon 5, which appears at 30.4 ppm as would be predicted for a methylene carbon. The values of the phosphorus-carbon coupling constants observed for phosphonium salt **126** compare reasonably favourably with literature values. For example the conjugated naphthalene derivative prepared by Verkade and coworkers shown in *Figure 46* exhibits $^4J_{P-C}$ coupling constants of between 2 and 5 Hz, similar to the $^4J_{P-C}$ values of between 2 and 6 Hz observed for **126**.[24] As would be expected, the ^1H NMR spectrum of **126** also appears to exhibit long range couplings, although quantification of these was unfortunately inconclusive as the spectrum is not first order and modelling of the spin system has not been undertaken.

3.4.2: Stilbene Synthesis *via* the Horner-Wittig Reaction.

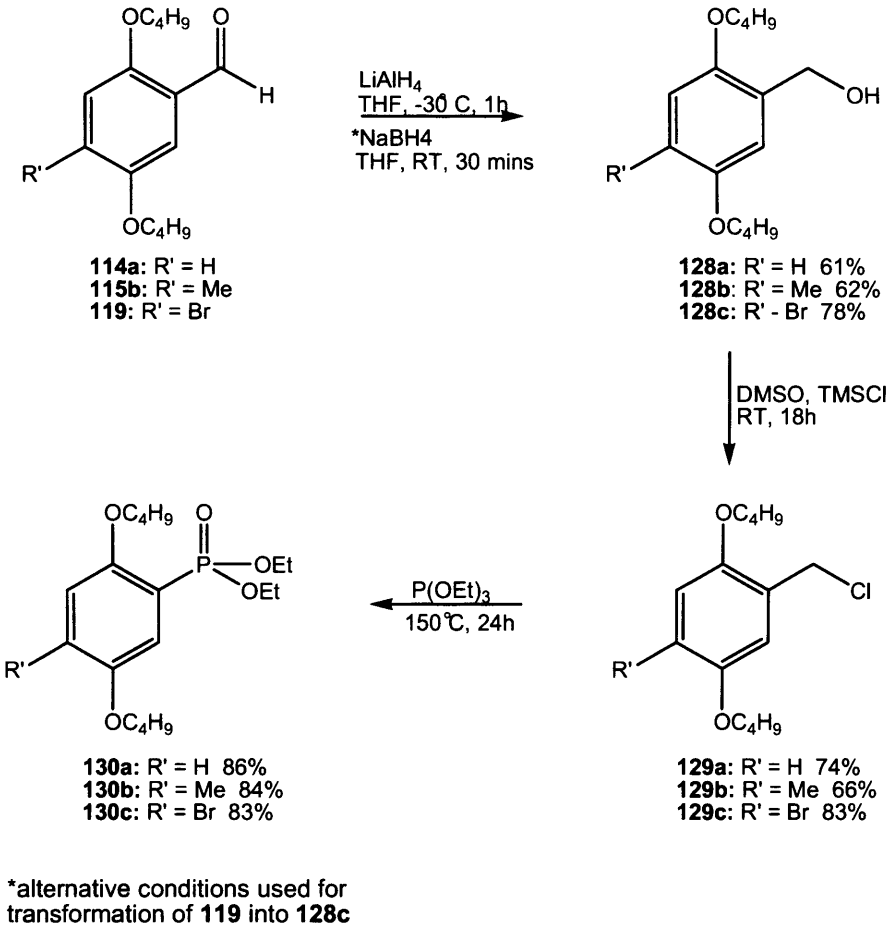
In order to avoid the lengthy purification encountered using the traditional Wittig reaction due to the necessity to remove triphenylphosphine oxide, it was perhaps the obvious step to move from the Wittig reaction towards the Horner-Wittig reaction, which creates water-soluble by-products that can be easily washed from the desired product at the end of the reaction. The reaction conditions employed are shown below in *Scheme 61.*



Scheme 61: Reagents and conditions for a generalised stilbene synthesis *via* Horner-Wittig reaction.

3.4.2.1: Preparation of Phosphonate Esters as Precursors to Stilbenes *via* the Horner-Wittig Reaction.

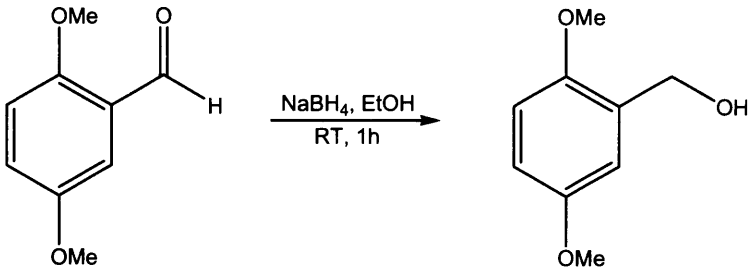
In order to prepare the desired stilbenes **131** using this methodology, it was first necessary to synthesise the phosphonate esters **130** from their corresponding starting aldehydes, using the method shown in *Scheme 62.*



Scheme 62: Preparation of 2,5-dibutoxybenzylphosphonic acid diethyl esters **130a-c.**

A test reaction carried out using methyl 2,5-dibutoxybenzaldehyde **115b** showed that sodium borohydride appeared not to be a strong enough reducing agent to prepare the desired benzyl alcohols **128a** and **b**, as ^{1}H NMR analysis of the crude product isolated after aqueous work-up showed that a significant quantity of the starting aldehyde **115b** (approximately 35%) had been recovered unchanged. Literature precedent[25] indicates that this low reactivity of alkoxy aldehydes towards reducing agents is not the norm, for example, Hartzfeld and Rose were able to prepare 2,5-dimethoxy benzyl alcohol (**133**) from 2,5-dimethoxybenzaldehyde (**132**) in good yield using sodium borohydride in 95% ethanol (*Scheme 63*).[26] However, for the purposes of this research a stronger reducing agent

was required, and upon changing from sodium borohydride to lithium aluminium hydride, the 2,5-dibutyloxy benzyl alcohols **128a** and **b** could be isolated cleanly after work-up in up to 78% yield. Conversely, for reduction of 4-bromo-2,5-dibutyloxybenzaldehyde **119** lithium aluminium hydride proved too harsh a reagent, destroying the aldehyde and returning only the parent 1,4-dibutyloxybenzene **112a** after work-up. Thus, sodium borohydride was employed for this reduction, furnishing the desired 4-bromo 2,5-dibutyloxy benzyl alcohol **128c** in 78 % yield. A comparison of the ^{1}H NMR chemical shift values for benzyl alcohols **128** show that these are in reasonable agreement with literature values. To illustrate, Hartzfeld and Rose quote a value of 2.61 ppm for the hydroxyl proton of 2,5-dimethoxybenzaldehyde,[27] while the chemical shifts of the same proton in benzyl alcohols **128a-c** are 2.39, 2.24 and 2.26 ppm respectively.

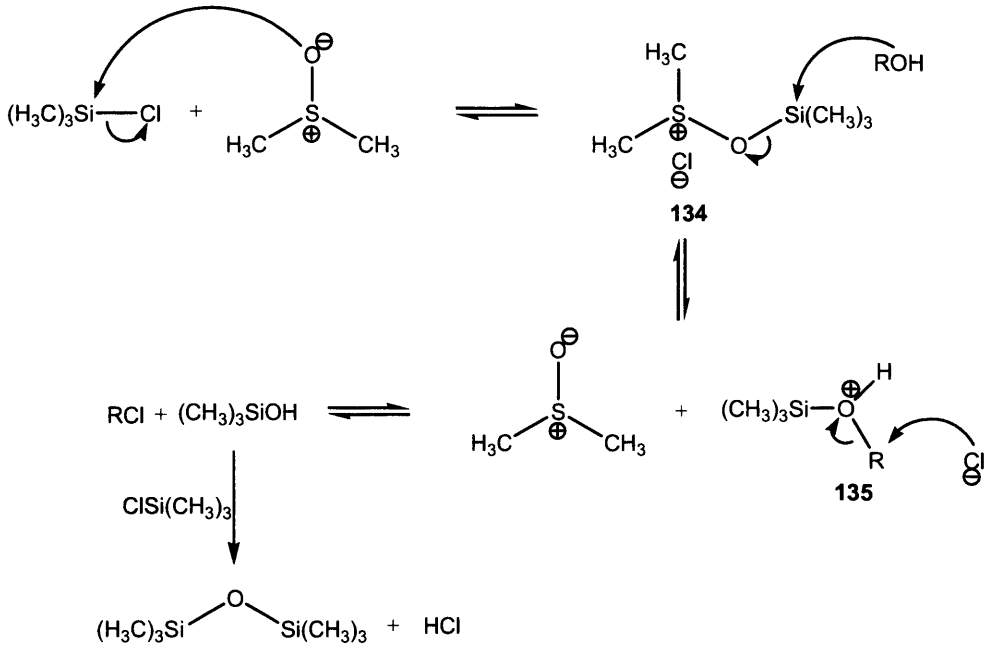


132 **133**

Scheme 63: Preparation of 2,5-dimethoxy benzyl alcohol using sodium borohydride, as demonstrated by Hartzfeld and Rose.[41]

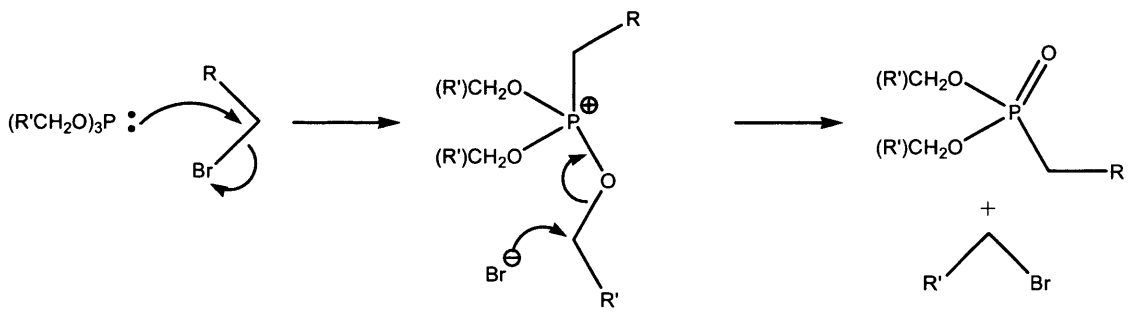
Transformation of compounds **128a-c** into the corresponding benzyl chlorides **129a-c** was firstly attempted using thionyl chloride,[27] but this approach was ineffective, with the reaction only achieving 50% conversion of **128a** into **129a** after an extended reaction time of 48 hours. This result is thought to be due to the reasonably low reactivity of the benzyl alcohol substrates used here. The reaction therefore required the use of a slightly complex method using trimethylsilyl chloride (TMSCl) and a catalytic amount of dimethyl sulfoxide (DMSO), following the method of Snyder.[28] This reaction is thought to proceed *via* the more reactive Si-O-S intermediate, generated through the reaction of DMSO with TMSCl as shown in the mechanism described in *Scheme 64*. This reactive cation **134** can then go on to combine with an alcohol to form a second reactive silicon intermediate **135**, and regenerate DMSO, which is hence a true catalyst in this reaction. Intermediate **135** is in turn attacked by chloride ion to form the desired benzyl chloride product, and

trimethylsilanol, which is itself attacked by a further molecule of TMSCl to form the stable hexamethyldisiloxane and HCl.



Scheme 64: Mechanism of chlorination of a substituted alcohol using TMSCl and DMSO.

With the necessary benzyl halides in hand, formation of the target phosphonate esters **130a-c** was subsequently achieved by use of the Michaelis-Arbusov reaction, involving heating the precursor benzyl chlorides **129a-c** with one molar equivalent of triethylphosphite for 48 hours at 150°C. This is a well-known conversion; with the preparation of many similar compounds to phosphonate esters **130** having been documented in the literature. For example, an analogous compound to **130b**, methyl-2,5-dioctyloxy phosphonic acid diethyl ester, has been prepared by Detert *et al.* as a precursor for the synthesis of alkoxy-substituted PPV oligomers *via* Horner-Witting coupling.[29] The mechanism of the Michaelis-Arbusov reaction is shown in *Scheme 65.*

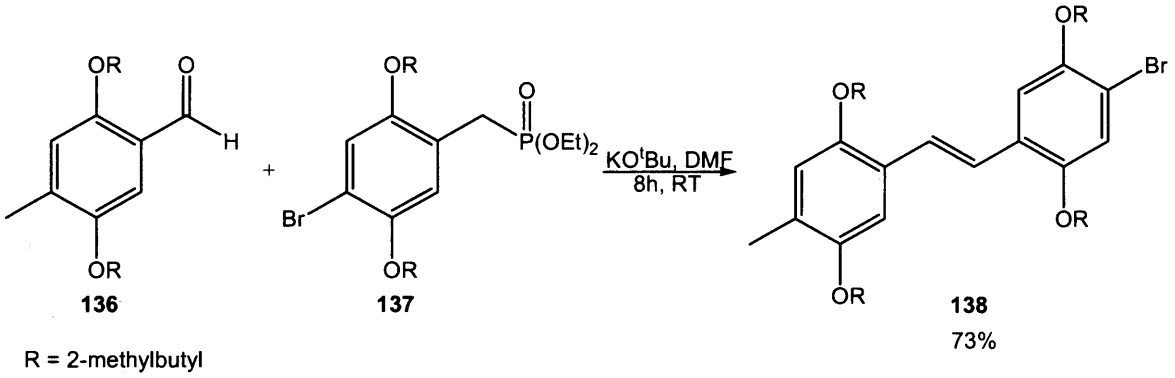


Scheme 65: Mechanism of the Michaelis-Arbusov reaction.

Despite the somewhat harsh conditions, which were necessary to overcome the unreactive nature of the benzyl chlorides **129**, the desired phosphonate esters **130** were successfully prepared in reasonable yields (over 60%). Vacuum distillation, using a Kügelrohr apparatus, was required to sufficiently purify the phosphonate esters prior to use in the next reaction step, something that mainly removed unreacted triethylphosphite. Examination of the ^{13}C NMR spectra of phosphonate esters **130** shows that, similarly to phosphonium salt **126** discussed earlier in this chapter, these compounds also exhibit long-range P-C couplings due to the conjugated nature of the system.

3.4.2.2: Preparation of Dialkoxy-Substituted Stilbenes *via* the Horner-Wittig Reaction.

With the necessary phosphonate esters having been successfully prepared and purified, it was then possible to carry out the Horner-Wittig reaction itself in order to synthesise the desired alkoxy-substituted stilbenes. This is a commonly employed method for the preparation of such stilbenes, with recent examples being found in the work of Janssen and coworkers,[30] and Detert *et al.*[44] The method of Janssen is illustrated below in *Scheme 66*, where a very similar stilbene to 4,4'-dibromo-2,5,2',5'-tetrabutyloxy-*trans*-stilbene **131c** is prepared from the corresponding aldehyde and phosphonate ester.

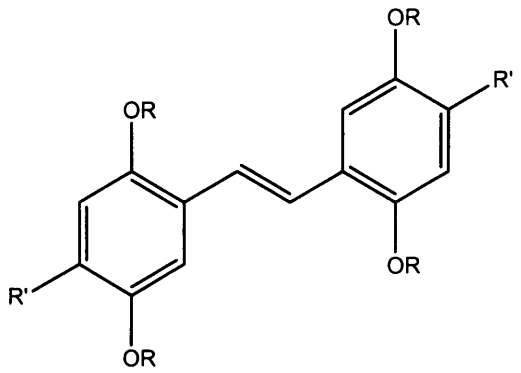


Scheme 66: Preparation of 4-bromo-4'-methyl-2,5,2',5'-tetra(2-methylbutoxy)-*trans*-stilbene, as described by Janssen and coworkers.[45]

Preparation of stilbenes **81** was a reasonably straightforward undertaking, involving mixing of the phosphonate ester and corresponding aldehyde in dry THF under an inert atmosphere, then addition of potassium *t*-butoxide. Approximately 10 mol % 18-crown-6 was added to the reaction mixture at this stage, to act as a phase transfer catalyst to aid dissolution of the base and hence generation of the reactive ylide. This is in contrast to the

preparation of 4-vinyl-4'-bromostilbene *via* the Wittig reaction discussed previously in this chapter (*Section 3.4.1.1*), where the precursor phosphonium salt **126** itself acted as a phase-transfer catalyst to enable the reaction to occur successfully.

Stirring at room temperature was sufficient to bring about reaction and, after quenching with water, the crude products could be simply extracted from the solution with diethyl ether, in relatively low yields (~40%). Following removal of the solvent, the crude solids could be recrystallised from hot methanol to yield the stilbenes **131** (*Figure 49*) as yellow needle-like crystals, no crystals suitable for X-ray diffraction studies could be obtained. As with the stilbenes **122** prepared *via* the McMurry coupling (see *Section 3.2.1*), stilbenes **131** are symmetrical, hence their geometry cannot easily be elucidated by proton NMR. The geometry of the stilbenes could not therefore be unequivocally determined, although they are most likely to adopt a *trans* configuration on steric grounds.



$R = C_4H_9$

131a: R' = H 33%
131b: R' = Me 25%
131c: R' = Br 22%

Figure 49: Stilbenes synthesised *via* the Horner-Wittig reaction.

3.5: Conclusions.

This chapter has described the preparation of functionalised stilbenes *via* the McMurry, Wittig, and Horner-Wittig reactions. ^{13}C and ^{1}H NMR spectroscopy, and X-Ray crystallographic studies, have shown that the stilbenes prepared adopt a *trans* configuration about the central C=C bond, and are largely planar in the solid state.

Through the routes described here, it has been shown possible to prepare a range of stilbenes bearing either two or four alkoxy substituents. The additional functionality introduced at the *para* position to the stilbene C=C bond will, after further transformations, provide a route into ring-closing strategies to form [2.2] *para*-cyclophenes.

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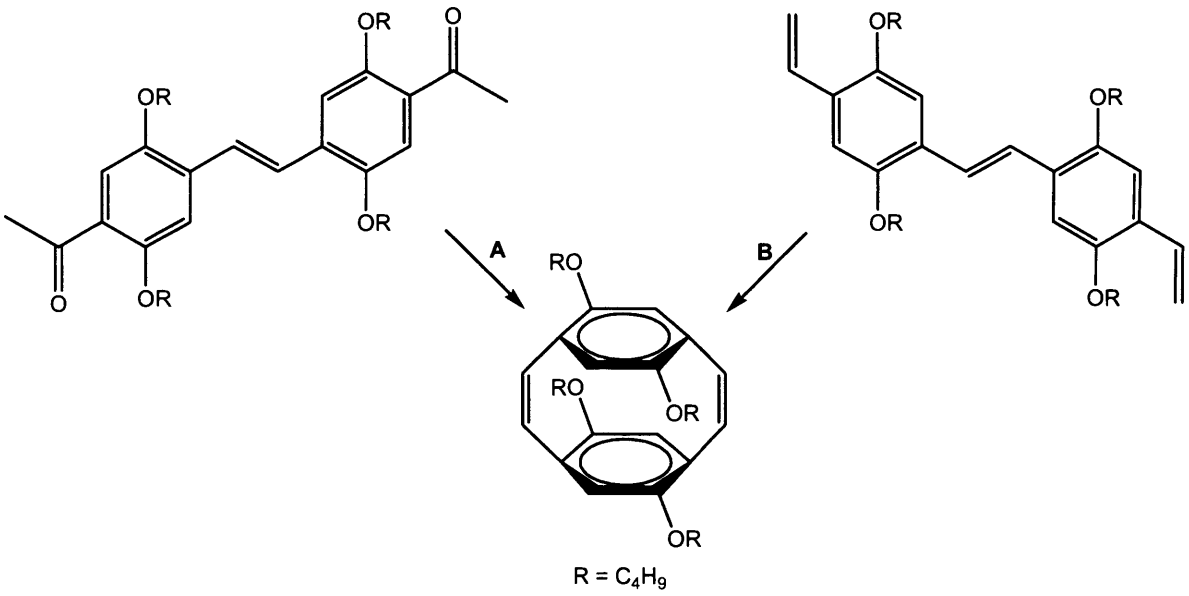
CHAPTER FOUR

Further Studies on Alkoxy-Substituted Stilbenes: Towards [2.2] *para*-Cyclophenes and [2.2] *para*-Cyclophane-1-enes

4.1: Introduction.

In order for the stilbenes **131** discussed in *Chapter Three* to act as effective precursors to the target [2.2] *para*-cyclophenes it was necessary to introduce further functionalisation at the aromatic rings, in order to be able to subsequently achieve the desired ring-closing reactions (see *Scheme 67*). Two methods for this were proposed. Firstly, formylation of either **131a** or **131b** in order to generate a compound suitable for ring-closing using the McMurry coupling (Route **A**, *Scheme 67*) is proposed. Secondly, the use of dibromo stilbene **131c** in a Stille coupling to yield a divinyl stilbene which could then be ring-closed *via* RCM (Route **B**, *Scheme 67*) was envisaged.

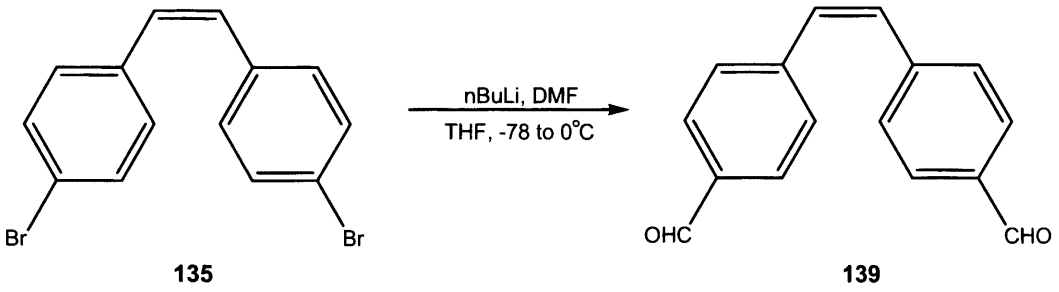


Scheme 67: Ring-closing to prepare [2.2]-*para*-cyclophene *via* route **A**-McMurry coupling, or route **B**-RCM.

4.2: Formylation of Alkoxy-Substituted Stilbenes.

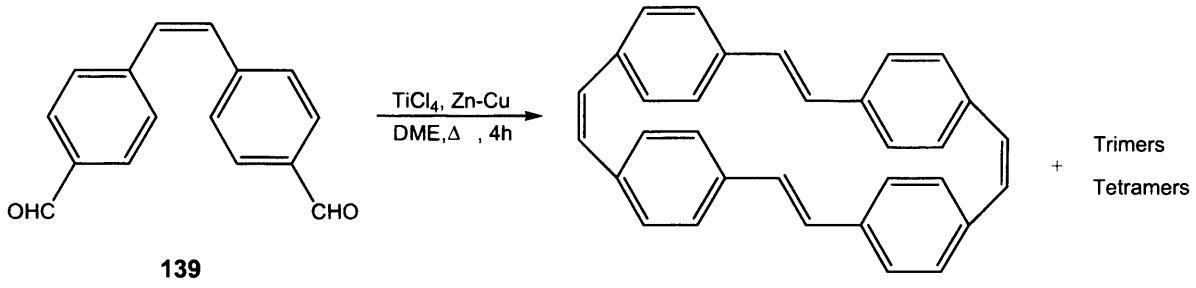
With a view to preparing the desired ring-closed [2.2] *para*-cyclophene *via* the McMurry coupling (strategy **A**, *Scheme 67),* it was necessary to synthesise substituted diformyl stilbene **134.** Synthesis of the unsubstituted form of this compound, 4,4'-formylstilbene **139**, has been reported by a number of groups;[1] for example *cis*-4,4'-formylstilbene has been prepared from *cis*-4,4'-dibromostilbene **83** by Bosanac and Willcox, according to the method shown below in *Scheme 68.*[2] The same reaction methodology has also been employed by Peris *et al.,* starting from *trans*-4,4'-dibromostilbene to yield the *trans* form of 4,4'-diformylstilbene.[3] Interestingly, unsubstituted 4,4'-diformylstilbene **139** has been employed as a precursor to macrocyclic cyclophenes. For example Oda and coworkers

used the McMurry reaction to couple **139**, yielding primarily (E,Z,E,Z)[2.4]-*para*-cyclophane (**140**) and a mixture of other macrocyclic cyclophenes (*Scheme 69*).[4]



135 **139**

Scheme 68: Preparation of unsubstituted *cis*-4,4'-diformyl stilbene.

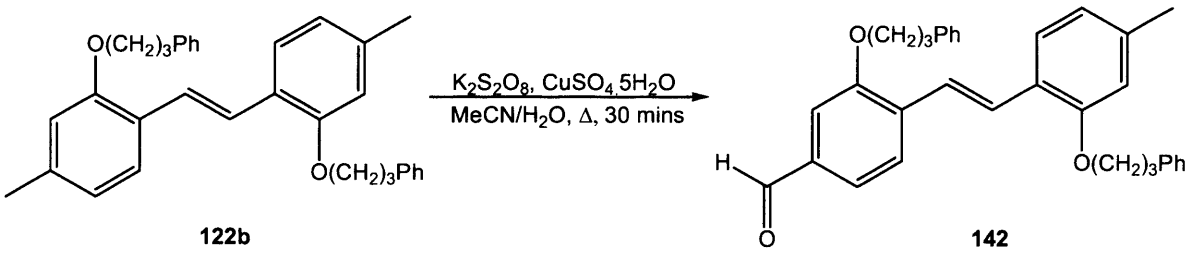


139 **140**

Scheme 69: Synthesis of macrocyclic *para*-cyclophanetetraenes *via* McMurry coupling of 4,4'-diformylstilbene **139.**[49]

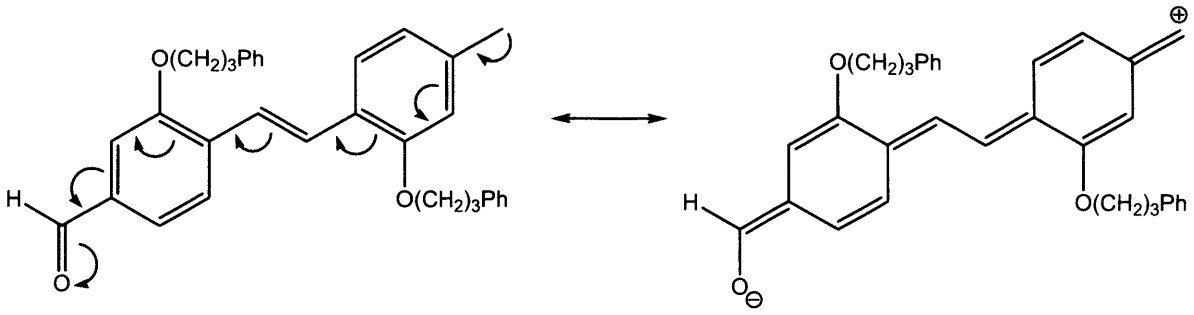
4.2.1: Attempted Formylation *via* Single-Electron Oxidation.

An attempt to prepare 4,4'-diformyl-2,2'-di(phenylpropoxy) stilbene **141** from **122b** using the single-electron oxidation method of Bhatt and Perumal previously described in *Chapter 2, Section 2.3* (*Scheme 70*)[5] was unsuccessful, this is thought to be due to the conjugated nature of the molecule causing deactivation of the remaining methyl group once one formyl moiety has been added (*Scheme 71*). ^{1}H NMR spectroscopic analysis of the crude product after work-up indicated that only the mono-derivatised product **142** had been formed. As there appears to be no straightforward method to bring about cyclisation of **142**, no further studies were undertaken using this reaction and crude **142** was not purified.



122b 142

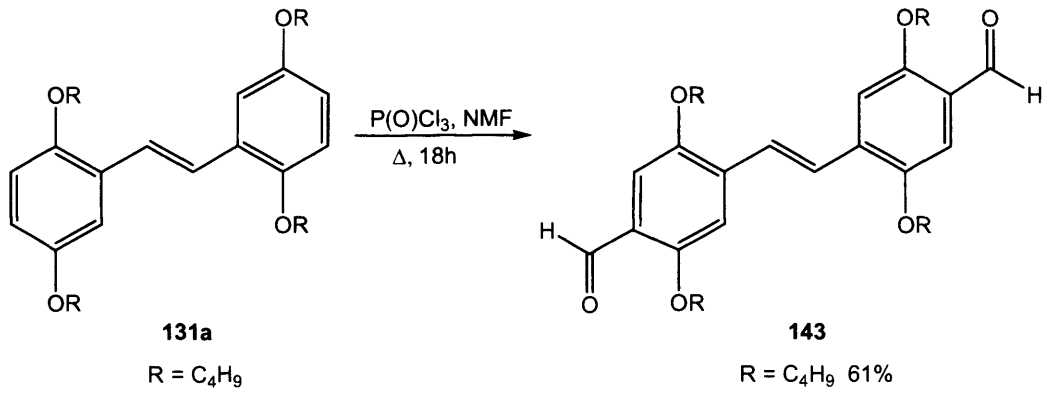
Scheme 70: Formylation using single-electron oxidation.



Scheme 71: Proposed deactivation pathway through stilbene conjugation.

4.2.2: Formylation *via* the Vilsmeier Reaction.

As diformylation of **122b** using the single-electron oxidation method was unsuccessful, attention was turned to the Vilsmeier formylation as a method of adding the desired aldehyde moieties to the stilbene backbone. Formylation of **131a** using the same Vilsmeier reaction conditions as were used to prepare alkoxy benzaldehydes **114** and **115** (see *Chapter 2, Section 2.3*) (*Scheme 72*) successfully introduced two formyl groups onto the stilbene framework, as was proven by ^{1}H NMR spectroscopy, mass spectrometry and elemental analysis. The ^{1}H NMR spectrum of 2,5,2',5'-tetrabutyloxy-4,4'-diformyl-*trans*-stilbene **(143)** is shown in *Figure 50* below; note the aldehyde signal integrates to two protons, illustrating that two formyl groups are indeed present, and that the two alkene protons give rise to a singlet, showing that the molecule is symmetrical. Unfortunately it was not possible to grow crystals of **143**, as recrystallisation from hot methanol yielded the product as a powder only; hence determination of the *cis-trans* geometry was not possible. From the ^{1}H NMR spectrum it is, however, evident that only one isomer of **143** is present, from consideration of previous results and due to the steric bulk of the compound, it can be postulated that the double bond adopts a *trans*-geometry.



Scheme 72: Formylation of stilbene **131a** *via* a Vilsmeier reaction.

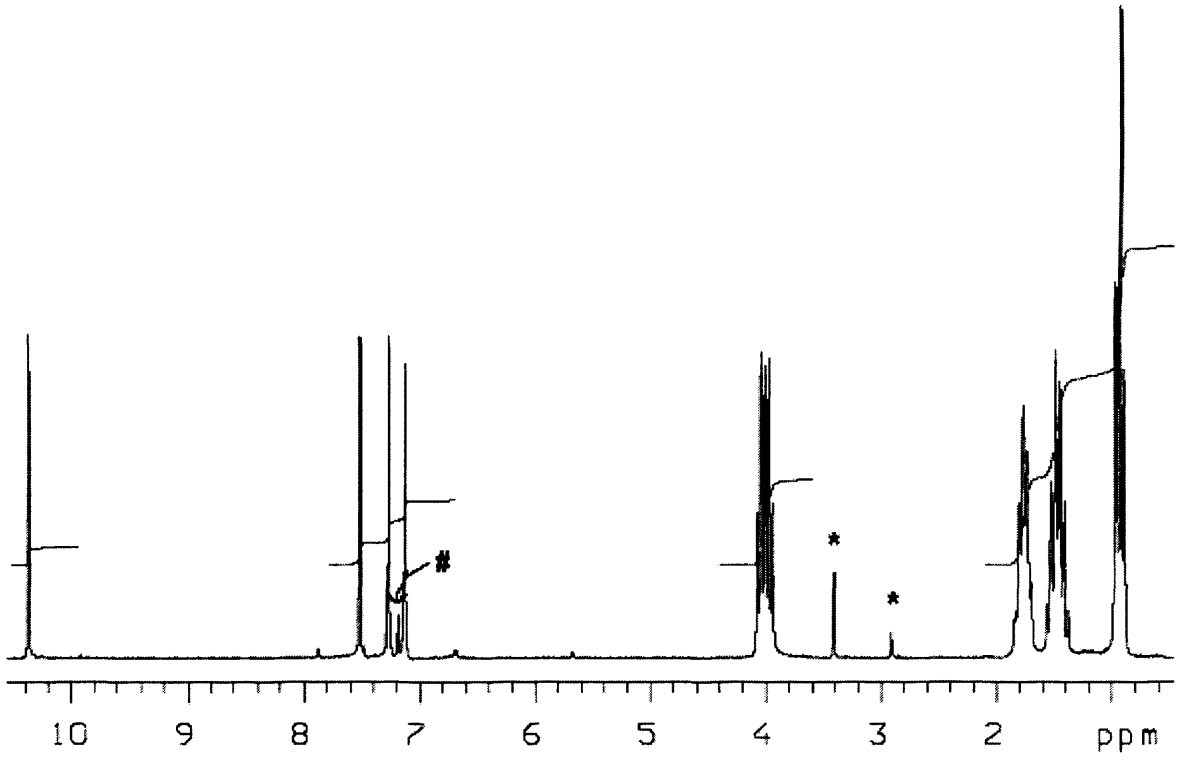
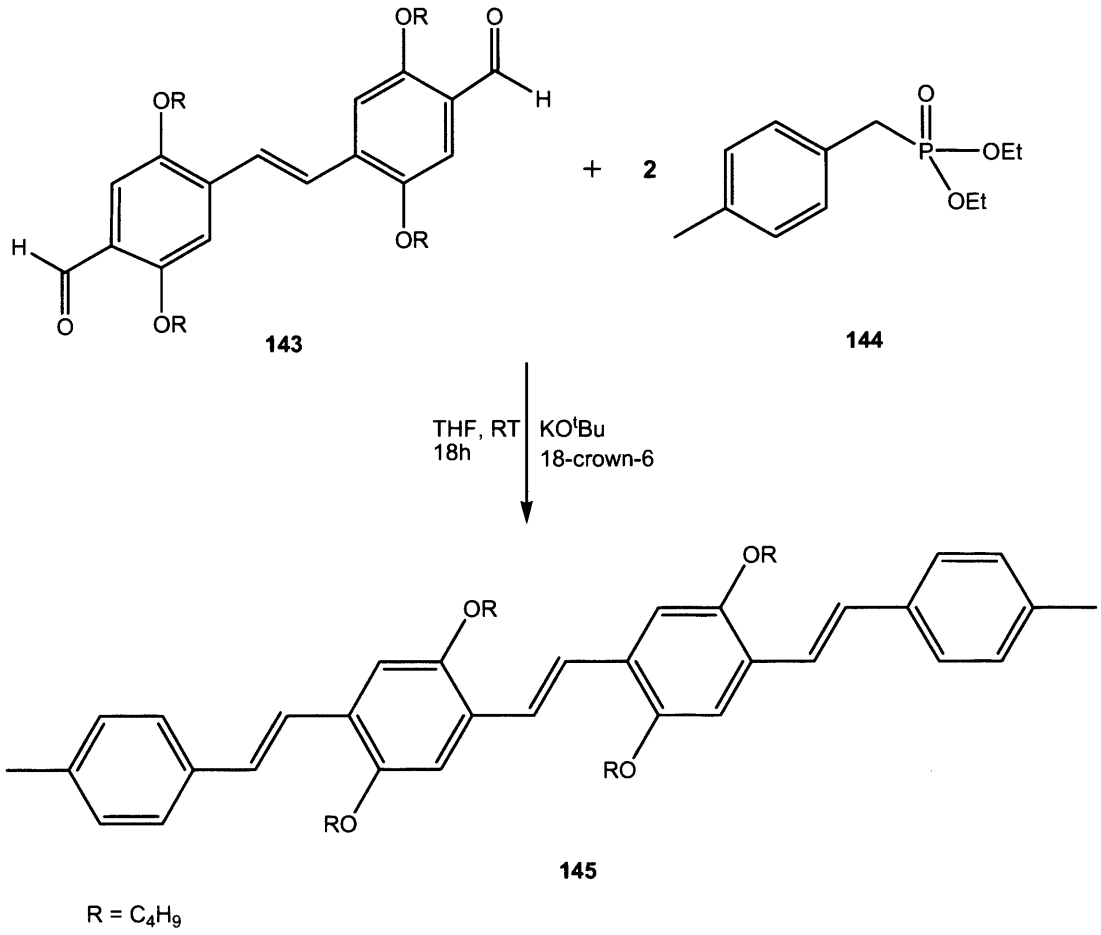


Figure 50: ^{1}H NMR (400 MHz, $CDCl_3$) of 2,5,2',5'-tetrabutyloxy-4,4'-diformyl-*trans*-stilbene **143,** where * indicates impurities, and # shows $CDCl_3$.

4.3: Preparation of Oligomeric PPV *via* Horner-Wittig Reaction.

In addition to being a suitable precursor to [2.2] *para*-cyclophenes, **143** can also be used as a synthetic intermediate for the preparation of oligomeric PPVs. As discussed in *Chapter 1*, these oligomers are considered highly valuable in the study of PPVs, the properties of a bulk PPV can often be inferred from data collected using these oligomeric forms, which allow for more straightforward characterisation and processing. Synthesis of PPV oligomer **145** was easily achieved *via* a Horner-Wittig reaction between **143** and two equivalents of 4-methyl phosphonic acid diethyl ester **144** as shown below in *Scheme 73.*



Scheme 73: Synthesis of PPV oligomer **145.**

4.3.1: Structure and Characterisation of PPV Oligomer 145.

Upon work-up and recrystallisation from hot methanol, the oligomer **145** was isolated as a yellow powder which fluoresced yellow/green in solution. The structure of **145** was confirmed by ^1H and ^{13}C NMR spectroscopy, the relevant spectra are shown below in *Figures 51* and *52*. A summary of the assignments for these spectra is shown in *Figure 53*; these were elucidated with the aid of COSY and HETCOR experiments.

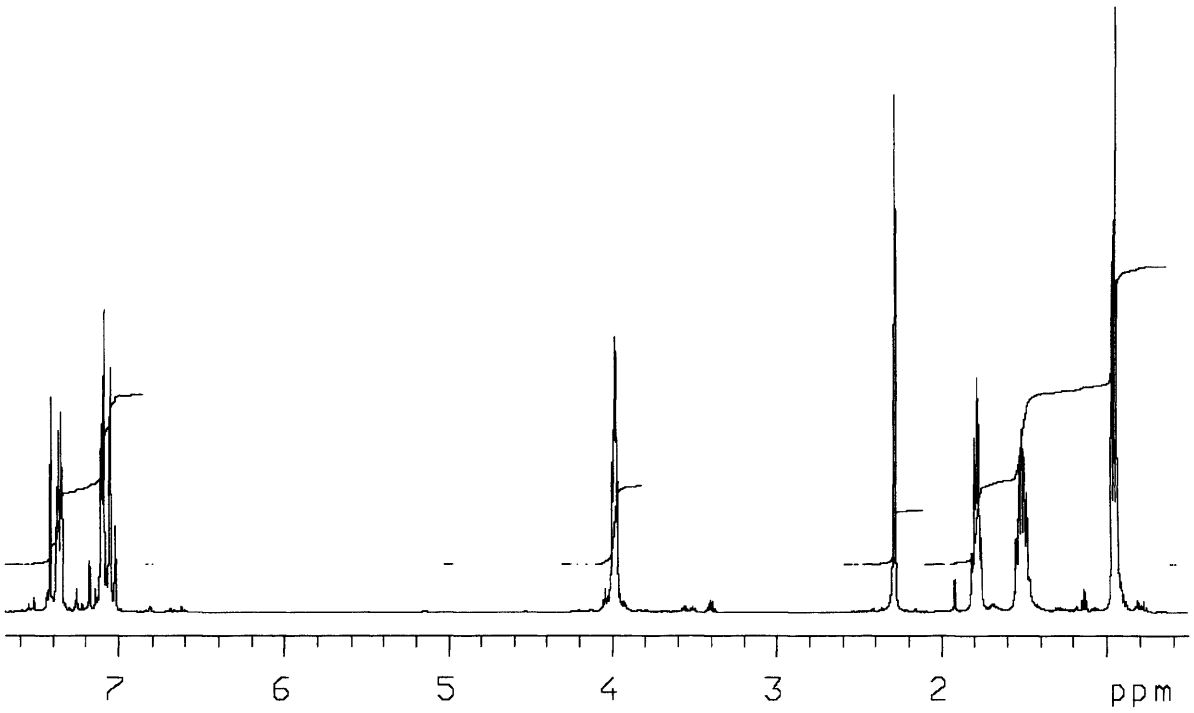


Figure 51: ^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **145,** showing integration.

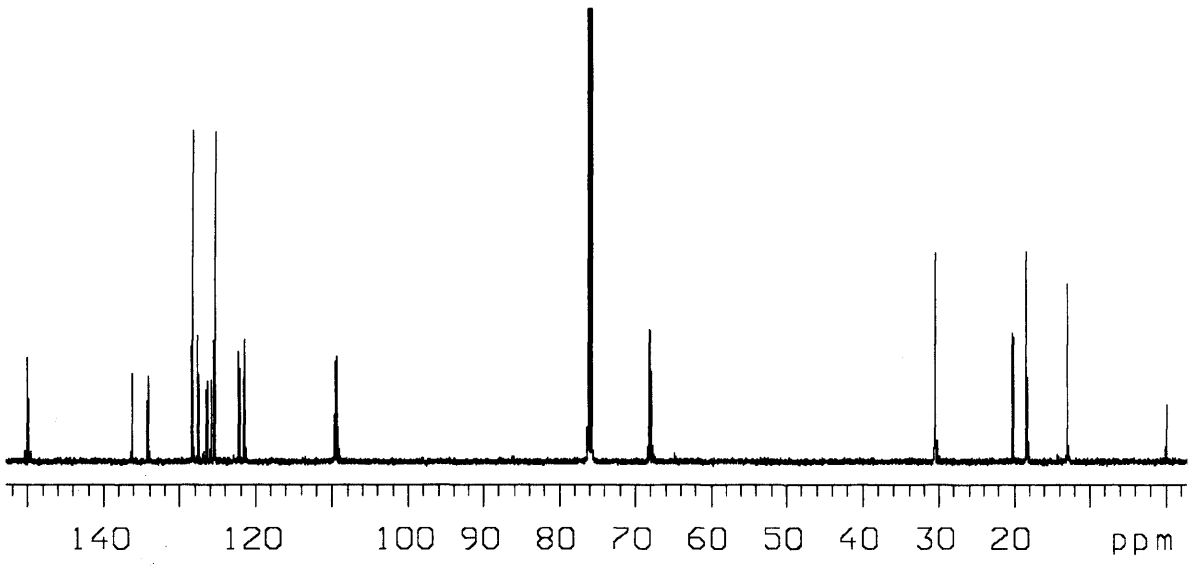
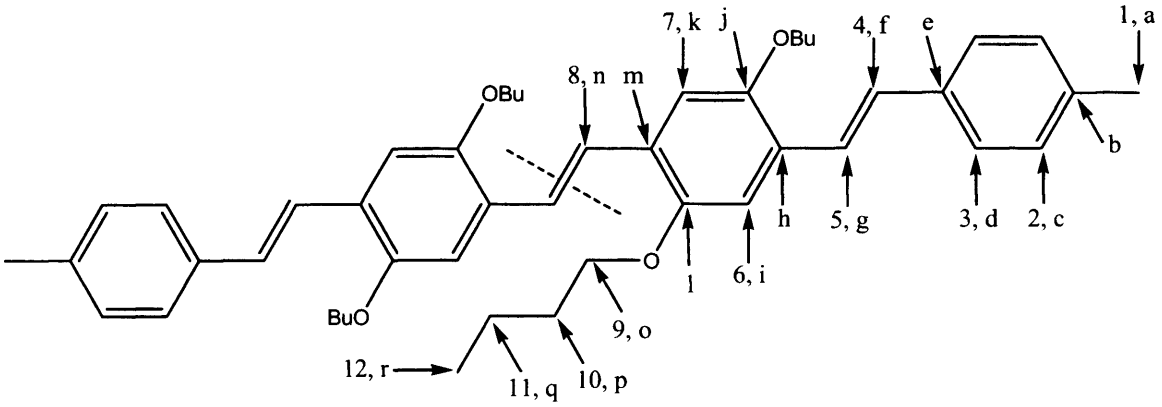


Figure 52: ^{13}C NMR spectrum (125 MHz, $CDCl_3$) of **145.**



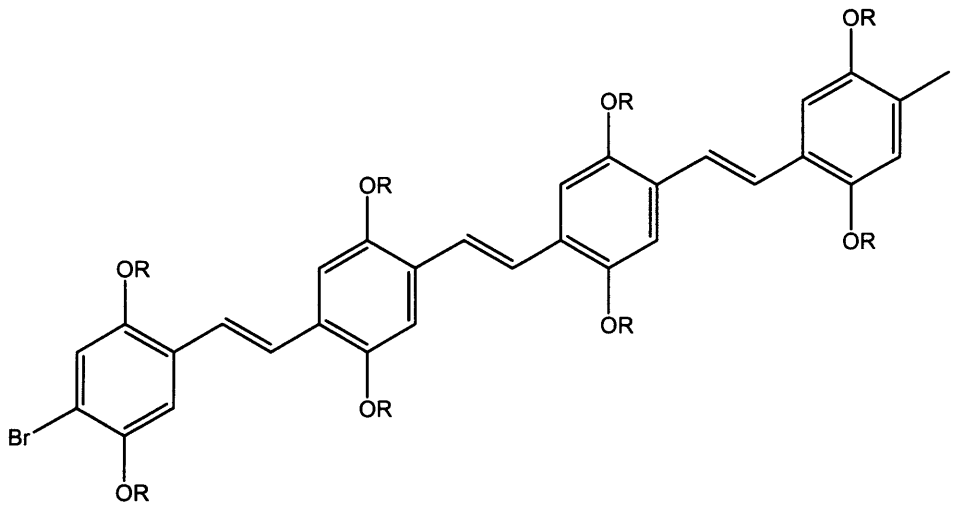
^{1}H NMR Assignment	δ (ppm)	^{13}C {^{1}H} NMR Assignment	δ (ppm)
1	2.30	a	16.3
-	-	b	136.2
2	7.43	c	121.6
3	7.46	d	125.4
-	-	e	134.3
4	7.20*	f	128.3
5	7.15*	g	127.6
-	-	h	125.9
6	7.14	i	109.7
-	-	j, l	150.1
7	7.18	k	109.5
-	-	m	126.5
8	7.50	n	122.2
9	4.08, 4.09§	o	68.3
10	1.88	p	30.6
11	1.60*	q	18.5
12	1.04	r	12.9

* Peaks overlapping.

§ Two overlapping triplets

Figure 53: Assignments for ^{1}H and ^{13}C{^{1}H} NMR spectra of **145** (^{1}H 400 MHz, $CDCl_3$, ^{13}C 125 MHz, $CDCl_3$).

The data presented in *Figure 53* compare favourably with examples of similar oligomers, although a comparison of the exact chemical shifts and coupling constants of specific protons with literature values is unfeasible, as full assignments are not generally reported. The chemical shifts of the vinylene protons of oligomer **145** (7.15 and 7.20 ppm) fall in the same region of the NMR spectrum as those in related oligomers, such as those for the vinylene protons of the oligomer **146** prepared by Janssen *et al.*[45] (*Figure 54*), which appear between 7.36-7.56 ppm. The slight shift to lower field of these protons when compared to those in oligomer **145** can be attributed to the greater number of electron-withdrawing alkoxy groups present in **146**. The longer-chain oligomers of Yu *et al.* discussed in *Chapter One, Section A3.2.2*, which only contain alkoxy substituents on alternating aromatic rings, exhibit chemical shifts of the vinylene protons in the range 7.14-7.32 ppm,[6] which is more similar to the values seen for oligomer **145**.



R = 2-methylbutoxy **146**

Figure 54: An example of the oligomeric PPV prepared by Janssen and coworkers.[45]

4.4: Photophysical Studies of Alkoxy-Substituted Stilbenes and PPV Oligomer 145.

The photophysical properties of PPV-type compounds such as stilbenoid precursors, oligomeric PPVs and also the polymers themselves are often evaluated using absorption and fluorescence spectroscopy, as these measurements can then be related to their electroluminescent properties. As all the stilbenes prepared during the course of this work were designed as precursors to light-emitting polymers, it was felt that further investigation of their photophysical properties was merited. Spectra were measured for four stilbenes and also PPV oligomer **145** (*Figures 56 and 57*). These compounds are shown in *Figure 55.*

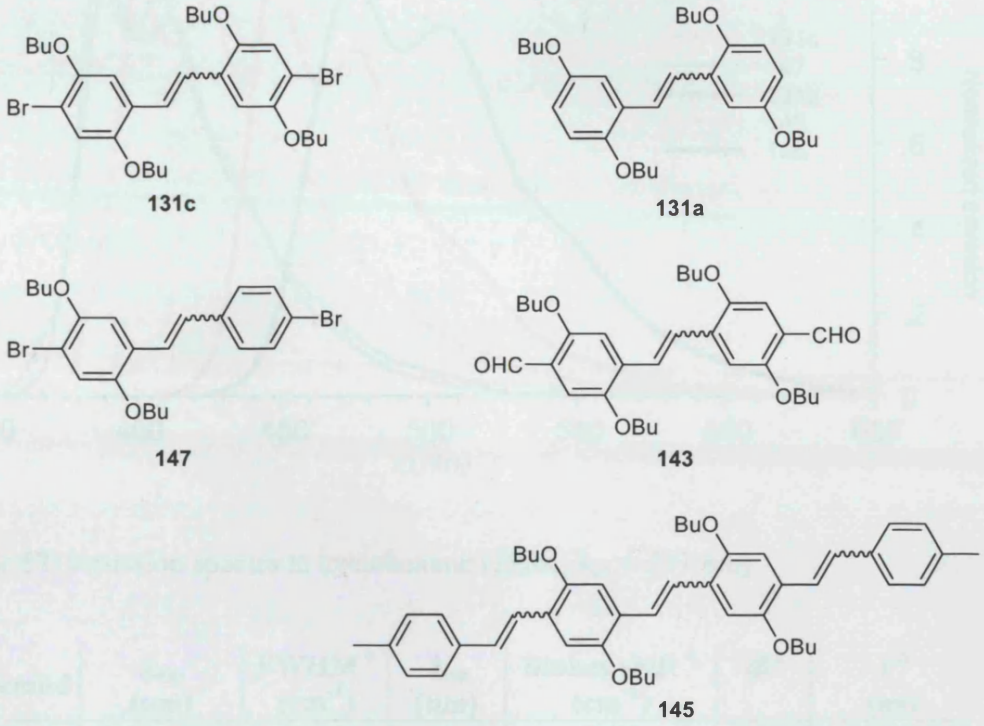


Figure 55: Compounds used in absorption and fluorescence studies.

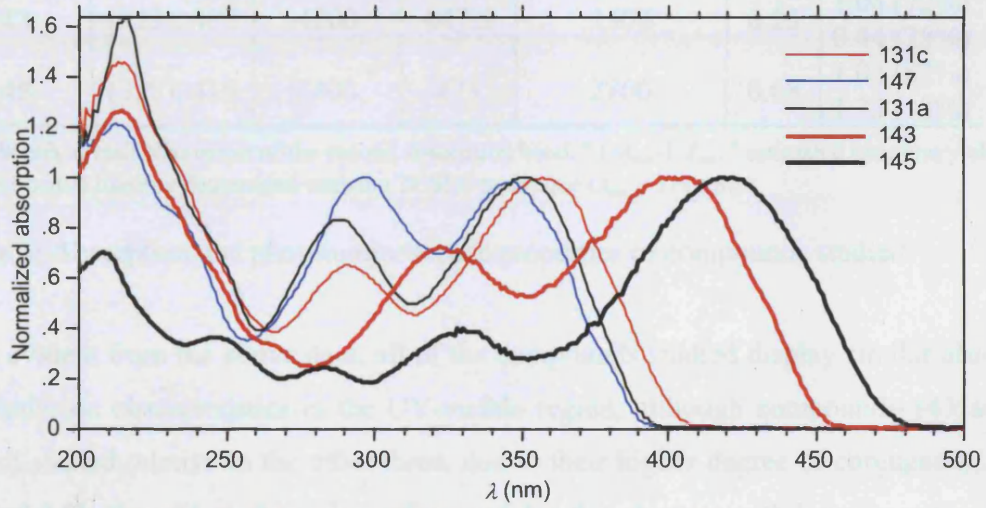


Figure 56: Absorption spectra in cyclohexane (298K).

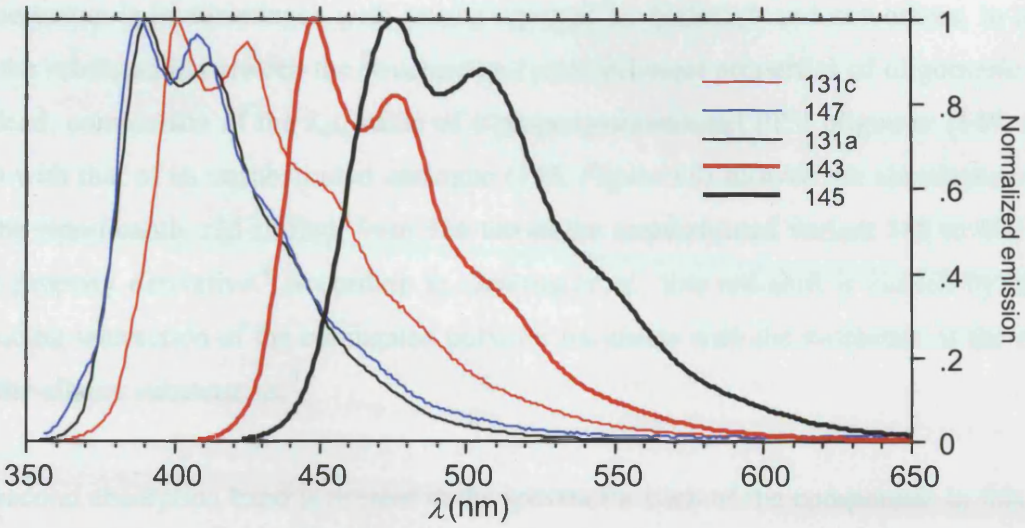


Figure 57: Emission spectra in cyclohexane (298K, λ_{ex} = 371 nm).

Compound	λ_{abs} (nm)	FWHM [a] (cm^{-1})	λ_{em} (nm)	Stokes shift [b] (cm^{-1})	Φ [c]	τ [d] (ns)
131c	(291), 357	5200	401	3100	0.06	0.18
147	296, (346)	≈ 5000	388	3100	0.025	0.12
131a	(288), 352	5100	391	2800	0.43	1.82
143	(323), 403	4200	447.5	2500	0.23	1.04 (72%) 0.44 (28%)
145	(328), 419	5400	475	2800	0.68	1.04 (82%) 1.73 (18%)

[a] Full Width at Half Maximum of the second absorption band. [b] $1/\lambda_{abs}$-$1/\lambda_{em}$. [c] estimated quantum yields.
[d] Experimental lifetime determined with the TCSPC technique (λ_{ex} = 371 nm).

Table 2: Absorption and photoluminescence properties of compounds studied.

As is evident from the above data, all of the compounds studied display similar absorption and emission characteristics in the UV-visible region, although compounds **143** and **145** are red-shifted relative to the other three, due to their higher degree of conjugation. In the case of **143**, the red shift is also influenced by the electron-withdrawing nature of the aldehyde substituents. Closer examination of the spectra for compounds **131c** and **131a** shows that the absorption and emission of **131a** is also slightly red-shifted compared to that of **131c.** This demonstrates that the addition of electron-withdrawing bromine atoms to the parent stilbene also causes a red shift in the absorption and emission. Studying the absorption spectra, the broad, structureless bands observed between 325 and 400 nm are believed to be due to a π-π* transition localised to the olefinic C=C bond,[7] similar to those observed for *trans* stilbene (*Figure 58*), however this band has been significantly red-shifted due to the pendant alkoxy groups present on the compounds studied. This

observation is in accordance with results reported by Stalmach and coworkers, in a study of the relationship between the structure and photophysical properties of oligomeric PPVs. Indeed, comparison of the λ_{abs} value of a propoxy-substituted PPV oligomer (**149**, *Figure 60*) with that of its unsubstituted analogue (**148**, *Figure 60*) showed the absorbance of **148** to be significantly red-shifted, from 356 nm in the unsubstituted variant **148** to 402 nm in the propoxy derivative.[8] According to Oelkrug *et al.*, this red-shift is caused by an anti-bonding interaction of the conjugated polymer backbone with the π-orbitals of the oxygen in the alkoxy substituents.[9]

A second absorption band is present in the spectra for each of the compounds in this study, which is not observed in the absorption spectra of unsubstituted stilbenoid compounds and PPV oligomers. This band has a value of λ_{abs} of between 288 and 328 nm, and is attributed to perturbation of the HOMO and LUMO by the alkoxy substituents.[41]

Examination of the emission spectra (*Figure 57*) reveals that all the compounds exhibit similar fluorescence profiles, but due to their extended conjugation pathways, compounds **143** and **145** are significantly red-shifted. A comparison of the emission spectra of compounds the compounds studied for this thesis with those of Stalmach and coworkers shown in *Figure 60*[52] shows a reasonable correlation, although as would be expected due to their shorter conjugation path length, a lower value of λ_{em} is observed for the shorter stilbene compounds **131c, 147** and **131a** than for both the oligomers of Stalmach and compounds **143** and **145** studied, although the value is still higher than that of unsubstituted trans-stilbene (see *Figure 59*).

Kvaran *et al.* have reported, in a study of halo-substituted stilbenes *via* absorption spectroscopy, that compounds which are planar in solution give rise to absorption spectra showing vibrational structure, whereas those compounds that are non-planar in solution show only broad, structureless peaks.[7] Comparison of the absorption and emission spectra of the compounds studied reveals that, while the bands observed in the absorption spectra are all broad and structureless, some degree of vibrational structure can be seen in the emission spectra. This indicates that in the ground state, rotation about the phenyl-olefin single bond is rapid causing the absorption spectrum measured to be an average over all possible conformers. In the first excited state however, the lowest energy conformer is the planar structure, hence the majority of the sample rapidly planarises and thus emits from this low-energy, planar conformer.

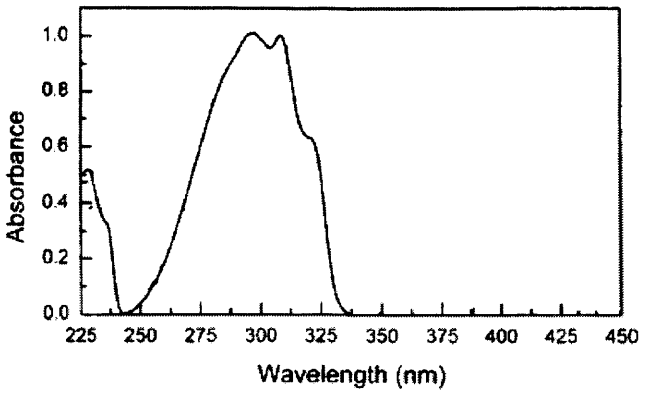


Figure 58: Absorbance spectrum of *trans*-stilbene in water/methanol (1:1).

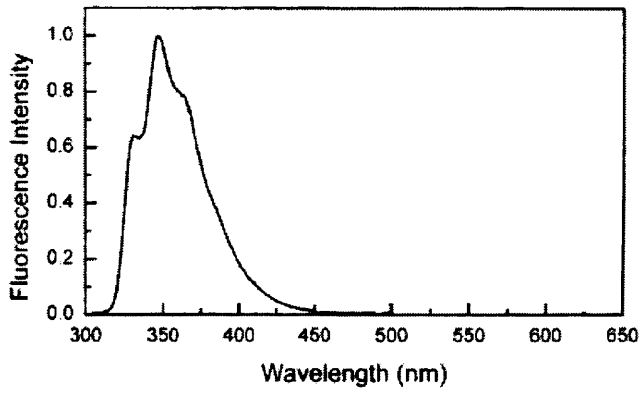


Figure 59: Emission spectrum of *trans*-stilbene in water/methanol (1:1).

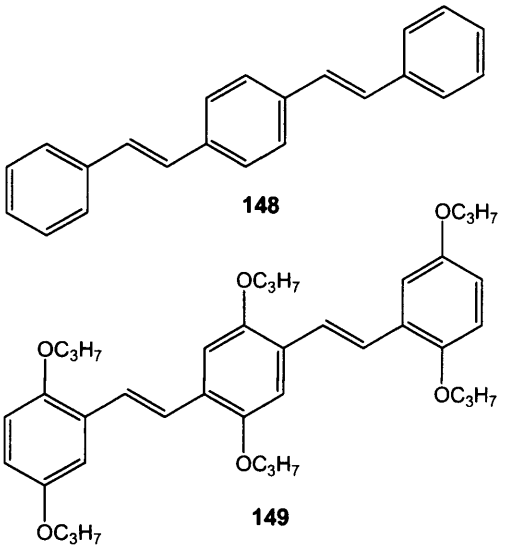


Figure 60: Unsubstituted and propoxy-functionalised PPV oligomers compared by Stalmach *et al.*[52] (absorption and emission measured in solution in $CHCl_3$).

Referring to *Table 2*, compounds **131c** and **147** have far lower quantum yields (0.06 and 0.025, respectively) than the other three compounds tested, although all five compounds have higher quantum yields than that of *trans*-stilbene. The low quantum yields observed

for **131c** and **147** can be attributed to the presence of the bromine atoms on the aromatic rings causing quenching of the fluorescence *via* spin-orbit coupling and intersystem crossing to the triplet state. These effects can be illustrated by use of *Equation 4,* and the simplified Jabłoński diagram shown below in *Figure 61*, where the value K_{nr}, the rate of nonradiative decay to S_0, is increased due to these quenching processes. The fluorescence lifetimes of the two compounds AHD1 and AHD2 are also significantly shorter than those observed for the non-brominated species tested, this can also be attributed to the quenching effect of the bromine.

$$\textbf{Quantum Yield } \Phi_F = k_F / K_F + K_{nr}$$

K_F = emissive rate of the fluorophore

K_{nr} = rate of nonradiative decay to S_0

Equation 4: Calculation of the Quantum Yield.

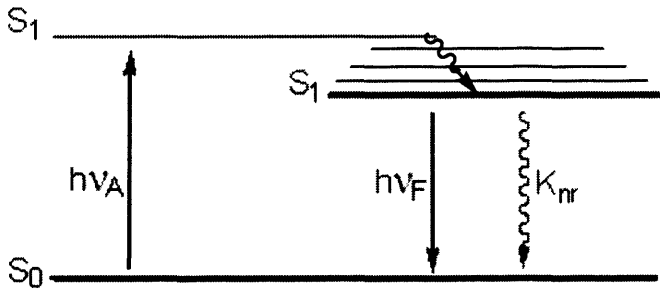


Figure 61: Simplified Jabłoński diagram illustrating fluorescence ($H\nu_F$) and nonradiative decay (K_{nr}) pathways.[10]

Also referring to *Table 2*, the lifetimes of the compounds studied reflect the same trends as their quantum yields, with **131c** and **147** having far shorter fluorescence lifetimes than the other three compounds studied, due to the quenching effects of the bromine substituents. Upon measurement of the fluorescence lifetimes of **143** and **145**, two separate values were obtained for each. In the case of **145**, these two values are very similar (1.04 ns for 82% of the sample, and 1.73 ns for the remaining 18%), suggesting that two isomers of the same compound are present in the sample. For the case of **143**, the two lifetime values measured are extremely different (1.04 ns for 72% of the sample, and 0.44 ns for the remaining

28%), something that indicates that the lower lifetime measurement is most probably due to an impurity in the sample.

4.5: The Reactivity of the Stilbene Double Bond.

Although the stilbenes (**131**) prepared were designed as precursors to [2.2] *para*-cyclophenes, their *trans* geometry posed an additional problem; the functional groups added to bring about the ring-closing in order to prepare the desired [2.2] *para*-cyclophenes are held at opposite ends of the stilbene framework, and hence have little opportunity to react intramolecularly. (*Figure 62*).

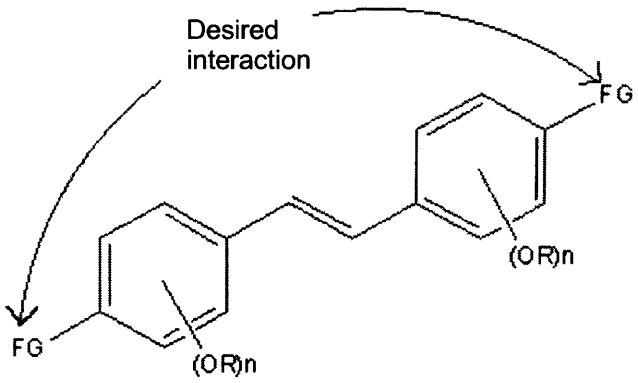


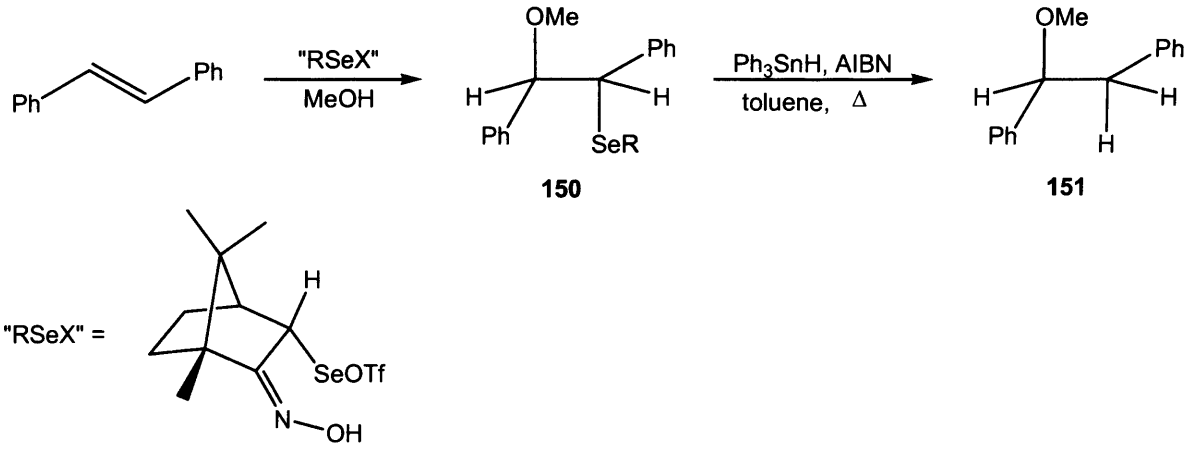
Figure 62: *trans*-Geometry of stilbenes prevents interaction of functional groups necessary to enable ring-closing.

It would be likely that if ring-closing were to be attempted on stilbenes **131**, polymerisation or oligomerisation would be most likely to occur. This would, of course, lead to PPV in itself, but not in the controlled manner possible through the ROMP of [2.2] *para*-cyclophene monomers. Referring back to *Chapter 1, Section D*, it will be recalled that in addition to these [2.2] *para*-cyclophenes, a family of [2.2] *para*-cyclophane-1-enes were also of interest as monomers to be used in ROMP, in order to prepare a series of precursor polymers to PPV, which being non-conjugated, would prove inherently more soluble and processable than their fully-conjugated PPV counterparts.

4.5.1: Attempted Addition of 'H-X' Across the Stilbene Double Bond.

The points mentioned in *Section 4.5* being taken into consideration, it was decided that 'removal' of the stilbene double bond by addition of suitable groups H-X (where X = halogen, -OH, -OME), across it was the best approach to engender greater flexibility. As was discussed in *Chapter 1, Section B2.5*, the central C=C bond in stilbene is much less

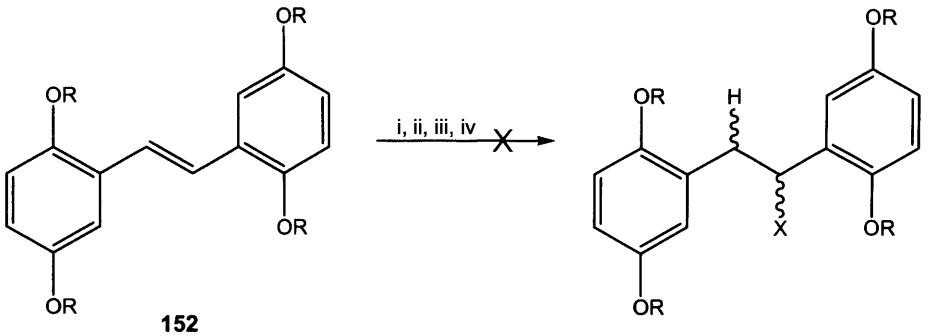
reactive than would be expected in comparison with other alkenes. This being the case, the addition of H-X across the stilbene double bond is relatively hard to achieve. A variety of examples exist in the literature of such addition reactions using unsubstituted *trans*-stilbene, but none have yet been reported using alkoxy-functionalised substrates. For example, Back and coworkers have described the addition of MeOH across the double bond of *trans*-stilbene using an organoselenium reagent to afford the corresponding ether **151** (*Scheme 74*).[11] The addition of HCl to *trans*-stilbene was reported by Kaupp and Ringer in 1986. However, spectroscopic analysis showed that a mixture of products had been obtained, α-chloro bibenzyl only comprising 47% of the mixture, which was not separated.[12]



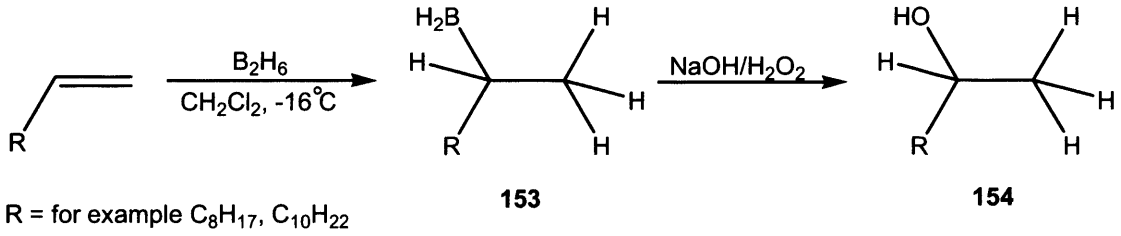
Scheme 74: Addition of MeOH across the stilbene double bond using an organoselenium reagent.

Work both within the Dyer group and by collaborators at the University of York (Dyson *et al.*) has shown that the addition of suitable leaving groups 'H-X' across the double bond in alkoxy-functionalised stilbenes (*Scheme 75*) is far from trivial. Repeated attempts to add HBr and HCl both with and without a lewis acid catalyst such as $FeCl_3$ were unsuccessful. This lack of reactivity is thought to be due to the destabilising effect of the *meta*-alkoxy group disfavouring the formation of the necessary benzylic carbocation. Several attempts by Dyson *et al.* to add MeOH across the double bond of 3,3'-dimethoxy stilbene (**152**), by various modified literature methods including reaction with sodium methoxide in methanol,[13] reaction with hydrochloric acid in methanol,[14] irradiation at 315 nm in methanol,[15] and finally methoxymercuration[16] all proved unsuccessful, returning only the starting stilbenes after work up in all cases.

An attempt was also made to add 'H_2O' across the stilbene double bond, using the hydroboration method described by Brown *et al.* (*Scheme 76*), where the use of diborane in dichloromethane rapidly generates an organoborane (**153**), which can be converted to the corresponding alcohol (**154**) by the use of standard oxidation procedures such as sodium hydroxide/hydrogen peroxide.[17] Tests by Brown *et al.* on 'standard' aliphatic alkenes, for example 1-octene and 1-decene, showed this reaction to occur rapidly even at -16°C. However results using the stilbenes described in this thesis proved inconclusive, showing complex mixtures of products by ^1H NMR spectroscopy. This is probably again due to the low reactivity of the stilbene C=C bond when compared to other olefins.



Scheme 75: Attempted addition of H-X across the stilbene double bond.



Scheme 76: Addition of 'H_2O' across alkenes *via* hydroboration.

4.5.2: Dihydroxylation of Stilbenes.

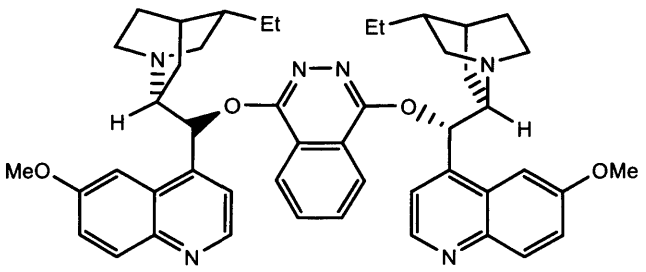
As addition of H-X across the double bond proved more complex than was expected, an alternative reaction involving the C=C bond was sought to provide a 'model' substrate for the testing of ring-closing procedures. Stilbenes have been shown (See *Chapter 1, Section B2.5.3*) to be suitable substrates for dihydroxylation across the olefinic bond, hence a method of preparing the corresponding 1,2-ethanediols from the functionalised stilbenes described in previous sections was investigated. These diols, although appropriate for use as models for the desired ring-closing, will not, when ring-closed, yield suitable [2.2] *para-*

cyclophane-1-enes for polymerisation. This is due to the fact that a PPV precursor polymer prepared using a diol-functionalised [2.2] *para*-cyclophane-1-ene cannot be straightforwardly transformed to PPV, as the transformation of a 1,2-diol functionality into an alkene is not trivial and cannot be performed in the solid state.

4.5.2.1: Asymmetric Dihydroxylation of Alkoxy-Substituted Stilbenes.

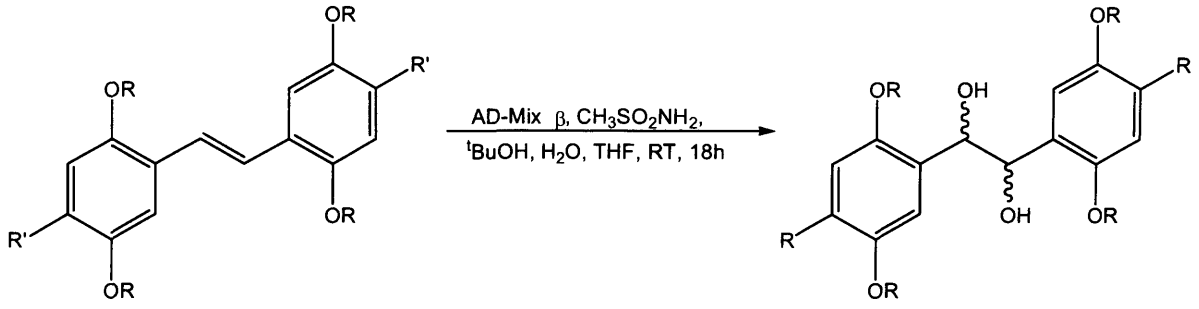
The asymmetric dihydroxylation (AD) of *trans*-stilbene has been demonstrated to occur in almost quantitative yield under 'standard' AD conditions.[18] In fact, *trans*-stilbene is one of the best substrates for the AD reaction, being an almost perfect match for the catalytic binding site in many of the commonly employed chiral ligands used in this reaction. The product of this dihydroxylation, 1,2-diphenylethanediol, has been employed as a chiral ligand for both catalysts and auxiliaries in, for example, the asymmetric Diels-Alder reaction,[19] and the catalytic asymmetric oxidation of aryl sulfides.[20]

Enantioselectivity was not an issue during the course of this work, as the dihydroxylation was undertaken simply to introduce free rotation about the previously conformationally locked C=C bond. However, the commercially available reagent 'AD-Mix β' was chosen as the preferred reagent to bring about dihydroxylation of the stilbenes **131**, primarily due to its ease of manipulation and handling. Additionally, this method avoided the use of reasonably large quantities of highly toxic osmium tetroxide. This pre-mixed reagent can be regarded as a non-volatile source of osmium tetroxide, and contains the chiral ligand $(DHQD)_2PHAL$ (**155**) (*Figure 63*) in addition to the correct proportions of potassium carbonate, potassium hexacyanoferrate and potassium osmate required to bring about the desired dihydroxylation. The dihydroxylated stilbenes were prepared according to the method shown in *Scheme 77,* adapted from previous work carried out in the Dyer group.[21] The addition of methane sulfonamide to the reaction mixture when using AD-Mix reagents has been demonstrated to greatly enhance the rate of hydrolysis of the osmium (VI) glycolate intermediate,[22] for non-terminal olefins such as *trans*-stilbene this hydrolysis step is catalyst turnover-limiting, hence increasing the rate of this step increases the rate of the overall AD reaction.



155

Figure 63: $(DHQD)_2PHAL$ (**155**), the chiral ligand used in AD-Mix β.



131a: R = n-butyl, R' = H
131c: R = n-butyl, R' = Br

156a: R = n-butyl, R' = H 15%
156b: R = n-butyl, R' = Br 72%

Scheme 77: Dihydroxylation of stilbenes **131a** and **131c** using Ad-Mix β.

Dihydroxylation was initially tested on a small scale (0.5 g of substrate), and the desired ethane 1,2-diols were successfully prepared, although unfortunately in very low yield (~15%). ^1H NMR analysis of the crude diols **156** showed significant impurities, and purification proved difficult, as column chromatography was unsuitable; the acidic nature of the silica gel caused the diols to decompose on the column. Recrystallisation of 1,2-di-(2,5-dibutoxy-phenyl)-ethane-1,2-diol **156a** from warm pentane was, however, successful. Upon scale-up of dihydroxylation of both **131a** and **131c** (*Scheme 77)*, yields of **156a** remained disappointingly low, whereas **156b** was produced cleanly in good yield.[23] Reasons for this observation are, as yet, unknown.

4.5.2.2: Structure and Characterisation of the 1,2-Ethane Diols 156

The ^1H NMR spectrum of **156a** is shown in *Figure 64*. The presence of trace amounts of water in the deuterated solvent led to subsequent broadening of the resonances attributed to the hydroxyl protons, hence these signals were not observed. The ^1H NMR spectrum of the starting material 2,5,2',5'-tetrabutoxy stilbene **131a** is shown below in *Figure 65,* for comparison. Compound **156a** is highly symmetrical; hence the methyne protons appear in

the spectrum as a singlet resonance. From integration, only one set of signals is observed in the spectrum, suggesting, as would be expected through the employment of asymmetric dihydroxylation reagent Ad-Mix β, that only one enantiomer of the product has been formed. However, no formal determination of the stereochemistry was attempted for the ethane-1,2-diols prepared.

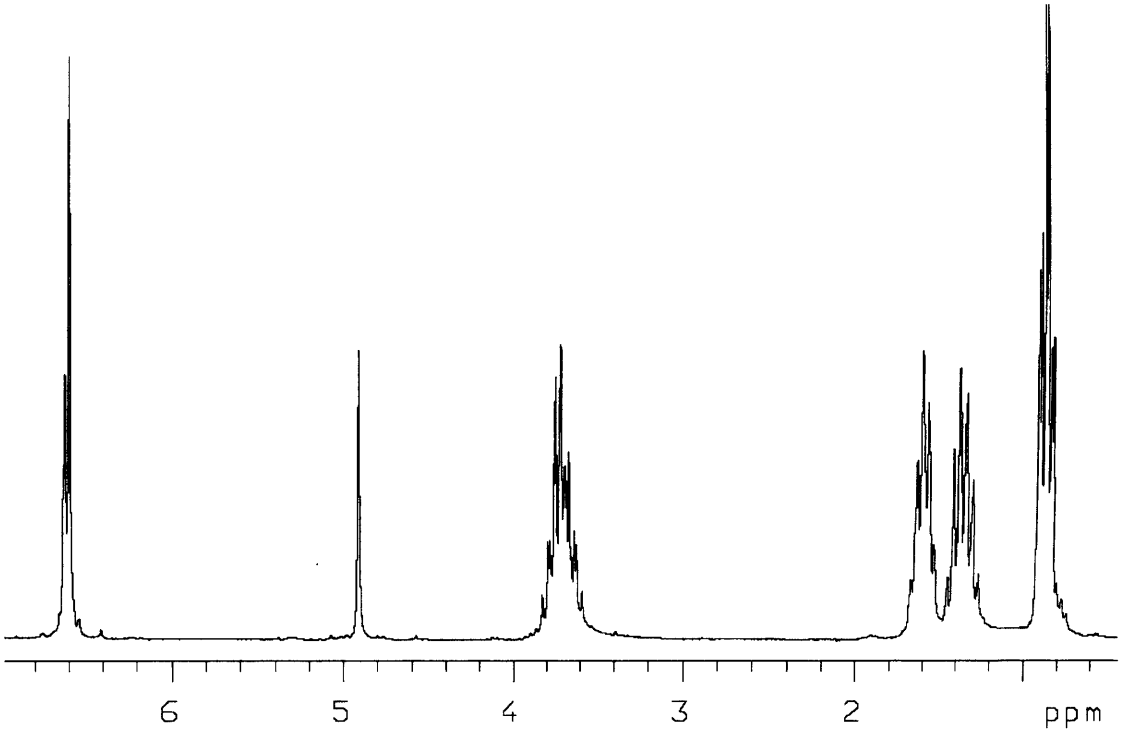


Figure 64: ^{1}H NMR spectrum (400 MHz, $CDCl_3$) of 1,2-di-(2,5-dibutoxy-phenyl)-ethane-1,2-diol **156a.**

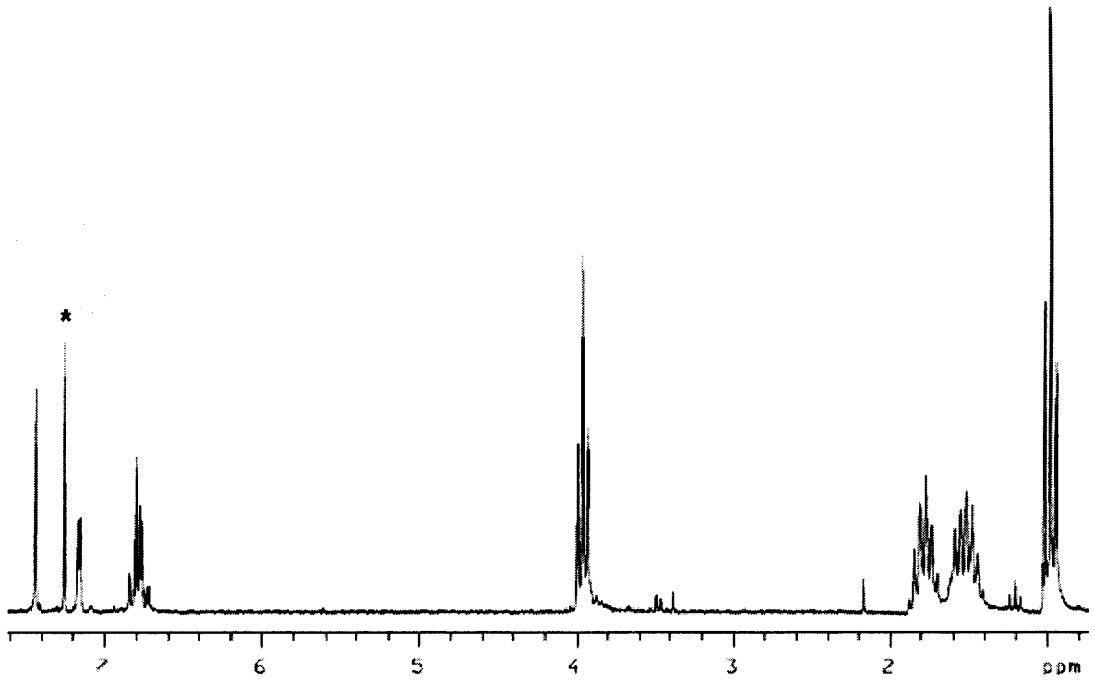
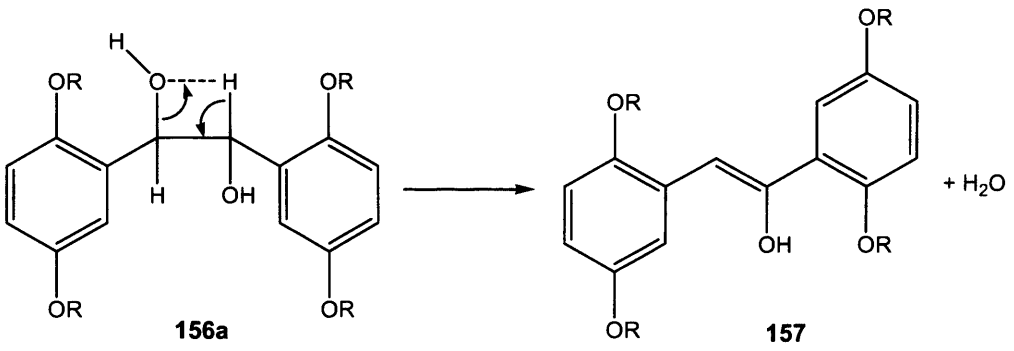
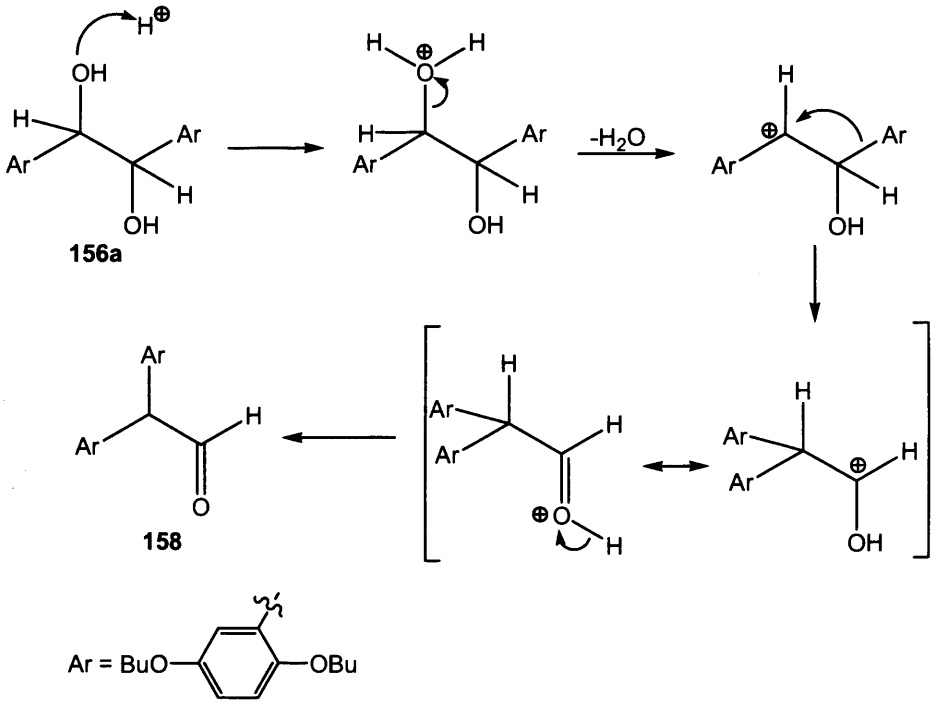


Figure 65: 1H NMR spectrum (200 MHz, $CDCl_3$) of 2,5,2',5'-tetrabutoxy stilbene **131a.**
* $CDCl_3$

Rather than the expected parent ion, the ES+ mass spectrum of 1,2-di-(2,5-dibutoxy-phenyl)-ethane-1,2-diol **156a** presents a peak at *m/z* = 484 , which corresponds to a species resulting from loss of a molecule of water from the target molecule. It is proposed that this loss of water can occur in one of two ways: either through an elimination pathway to yield the corresponding alkene **157** (*Scheme 78*), or *via* a pinacol rearrangement to give the related aldehyde **158** (*Scheme 79*). However, it cannot be conclusively stated which of these reactions actually occurs in the mass spectrometer, the isotope pattern being identical for both products.[24]



Scheme 78: Loss of water from **156a** *via* an elimination pathway.



Scheme 79: Loss of water from **156a** *via* a Pinacol rearrangement to yield aldehyde **158.**

Generally, the pinacol rearrangement of a 1,2-diol can yield either an aldehyde or a ketone, depending on the migratory aptitude of the groups present on the sp^3 carbon of the carbocation intermediate. In the case shown above in *Scheme 79*, the aryl group is believed to have a higher probability of migrating, due to its bearing electron-donating alkoxy groups in the *meta* position, although the alkoxy substituents in the *ortho* position could be seen as decreasing this probability somewhat.[25] Therefore, it is predicted that should a pinacol rearrangement be the decomposition pathway, the product observed in the mass spectrum will be the aldehyde, and not the ketone.

In contrast, the related compound 1-(4-bromo-2,5-dibutoxy-phenyl)-2-(4-bromo-phenyl)-ethane-1,2-diol **156b** does not exhibit a loss of water in its mass spectrum, showing instead a molecular ion peak for its sodium salt at m/z = 539, a feature commonly observed by Electrospray ionisation. The fact that brominated diol **156b** survives the ionisation process intact, whilst 1,2-di-(2,5-dibutoxy-phenyl)-ethane-1,2-diol **156a** does not, has been attributed to the stabilising effect of the bromine which disfavours any rearrangement.

4.6: Protection of 1,2-Ethane Diols 156.

In order for further transformations to be carried out upon the ethane 1,2-diols described above in *Section 4.5,* it was deemed necessary to protect the alcohol functionality to prevent unwanted side-reactions from occurring. Although a cyclic protecting group, for example a cyclic acetal, is commonly preferred for this type of protection due to its increased stability, in the context of the work carried out in this thesis a cyclic protecting group would not be suitable, as it would prevent free rotation about the HOC-COH bond in the diol (*Figure 66*). This free rotation is vital to the next step in the synthesis, as the molecule must be able to adopt a suitable *'cis'* geometry in order for ring-closing to occur and hence generate the desired [2.2] *para*-cyclophane.

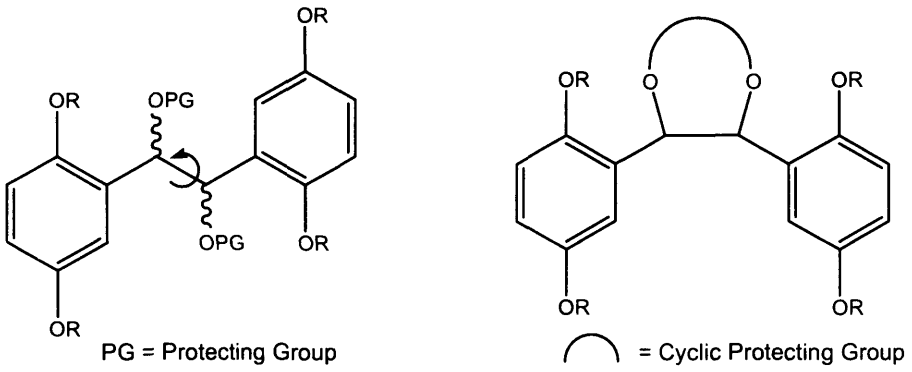
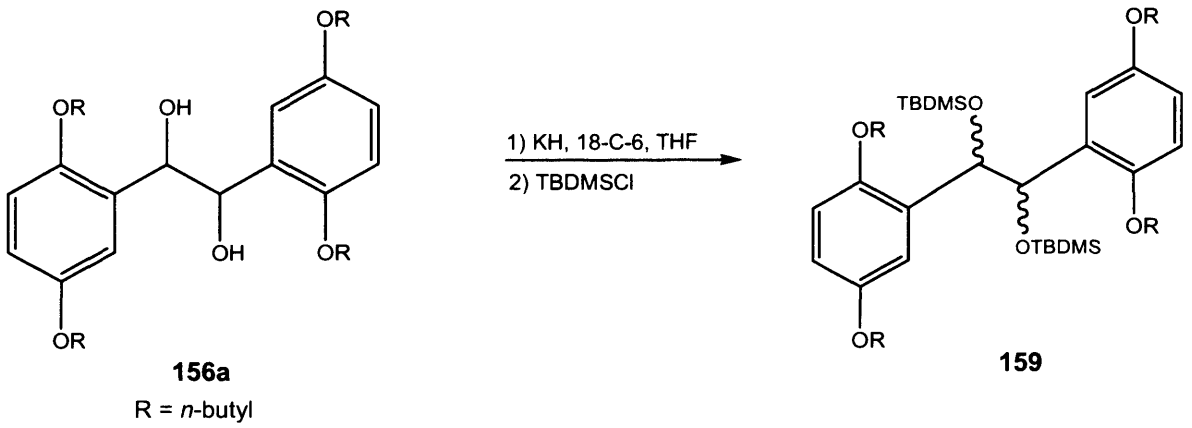


Figure 66: Illustration of 'conformationally locked' cyclic protecting group, and 'freely rotating' acyclic protecting group.

The choice of protecting group was hence governed by two factors: the necessity of using an acyclic protecting group, and its stability towards the reagents to be used in the next steps of the synthesis. Silyl ethers appeared the most promising of protecting groups to use, being both introduced and cleaved in a straightforward manner using a variety of reagents. Also their reactivity, and hence stability, can be easily tuned both electronically and sterically through alteration of the substituents present at silicon.[26] The eventual choice of the *t*-butyl dimethylsilyl ether group (TBDMS) as the protecting group for ethane 1,2-diols **156** was made on the basis that these diols are reasonably sterically hindered, being adjacent to an alkoxy-substituted phenyl ring. The TBDMS group has been demonstrated to be effective in protecting such hindered alcohols, and is generally introduced by initial deprotonation of the alcohol moiety by potassium hydride in THF, followed by trapping using TBDMSCl .[27, 28, 29] An identical methodology was employed in protecting 1,2-di-(2,5-dibutoxy-phenyl)-ethane-1,2-diol **156a,** and is illustrated below in *Scheme 80.*



156a
R = *n*-butyl

159

Scheme 80: Protection of 1,2-di-(2,5-dibutoxy-phenyl)-ethane-1,2-diol **156a** with TBDMS.

After removal of solvent from the reaction mixture, a yellow residue remained, which was washed with hexane to give a pale yellow solid which was hoped to be the desired protected diol. Unfortunately, ^{1}H NMR spectroscopy showed the reaction to have been only partially successful, with a large proportion of the diol (approx 50 % by ^{1}H NMR) remaining unreacted.

Regrettably, due to time constraints, it was not possible during the course of this thesis to further investigate and optimise the protection reaction detailed above. Further study is evidently necessary in order to successfully protect the 1,2-ethane diols **156**, either by adjustment of the reaction conditions employed to protect using the TBDMS group, or by exploring alternative protecting strategies which can be applied to the 1,2-ethane diols in question.

4.7: Conclusions.

This chapter has described the synthesis of a range of alkoxy-substituted stilbenes, *via* both the McMurry and Horner-Wittig reactions. These stilbenes can be further functionalised at the position *para* to the central C=C bond, in order to prepare suitable substrates for a ring-closing reaction to form an alkoxy substituted [2.2] *para*-cyclophene. Before this ring-closing could take place, it was found necessary to add a leaving group 'H-X' across the olefinic stilbene bond in order to introduce free rotation about this C-C linkage to allow the molecules to adopt an appropriate conformation for ring-closing to occur. This ring-closing would then lead to the desired [2.2]-*para*-cyclophane-1-ene monomer required to prepare a precursor polymer to PPV *via* ROMP. Unfortunately the introduction of such leaving groups H-X, for example HCl, MeOH and H_2O, across the stilbene C=C bond proved extremely complex, hence this bond was instead dihydroxylated *via* the AD reaction to provide a 'model' compound towards the testing of ring-closing strategies.

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CHAPTER FIVE

Attempted Synthesis of [2.2] *para*-Cyclophenes *via* Ramberg-Bäcklund Rearrangement.

5.1: Introduction.

Referring back to *Chapter 1, section C,* it was described how a ring-contraction of dithiacyclophanes through, for example, a Stevens-Benzyne reaction followed by sulfoxide pyrolysis yields [2.2] *para*-cyclophanes,[1] however these reaction conditions are harsh. This section describes how a previously untried Ramberg-Bäcklund rearrangement was attempted in order to bring about the same transformation under milder conditions.

Discovered in 1940 by Ramberg and Bäcklund,[2] and involving the base-mediated, regiospecific conversion of an α-halogenated sulfone (*e.g.* **159**) into an alkene, the Ramberg-Bäcklund rearrangement has been extensively studied as a versatile method of introducing an alkene moiety into a vast array of substrates (*Figure 67*, A). The development in 1969 of the Meyers' modification,[3] *i.e* reaction of the unsubstituted sulfone (*e.g.* **160**) with CCl_4 and strong base, has further opened up the synthetic possibilities of this reaction. In this latter procedure, an *in situ* halogenation-Ramberg-Bäcklund rearrangement takes place removing the necessity of having to use α-halogenated sulfones (See *Figure 67,* B).[4]

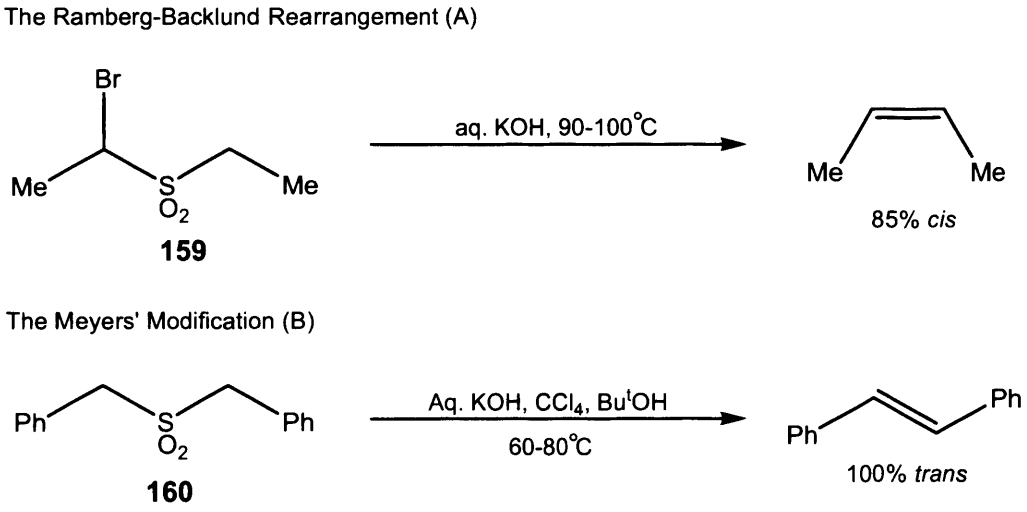
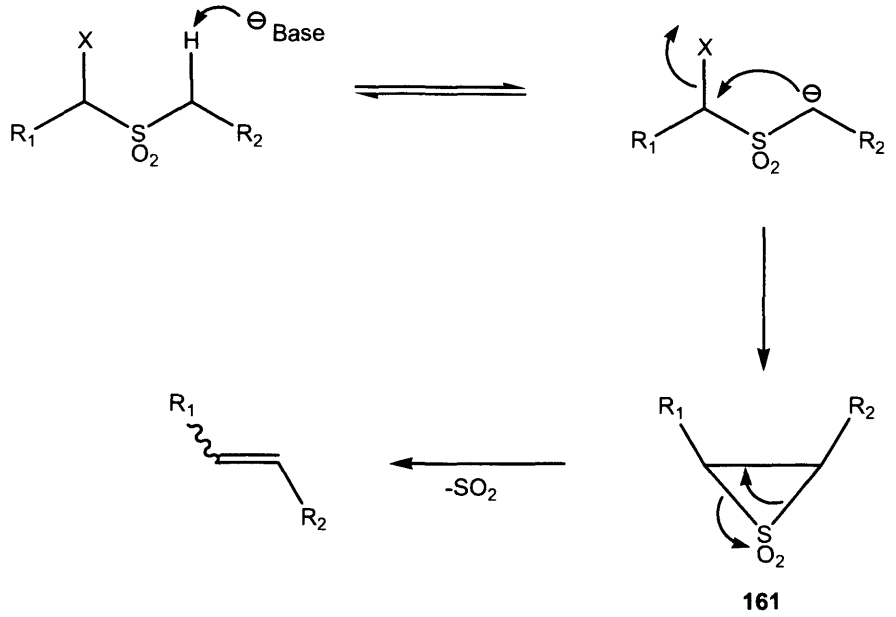


Figure 67: Examples of the Ramberg-Bäcklund Rearrangement (A) and Meyers' Modification (B).

The mechanism of the Ramberg-Bäcklund rearrangement is well-established, with the commonly accepted form being that shown in *Scheme 80.*[5] The procedure is generally cis-specific, due to the kinetically favoured *cis*-configuration of the 'R' groups during formation of the episulfone **161**, caused by a combination of diastereoselective carbanion formation and steric attraction.[6,7] However, it has been demonstrated that while the use of a

mild base further promotes the formation of *cis*-alkenes, employing a stronger base such as potassium t-butoxide favours formation of the *trans*-alkene, due to epimerisation of the sulfone prior to elimination of sulfur dioxide to generate the alkene.[8]



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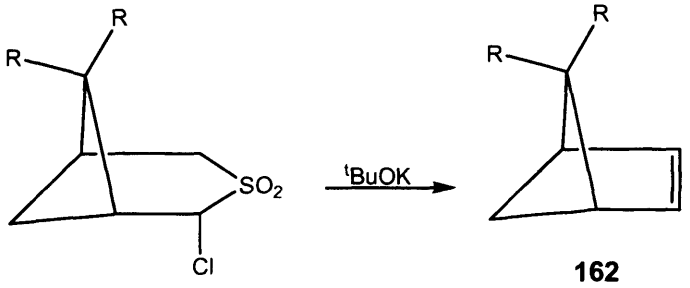
Scheme 80: The mechanism of the Ramberg-Bäcklund rearrangement.

The main advantages of preparing alkenes *via* the modified Ramberg-Bäcklund methodology include the regiospecificity of the reactions, the generally facile synthesis of the required sulfone starting materials,[9] and the wide applicability of the methodology, including the synthesis of highly strained ring systems[10] and tetra-substituted alkenes. An example of a strained ring system (**162**) prepared using the Ramberg-Bäcklund reaction is shown in *Scheme 81*.



162

Scheme 81: Ring-contraction of an α-halogenated sulfone to prepare a strained bicyclohexene.

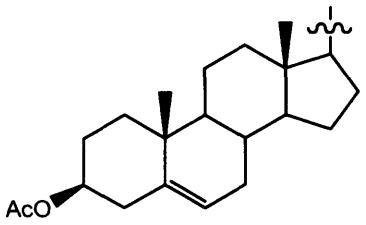
The Ramberg-Bäcklund approach is also frequently used in natural product synthesis, for example Schmittberger and Uguen observed that the Ramberg-Bäcklund rearrangement provided a convenient route for the preparation of the side-chains of sterols (*e.g.* **163**)-

structurally complex plant and animal hormones with antibiotic, phytohormonal and antifeedant properties (*Scheme 82*). In addition to the advantages discussed above, when compared to other olefination reactions commonly employed in this type of synthesis,[11] the Ramberg-Bäcklund rearrangement was shown to offer better stereoselectivity, and also avoids the use of a potentially reactive aldehyde moiety as a precursor to the desired alkene.

163

i) NCS, CCl_4, 90 C_o 15 mins
ii) mCPBA, $NaHCO_3$, RT, 3h
iii) ^tBuOK, THF, RT, 3-4h

St = Sterol backbone:

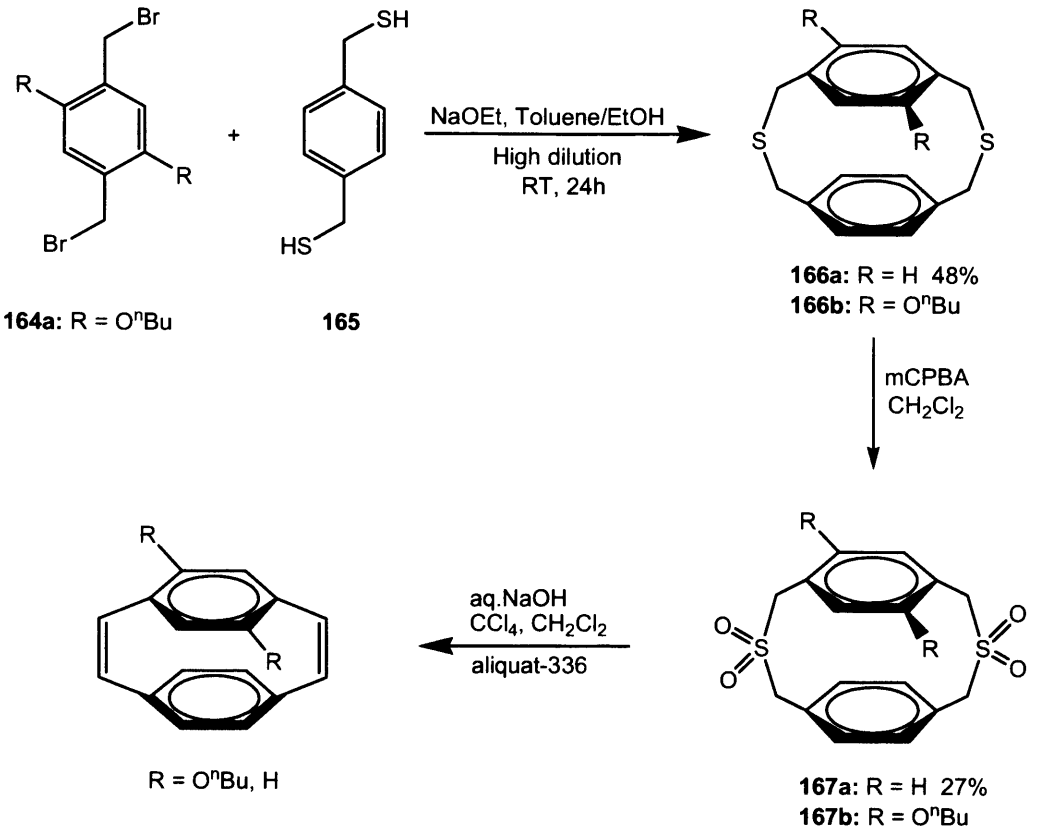


Scheme 82: Preparation of the side chain of a sterol, *via* a modified Ramberg-Bäcklund rearrangement.

5.2: Synthesis of [2.2] *para*-Cyclophenes *via* Ramberg-Bäcklund Rearrangement.

As part of this thesis, it was proposed that the Ramberg-Bäcklund methodology may provide a simple, effective route into functionalised [2.2] *para*-cyclophenes. Although unsubstituted [2.2] *para*-cyclophenes have previously been prepared *via* various thioether rearrangement methodologies (See *Chapter 1, Section C*), these literature routes do not allow for systematic functionalisation of the paracyclophene product. This functionalisation is, however, vital to the [2.2] *para*-cyclophane syntheses proposed in this thesis, as these compounds are to serve as monomers to prepare alkoxy-functionalised, soluble, PPV polymers.

The potential strategy developed towards [2.2] *para*-cyclophenes involves the use of a modified Ramberg-Bäcklund rearrangement to form the two double bonds, and is shown below in *Scheme 83.*



Scheme 83: Proposed strategy for the preparation of [2.2] *para*-cyclophenes *via* the modified Ramberg-Bäcklund rearrangement.

As is evident from *Scheme 83* above, the disadvantage in this modified Ramberg-Bäcklund approach is that it does not provide an easy opportunity for substitution at the double bonds, hence the product is a [2.2] *para*-cyclophene itself rather than the more desirable [2.2] *para*-cyclophane-1-ene. Thus, ROMP polymerisation of this [2.2] *para*-cyclophene would lead directly to PPV itself, rather than to the more processable non-conjugated precursor polymer.

Using this approach, substitution at only one of the two aromatic rings was attempted in the first instance due to the choice of starting materials for preparation of the precursor cyclic thiol **166**. Benzenedimethane thiol **165** is available commercially and thus a lengthy synthesis of this compound could be avoided. Preparation of 1,4-di(bromomethyl)-2,5-dialkoxybenzene **164** was achieved in high yield by reacting the corresponding dialkoxy benzene **112** with *para*-formaldehyde and HBr in acetic acid.[12]

Previous, preliminary unpublished work by the Dyer group has shown that it is possible to prepare the unsubstituted (R = H; *Scheme 83*) form of cyclic dithioether **166** in reasonable yield (48%) from benzenedimethanethiol and 1,4-dibromomethylbenzene, using sodium ethoxide (1.3M) or excess potassium carbonate as base.[13] The progress of the reaction was followed by TLC analysis in 3:2 toluene/cyclohexane, with R_f values of 0.58 for the cyclic dithioether product corresponding well to those documented in the literature of 0.6 in 3:2 benzene/cyclohexane.[14] A small amount of a white solid precipitated from the reaction solution during the course of the synthesis, this proved insoluble in all common organic solvents hence exact characterisation was impossible. However, this solid was believed to be a sulfur-bridged polymer formed where polymerisation, rather than cyclisation, of the reagents had occurred.

The cyclisation reaction attempted by Woodcock[12] was repeated several times in an attempt to optimise yields, the conditions used are summarised below in *Table 3*. Purification of the product was attempted using both recrystallisation and Soxhlet extraction, however the low solubility of the compound hindered recrystallisation and the high temperatures used in the soxhlet extraction caused decomposition of the thioether. The cyclic dithioether was, hence, used crude in the next step of the reaction scheme, namely oxidation to the sulfone **167**, which was carried out successfully but in low yields (27%), probably due to a combination of the impurity and insolubility of the cyclic dithioether precursor.

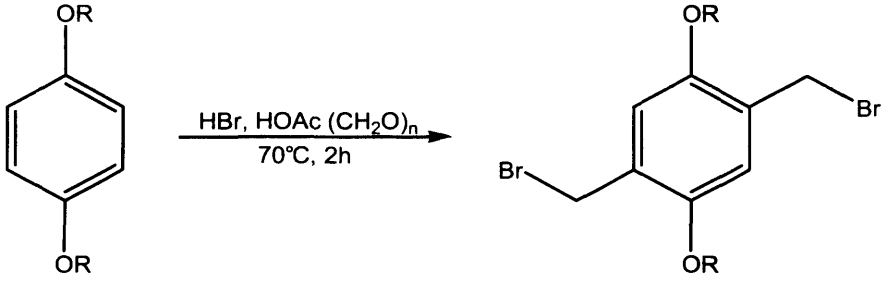
Reaction Attempt	**Reactant concentration (mmol dm^3)**	**Base**	**Time (h)**	**Addition Rate (mL / h)**	**Yield (%)**
1	17	K_2CO_3	1.5	200	10
2	17	NaOEt	80	3.75	48
3	17	NaOEt	100	3	26

Table 3: Variations in conditions and reagents for the synthesis of cyclic thioether **166**.

In order to achieve the desired modified Ramberg-Bäcklund rearrangement, dissolution of the sulfone **167** was attempted in a wide variety of organic solvents including THF, dichloromethane, chloroform, ethanol and methanol, but little or no solubility was observed even at elevated temperatures. The use of ultrasound irradiation was hoped to improve dissolution, but was also unsuccessful, as was an attempt at improving solubility

by carrying out the modified Ramberg-Bäcklund procedure in an alternative manner using a revised form of the biphasic conditions suggested by Hartman,[15] namely dichloromethane, aqueous sodium hydroxide, carbon tetrachloride and the phase-transfer catalyst octadecyltrimethylammonium bromide. However, this latter approach was unfortunately no more successful and hence, due to the insolubility of the sulfone **167**, it proved impossible to carry out the Ramberg-Bäcklund rearrangement, thus the [2.2] *para*-cyclophene could not be prepared.

In a further attempt to counteract the insolubility of the desired sulfone derivative, a revised methodology was developed for this thesis, whereupon addition of pendant alkoxy groups to the starting dibromomethylbenzene was hoped to increase solubility of the final sulfone. Towards this end, the two dibromomethyldialkoxy compounds 1,4-dibromomethyl-2,5-dibutyloxybenzene **164a** and 1,4-dibromomethyl-2,5-dipentyloxybenzene **164b** were synthesised according to *Scheme 84*, in good yield (78% and 53% respectively).



114a: R = C_4H_9
114b: R = C_5H_{11}

164a: R = C_4H_9 53%
164b :R = C_5H_{11} 78%

Scheme 84: Synthesis of 1,4-dibromomethyl-2,5-dibutyloxybenzene **164a** and 1,4-dibromomethyl-2,5-dipentyloxybenzene **164b** .

As was the case for the synthesis of the unsubstituted cyclic dithioether **166a** and sulfone **167** discussed in the preceding paragraphs, a further problem associated with the modified Ramberg-Bäcklund methodology was competing polymerisation of the substrates occurring, in preference to cyclisation. In order to promote cyclisation and hence avoid this problem of polymerisation, it was again necessary to carry out the preparation of the cyclic thioether **166b** under either true or *pseudo*- high-dilution conditions. This was achieved by the use of a syringe pump or dropping funnel, respectively, to add solutions of the two reagents, **164a** and benzenedimethanethiol, to a solution of sodium ethoxide as base (0.1 mol/dm^3). It proved extremely difficult to optimise these conditions, as either no reaction

at all took place and the starting materials were recovered unchanged, or an insoluble white solid was formed (see *Table 4*). Analogously to the work of Woodcock described earlier in this section, this white solid was believed to be a sulfur-bridged polymer,[13] however due to its intractable nature no data could be obtained.

Reaction	Method of Addition	Concentration of Solutions ($mmol/dm^3$)	Addition Rate (μL/hour)	Result
1	Syringe Pump	147	50	No Reaction
2	Syringe Pump	147	200	Polymerisation
3*	Dropping Funnel	3.8	~4100	Polymerisation

*Reaction under true high-dilution conditions, 1.53 mmol of each reagent in 400 mL solvent.

Table 4: Selected attempts to synthesise cyclic thioether **166b.**

In order to further investigate the theory that polymerisation occurs upon insufficient dilution of the reaction solution, an experiment was carried out under 'standard' dilution conditions. The two reagents were simply added to a 1:1 solution of sodium ethoxide (0.1 mol dm^{-3}) and toluene, and the mixture stirred at room temperature for 18h. As predicted, a white solid precipitated from the solution and was isolated *via* suction filtration, however attempts to characterise this material were severely hindered by its insolubility in all common organic solvents and a conclusive identification was not achieved. Elemental analysis (combustion) proved inconclusive.

5.3: Conclusions.

In conclusion, although the Ramberg-Bäcklund rearrangement appeared to be an attractive route towards the preparation of [2.2] *para*-cyclophenes, problems of solubility and reproducibility were encountered, both in the preparation of the precursor cyclic thiols and sulfones, and in the Ramberg-Bäcklund rearrangement itself. Attempts were made to counteract these problems, through both strict control of the reaction conditions to prevent polymerisation, and alteration of the substrates to combat insolubility issues, yet these measures proved insufficient and preparation of [2.2] *para*-cyclophenes *via* this route was ultimately unsuccessful.

References for Chapter Five

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CHAPTER SIX

Conclusions and Further Work

6.1:Conclusions.

Taking as a starting point the functionalised alkoxy benzaldehydes discussed in *Chapter Four,* a reliable route for the preparation of suitably derivatised stilbenes has been implemented and a number of such stilbenes synthesised and fully characterised. It was observed that in order to prepare the desired functionalised [2.2] *para*-cyclophenes, further reaction of the stilbene olefinic bond was required. This was in order to introduce free rotation about this bond and allow the molecules to take up an appropriate conformation for the proposed ring-closing reaction. Such a derivatisation of the olefinic bond also provided a route into [2.2] *para*-cyclophane-1-enes, the polymerisation of which *via* ROMP would hopefully furnish a soluble precursor polymer to PPV such as those described in *Chapter One*. Towards this end, a number of routes towards introducing suitable leaving groups 'H-X' across the stilbene alkene bond were investigated, but met with little success due to the low reactivity of the bond in question. Hence, the already proven 'AD' reaction was applied to the stilbene precursors and the resulting diols purified and characterised. An overall summary of the chemistry achieved is shown below in *Figure 68.*

Preparation of [2.2] *para*-cyclophenes was also attempted through the use of a Ramberg-Bäcklund rearrangement using a suitably substituted cyclic dithioether. However, this route proved ultimately unsuccessful, due to problems with the solubility of both the dithioether and sulfone substrates, and unwanted polymerisation reactions occurring preferentially to the desired cyclisations.

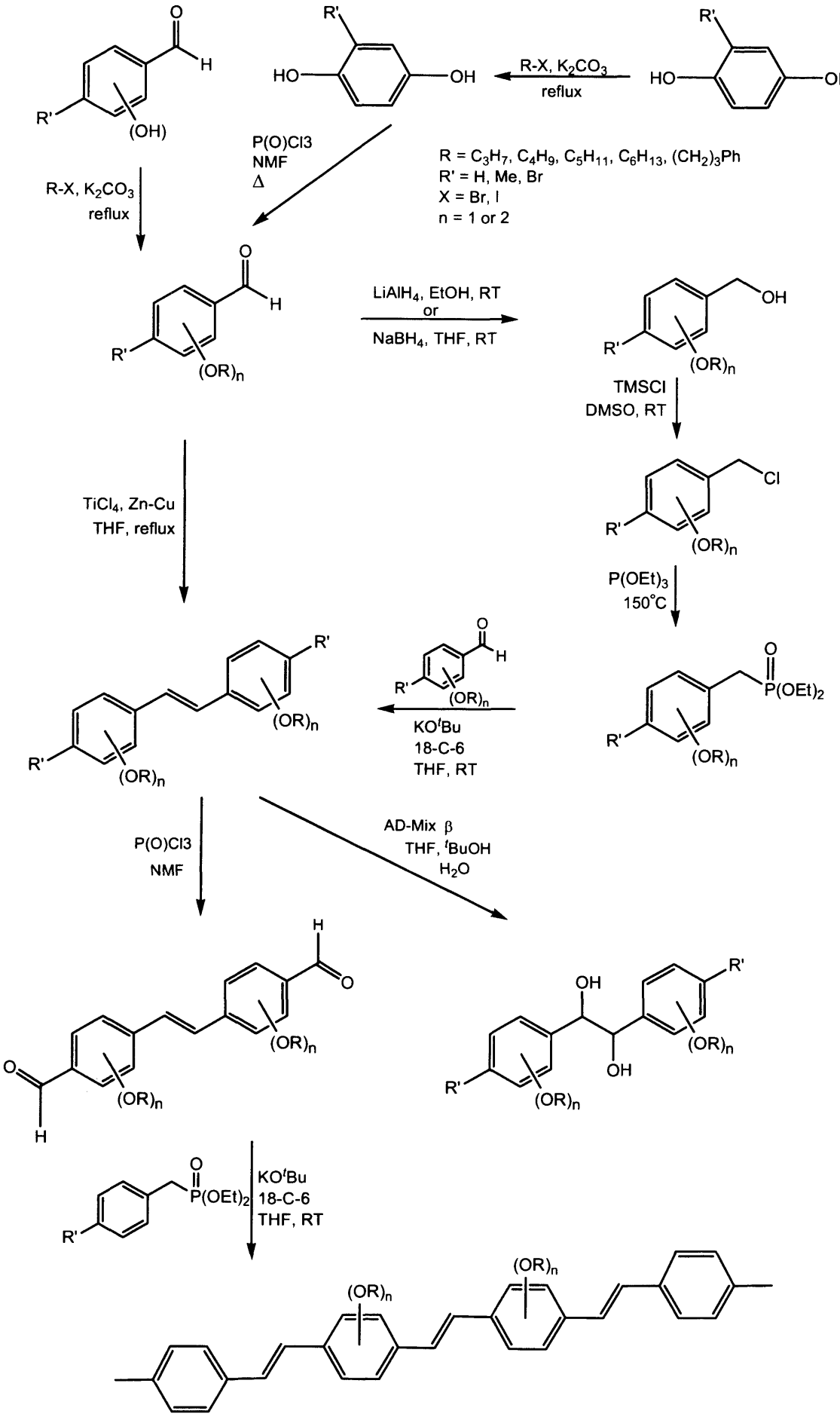
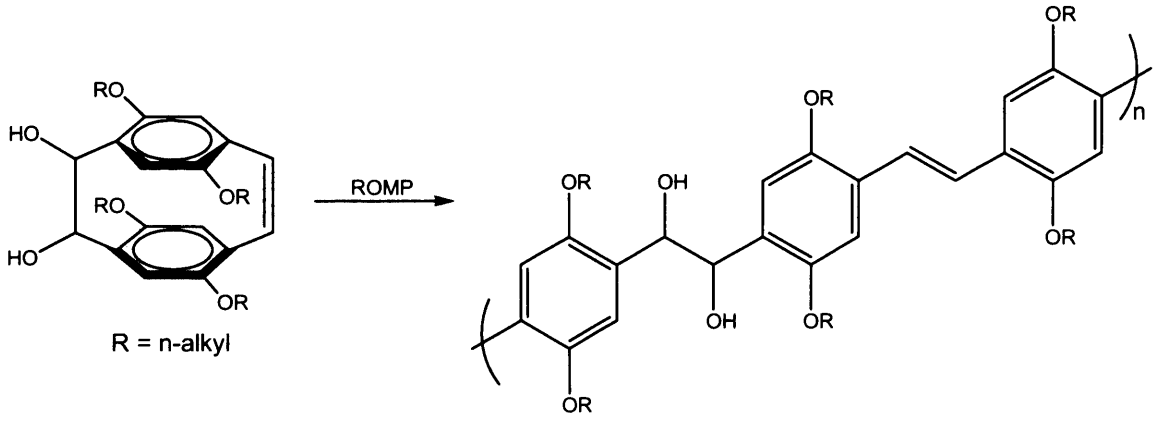


Figure 68: Summary of the chemistry described in this thesis.

6.2: Further Work.

Although a straightforward route for the preparation of suitably functionalised stilbenes and 1,2-ethane diols has been developed during the course of research for this thesis, the later synthetic steps, namely the McMurry and Horner-Wittig reactions and stilbene dihydroxylation, still suffer from low yields. Further optimisation of these steps is therefore necessary in order to allow for the straightforward preparation of multigram quantities of the desired stilbenes and 1,2-ethane diols.

Once suitably functionalised 1,2-ethane diols are readily available, research must be directed into achieving ring-closing to furnish [2.2] *para*-cyclophane-1-enes, *via* either the McMurry reaction, or RCM. From the discoveries made whilst investigating the Ramberg-Bäcklund route described in *Chapter Five,* it is already evident that these reactions must be undertaken at high dilution, to avoid polymerisation of the substrate occurring in place of cyclisation. Optimisation of the most successful ring-closing methodology must be carried out, in order to facilitate the preparation of a series of alkoxy-substituted [2.2] para-cyclophane-1-enes carrying various alkyl substituents. Polymerisation of these monomers *via* ROMP, using a Grubbs-type ruthenium-based initiator that will be stable to the –OH functionalities present, can then be carried out (*Scheme 85*) and their structure and properties investigated. Processing of this dihydroxy-substituted polymer will not, however, be carried out, due to the difficulty of performing a dihydroxylation reaction upon a solid polymer substrate.



Scheme 85: Proposed polymerisation of diol-functionalised [2.2] *para*-cyclophane-1-ene.

As the polymers synthesised through ROMP of diol-substituted [2.2] *para*-cyclophane-1-enes will not be suitable for the preparation of PPV, further research must therefore be directed into the introduction of some form of leaving group 'H-X' across the central

double bond in the stilbene precursors. As this bond in alkoxy-substituted stilbenes has been demonstrated to be highly unreactive, an alternative method must therefore be devised to prepare the desired compounds for ring-closing, which are, in effect, α-substituted bibenzyls (*Figure 69*).

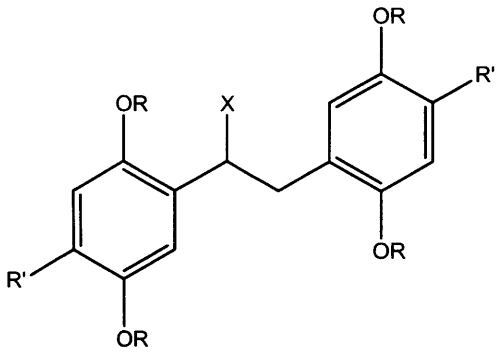
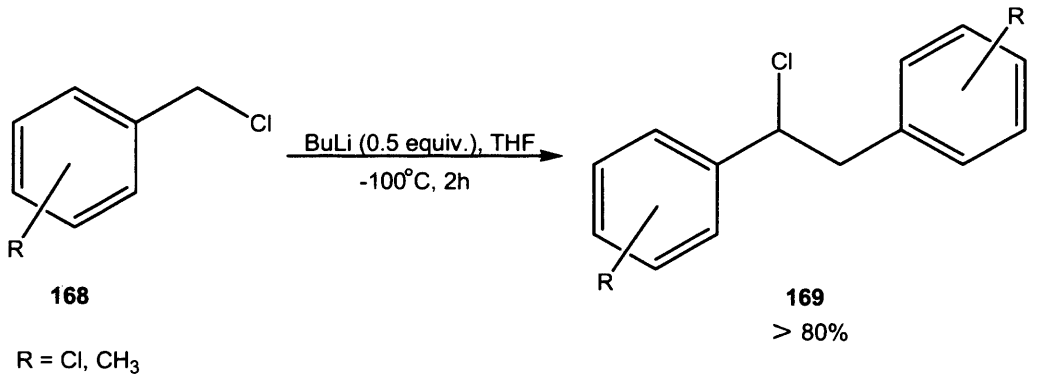


Figure 69: Example of an α-substituted bibenzyl precursor to [2.2]-*para*-cyclophane-1-enes.

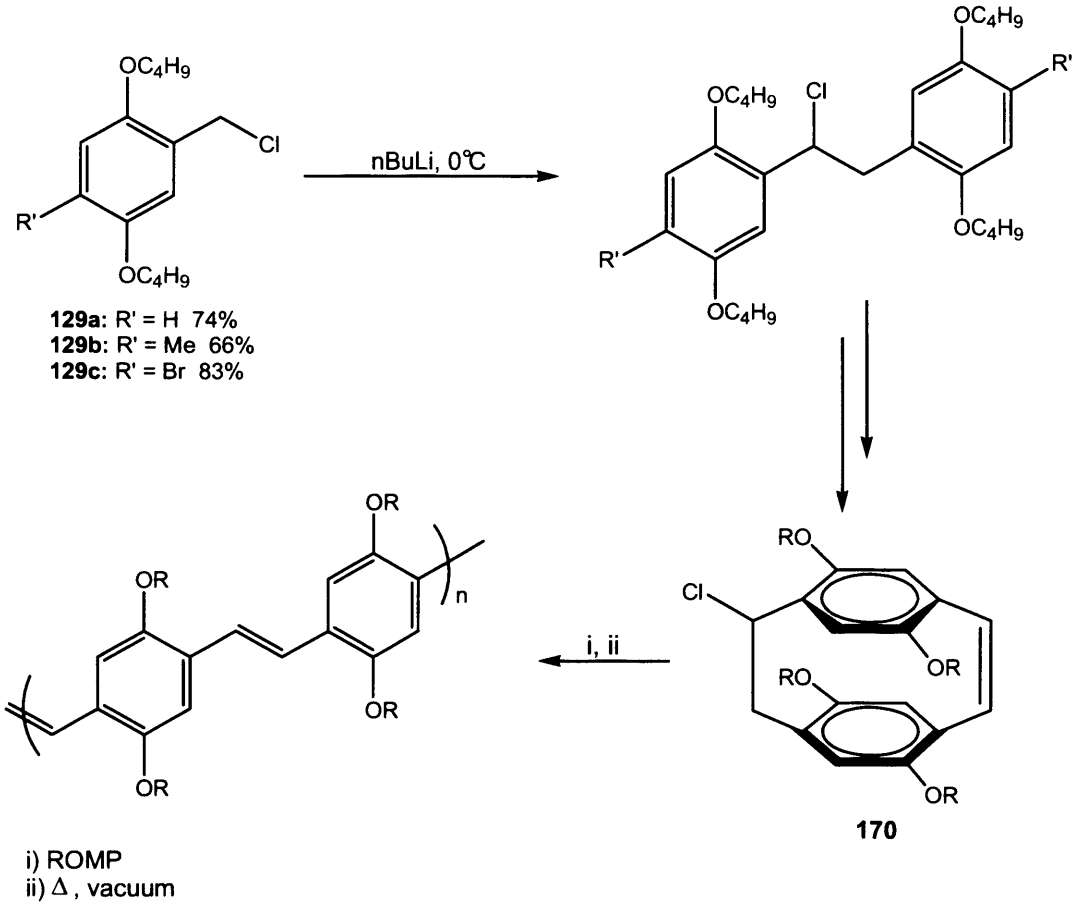
Hoeg and Lusk have reported a method of preparing α-chloro bibenzyls **169** through the reaction of benzyl chlorides **168** with *n*-butyl lithium as illustrated in *Scheme 86*.[1] This reaction is thought to proceed *via* an α-chloro benzyllithium intermediate, which reacts with a further equivalent of benzyl chloride to yield the α-chloro bibenzyl.



Scheme 86: Preparation of α-chloro bibenzyls **169** *via* reaction of benzyl chlorides **168** with *n*-butyl lithium.

Referring to *Scheme 86* above, it can therefore be postulated that a similar reaction of alkoxy-substituted benzyl chlorides **129** (*Chapter 3, Section 3.4.2.1)* with *n*-butyl lithium would yield the desired alkoxy-substituted α-chloro bibenzyls. Subsequent

functionalisation and ring-closing would then furnish alkoxy-substituted [2.2] para-cyclophane-1-ene **170** (*Scheme 87*), which could subsequently be polymerised to give a suitable precursor polymer to PPV. Elimination of HCl from this polymer, either by heating under vacuum, or by addition of base (similarly to the Gilch method of PPV synthesis, *Chapter 1, Section A3.2.2*) would yield an alkoxy-functionalised PPV.



Scheme 87: Postulated route to PPV *via* an α-chloro bibenzyl precursor.

Once a reproducible method of alkoxy-functionalised PPV synthesis has been established, study of the PPV prepared will be necessary, to examine both its photophysical and electroluminescent properties, and also the nature of the polymer itself, for example its MW, conjugation path length, and polydispersity. Variation of the alkoxy substituents, which is easily achievable through the synthetic pathway set out in this thesis, will yield a series of PPVs; the properties of which must be determined and hence the effect of substituent variation upon these properties evaluated.

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CHAPTER SEVEN

Experimental Details

General Considerations.

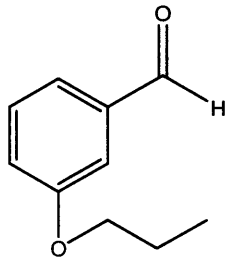
All experiments were conducted in standard Quickfit glassware. Where necessary, reactions were performed under an atmosphere of dry nitrogen using standard Schlenk and cannula techniques, or in a nitrogen-filled Saffron Scientific glove box. Dry solvents were freshly distilled under nitrogen from sodium / benzophenone (diethyl ether, toluene, THF and DME), sodium (hexane, pentane), calcium hydride (acetonitrile, DCM and petroleum ether 40 – 60), or P_2O_5 ($CDCl_3$, C_6D_6, CD_3CN) or obtained dry from an Innovative Technologies Solvent Purification System and deoxygenated prior to use.

Laboratory coat, safety spectacles and gloves were worn at all times and all experiments conducted in an efficient fume-hood, following completion of appropriate COSHH assessments. Waste products and residues were treated appropriately and returned for disposal following separation.

Routine NMR spectra were collected on Bruker AMX250, Bruker DPX300, Bruker AMX400, Varian 200, Varian 300 and Bruker Avance 400 machines, at ambient probe temperatures. Chemical shifts were referenced to residual protio impurities in the deuterated solvent (^1H), ^{13}C shift of solvent (^{13}C), or to external aqueous 85% H_3PO_4 (^{31}P). Solvent proton shifts: $CDCl_3$, δ 7.27 (s); C_6D_6, δ 7.16 (s) ppm. Solvent carbon shifts: $CDCl_3$, δ 77.2 (t); C_6D_6, δ 128.4 (t) ppm. All ^{13}C spectra were assigned with the aid of DEPT 135 experiments, chemical shifts are reported in ppm. Coupling constants are reported in Hz, where direct measurement from first-order spectra was possible.

EI mass spectra were recorded on a Kratos Concept 1H or Micromass Autospec instrument and are reported in *(m/z)*. GC-MS analyses were performed using a Perkin-Elmer Autosystem XL GC machine (PE-5MS 30m column, internal diameter 0.25mm, film thickness 0.25μm) coupled to a Perkin-Elmer 'Turbomass' spectrometer, or a Thermo Finnegan Trace instrument (Agilent HP-5MS 30m column, internal diameter 0.25mm, film thickness 0.25μm). GC analyses were performed on an Agilent 5890 series 2 spectrometer (5% diphenyl- 95% dimethyl-polysiloxane, 25 m column, internal diameter 0.32 mm). Elemental analyses were performed by the University of North London analysis service, or in-house at the University of Durham. Infrared spectra were recorded on a Perkin Elmer 1600 spectrophotometer between KBr plates. X-ray diffraction data were collected on a Bruker CCD area detector machine running Bruker SMART software. Data reduction and refinement were performed using Bruker SAINT software, SHELXS and SHELXL and molecular visualisation using SHELXTL.

3-Propyloxybenzaldehyde 109a



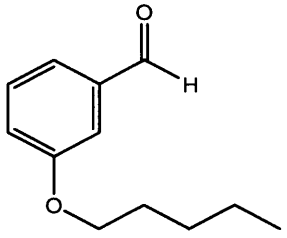
Potassium carbonate (12.1 g, 88 mmol) and caesium carbonate (3.1 g, 10 mmol) were stirred in acetone (200 mL) for 10 minutes at RT. 3-Hydroxybenzaldehyde (8.0 g, 65 mmol) was added and the reaction heated to reflux for 20 minutes. 1-Bromopropane (6.4 mL, 70 mmol) was then added *via* the condenser, and the solution heated at reflux for 18h. On cooling, the solution was isolated *via* suction filtration and reduced in volume using a rotary evaporator. Water (50 mL) was added, and the mixture extracted with diethyl ether (3 x 50 mL). Combined organic fractions were washed with aqueous sodium hydrogen carbonate (2 x 50 mL) and saturated brine (1 x 50 mL), before drying over magnesium sulfate. Solvent was removed *in vacuo* yielding a yellow oil, which was purified *via* Kügelrohr distillation (1 mmHg / 150°C) to give the desired product **109a** as a pale yellow oil, 4.9 g, 46%.

NMR: ^{1}H (200 MHz, $CDCl_3$): δ 1.04 (t, $^{3}J_{H-H}$ 7.4 Hz, 3H, CH_3); 1.82 (sext, $^{3}J_{H-H}$ 7.1 Hz, 2H, CH_2); 3.97 (t, $^{3}J_{H-H}$ 6.5 Hz, 2H, CH_2O); 6.87 (m, 1H, CH); 7.18 (m, 1H, CH); 7.38 (m, 1H, CH); 7.43 (m, 1H, CH); 9.90 (s, 1H, CHO).

$^{13}C\{^{1}H\}$ (100 MHz, $CDCl_3$): δ 10.5 (**C**H_3); 22.6 (**C**H_2); 69.8 (**C**H_2O); 113.8 (**C**H); 121.9 (**C**H); 123.2 (**C**H); 130.0 (**C**H); 137.8 (**C** ipso); 159.7 (**C** ipso); 192.2 (**C**HO).

MS (EI): Accurate mass: predicted M^+ = 206.2808, measured M^+ = 206.2897

3-Pentyloxy-benzaldehyde 109b



Potassium carbonate (11.7 g, 85 mmol) and 3-hydroxy benzaldehyde (10.0 g, 82 mmol) were heated gently in acetonitrile (180 mL) for 20 minutes. After this time 1-bromopentane (10.5 mL, 85 mmol) was added and the reaction heated to reflux for 18h. On cooling the solution was isolated by suction filtration and solvent removed *in vacuo* yielding the product **59b** as a pale yellow oil, 14.6 g, 93%.

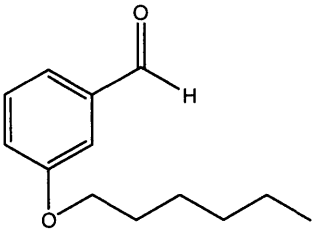
NMR: ^{1}H (300.1 MHz, $CDCl_3$): δ 0.92 (t, $^{3}J_{H-H}$ 7.0 Hz, 3H, CH_3); 1.40 (m, 4H, CH_2); 1.81 (pent, $^{3}J_{H-H}$ 7.0 Hz, 2H, CH_2); 3.98 (t, $^{3}J_{H-H}$ 6.6 Hz, 2H, CH_2O); 7.12 (m, 1H, CH); 7.40 (m, 1H, CH); 7.41 (m, 2H, CH); 9.95 (s, 1H, CHO).

$^{13}C\{^{1}H\}$ (75.5 MHz, $CDCl_3$): δ 14.0 (**C**H_3); 22.4 (**C**H_2); 28.1 (**C**H_2); 28.8 (**C**H_2); 68.2 (**C**H_2O); 112.8 (**C**H); 121.9 (**C**H); 123.2 (**C**H); 130.0 (**C**H); 137.8 (**C** ipso); 159.7, (**C** ipso); 192.1 (**C**HO).

MS (EI): Accurate mass: predicted M^+ = 192.1150, measured M^+ = 192.1146

IR: *υ max* (cm^{-1}) 2951 (s, aromatic ring); 2935 (s, aromatic ring); 2866 (s, aromatic ring) 1699 (s, CHO); 1593 (s); 1451 (s); 1261 (s); 1031 (m); 788 (s).

3-Hexyloxy-benzaldehyde 109c



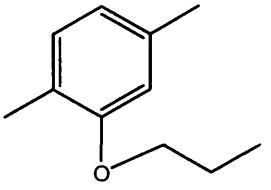
Potassium carbonate (14.6 g, 105 mmol) was stirred in acetone (300 mL) for five minutes, and a solution of 3-hydroxy benzaldehyde (8.6 g, 70 mmol) in acetone (50 mL) added. The reaction mixture was then heated at approximately 40°C for 20 minutes with stirring, before 1-iodohexane (21.5 mL, 70 mmol) was added. The solution was heated at reflux for 16h. On cooling, the reaction mixture was poured into water (200 mL), and extracted with diethyl ether (3 x 50 mL). Organic fractions were combined, dried over magnesium sulfate and the solvent removed *in vacuo*. Purification *via* Kügelrohr distillation (1 mmHg / 180°C) gave the desired product **59c** as a yellow oil, 4.3 g, 29%.

NMR: ^1H (200 MHz, $CDCl_3$): δ 0.9 (t, $^3J_{H-H}$ 6.6 Hz, 3H, CH_3); 1.34 (m, 4H, CH_2); 1.45 (m, 2H, CH_2); 1.79 (m, 2H, CH_2); 3.99 (t, $^3J_{H-H}$ 6.6 Hz, 2H, CH_2O); 7.16 (m, 1H, CH); 7.37 (m, 1H, CH); 7.41 (s, 1H, CH); 7.44 (s, 1H, CH); 9.95 (s, 1H, CHO).

$^{13}C\{^1H\}$: (100 MHz, $CDCl_3$): δ 14.0 (**C**H_3); 22.6 (**C**H_2); 25.7 (**C**H_2); 29.1 (**C**H_2); 31.6 (**C**H_2); 68.3 (**C**H_2O); 112.9 (**C**H); 122.0 (**C**H); 123.3 (**C**H); 130.0 (**C**H); 137.8 (**C** ipso); 159.8 (**C** ipso); 192.3 (**C**HO).

MS (EI): Accurate mass: predicted M^+ = 164.2011, measured M^+ = 164.2015

1,4-Dimethyl-2-propyloxybenzene 110a

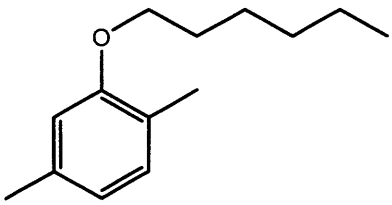


Sodium hydride (5.0 g, 60% suspension in oil, 125 mmol) was washed with dry hexane (3 x 100 mL), isolated by filtration using a cannula and dried *in vacuo*. The dry, washed sodium hydride was then suspended in dry diethyl ether (100 mL), and to this suspension was added a solution of 2,5-dimethylphenol (15.2 g, 125 mmol) in dry diethyl ether (150 mL), dropwise *via* a dropping funnel. The reaction was brought to reflux and stirred at this temperature until a thick white precipitate was formed. After cooling, excess diethyl ether was removed using a filter cannula, the isolated precipitate dried *in vacuo* and re-dissolved in dry DME (300 mL). To the solution was then added 1-bromopropane (11.9 mL, 130 mmol) *via* syringe, and the reaction heated to reflux for 18h. On cooling, the DME was removed using a rotary evaporator, and the residue taken into diethyl ether (200 mL). The solution was washed

with water (3 x 200 mL), dried over magnesium sulfate, isolated *via* suction filtration and the solvent removed *in vacuo*. The desired product **110a** was obtained pure (as determined by accurate mass spectrometry) as a pale yellow oil, 16.2 g, 78%.

NMR: ^{1}H (250 MHz, $CDCl_3$) δ 1.34 (t, $^{3}J_{H-H}$ 7.0 Hz, 3H, CH_3); 2.11 (pent, $^{3}J_{H-H}$ 7.0 Hz, 2H, CH_2); 2.59 (s, 3H, CH_3); 2.10 (s, 3H, CH_3); 4.19 (t, $^{3}J_{H-H}$ 6.6 Hz, 2H, CH_2O); 6.92 (s, 1H, CH); 6.95 (m, 1H, CH); 7.29 (m, 1H, CH).
$^{13}C\{^{1}H\}$ (62.9 MHz, $CDCl_3$) δ 9.9 (**C**H_3); 15.0 (**C**H_3); 20.6 (**C**H_3); 22.1 (**C**H_2); 71.0 (**C**H_2O); 111.2 (**C**H); 119.9 (**C**H); 122.8 (**C** ipso); 129.5 (**C**H); 135.5 (**C** ipso); 156.4 (**C** ipso).
MS (EI): Accurate mass: predicted M^+ = 164.2441, measured M^+ = 164.2443

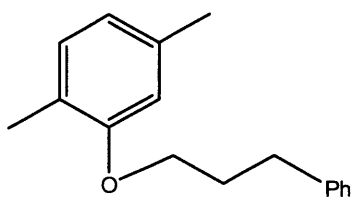
2-Hexyloxy-1,4-dimethylbenzene 110b



An identical procedure to that used for the preparation of 1,4-dimethyl-2-propyloxybenzene 110a was employed, using the following quantities:
Sodium hydride 0.3 g, 10 mmol; 2,5 dimethylphenol 1.1 g, 9 mmol; 1-iodohexane 1.5 mL, 10 mmol; diethyl ether as solvent 100 mL; DME as solvent 50 mL. The product **60b** was obtained pure (as determined by accurate mass spectrometry) as a clear oil, 1.6 g, 83%.

NMR: ^{1}H (300.1 MHz, $CDCl_3$): δ 1.55 (m, 3H, CH_3); 1.91-2.12 (m, 6H, CH_2); 2.43 (m, 2H, CH_2); 2.82 (s, 3H, CH_3); 2.95 (s, 3H, CH_3); 4.57 (t, $^{3}J_{H-H}$ 6.4 Hz, 2H, CH_2O); 7.27 (s, 1H, CH); 7.32 (m, 1H, CH); 7.64 (m, 1H, CH).
$^{13}C\{^{1}H\}$ (100 MHz, $CDCl_3$): δ 14.2 (**C**H_3); 15.8 (**C**H_3); 21.4 (**C**H_3); 22.7 (**C**H_2); 25.9 (**C**H_2); 29.5 (**C**H_2); 31.9 (**C**H_2); 67.9 (**C**H_2O); 112.1 (**C**H); 120.6 (**C**H); 123.7 (**C** ipso); 130.3 (**C**H); 137.0 (**C** ipso); 157.2 (**C** ipso).
MS (EI): Accurate mass: predicted M^+ = 206.1671, measured M^+ = 206.1675

1,4-Dimethyl-2-(3-phenylpropyloxy)benzene 110c



An identical procedure to that used for the preparation of 1,4-dimethyl-2-propyloxybenzene **110a** was employed, using the following quantities:
Sodium hydride 5.0 g, 125 mmol; 2,5 dimethylphenol 15.2 g, 125 mmol; 1-bromo, 3-phenylpropane 24 mL, 125 mmol. The product **110c** was isolated as a yellow oil, which

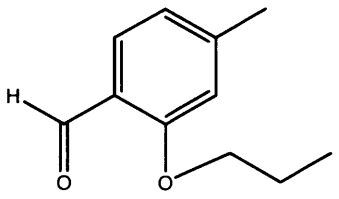
was subsequently purified using Kügelrohr distillation (1 mmHg / 120°C) to give the desired product, 25.9 g, 86%.

NMR: ^{1}H (300.1 MHz, $CDCl_3$) δ 2.02 (m, 2H, CH_2); 2.13 (s, 3H, CH_3); 2.20 (s, 3H, CH_3); 2.74 (t, $^{3}J_{H-H}$ 7.2 Hz, 2H, CH_2); 3.84 (t, $^{3}J_{H-H}$ 6.1 Hz, 2H, CH_2O); 6.50 (s, 1H, CH); 6.57 (m, 1H, CH); 6.92 (m, 1H, CH); 7.15 (m, 5H, CH).

$^{13}C\{^{1}H\}$ (75.5 MHz, $CDCl_3$) δ 16.4 (**C**H_3); 30.0 (**C**H_3); 31.6 (**C**H_2); 32.8 (**C**H_2); 67.1 (**C**H_2); 121.2 (**C**H); 124.1 (**C**H); 126.4 (**C**H); 126.7 (**C** ipso); 128.9 (**C**H); 129.1 (**C**H); 130.9 (**C**H); 137.0 (**C** ipso); 142.2 (**C** ipso); 157.5 (**C** ipso).

MS (EI): Accurate mass: predicted M^+ = 240.1514, measured M^+ = 240.1516

4-Methyl-2-propyloxybenzaldehyde 111a



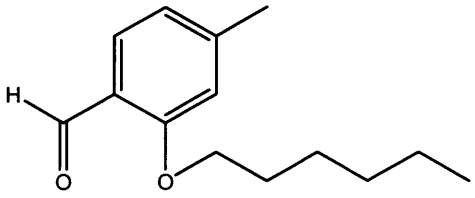
1,4-Dimethyl-2-propyloxybenzene **110a** (6.0 g, 30 mmol), copper sulfate pentahydrate (7.5 g, 30 mmol), and potassium persulfate (24.3 g, 90 mmol) were stirred vigorously in 1:1 water/acetonitrile (250 mL), and the reaction heated at reflux for 30 minutes. The cooled solution was extracted with dichloromethane (3 x 100 mL) and combined organic fractions washed with water (3 x 100 mL), separated and dried over magnesium sulfate. The solution was isolated *via* suction filtration and solvent removed *in vacuo* to give the desired product **61a** as a dark red oil, 5.1 g, 95%.

NMR: ^{1}H (200 MHz, $CDCl_3$) δ 1.35 (t, $^{3}J_{H-H}$ 7.4 Hz, 3H, CH_3); 1.79 (m, 2H, CH_2); 2.24 (s, 3H, CH_3); 3.95 (t, $^{3}J_{H-H}$ 6.4 Hz, 2H, CH_2O); 6.85 (m, 2H, CH); 7.25 (m, 1H, CH); 10.43 (s, 1H, CHO).

$^{13}C\{1H\}$ (68.9 MHz, $CDCl_3$) δ 10.9 (**C**H_3); 22.7 (**C**H_3); 22.9 (**C**H_2); 70.3 (**C**H_2O); 113.5 (**C**H); 121.9 (**C**H); 123.1 (**C** ipso); 128.6 (**C**H); 134.0 (**C** ipso); 147.8 (**C** ipso); 162.1 (**C** ipso); 190.0 (**C**HO).

MS (EI): Accurate mass: predicted M^+ = 178.2277, measured M^+ = 178.2273

2-Hexyloxy-4-methylbenzaldehyde 111b

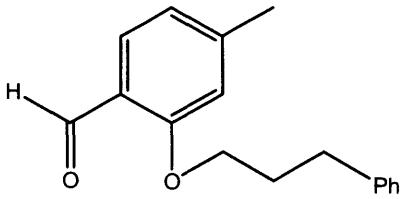


An identical procedure to that used for the preparation of 4-methyl-2-propyloxybenzaldehyde **111a** was employed, using the following quantities: 1-hexyloxy-2,5-dimethylbenzene 8.0 g, 39 mmol; copper sulfate pentahydrate 9.6 g, 39 mmol; potassium persulfate 31.3 g, 116 mmol; 1:1 acetonitrile/water as solvent 250 mL.

The desired product **111b** was isolated pure (as a pale orange oil, 6.3 g, 73%.

NMR: ^{1}H (300 MHz, $CDCl_3$) δ 0.93 (m, 3H, CH_3); 1.36 (m, 4H, CH_2); 1.45 (m, 2H, CH_2); 1.83 (m, 2H, CH_2); 2.40 (s, 3H, CH_3); 4.06 (t, $^{3}J_{H-H}$ 6.4 Hz, 2H, CH_2O); 6.78 (s, 1H, CH); 6.82 (m, 1H, CH); 7.73 (m, 1H, CH); 10.46 (s, 1H, CHO).
$^{13}C\{1H\}$ (100 MHz, $CDCl_3$): δ 12.2 (**C**H_3); 20.5 (**C**H_3); 20.7 (**C**H_2); 23.9 (**C**H_2); 29.7 (**C**H_2); 31.7 (**C**H_2); 66.6 (**C**H_2O); 111.4 (**C**H); 119.7 (**C**H); 121.0 (**C** ipso); 126.4 (**C**H); 145.5 (**C** ipso); 159.9 (**C** ipso); 187.7 (**C**HO).
MS (EI): Accurate mass: predicted M^+ = 220.3074, measured M^+ = 220.3076

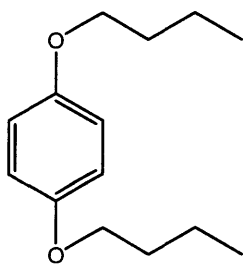
4-methyl-2-(3-Phenylpropoxy)benzaldehyde 111c



An identical procedure to that used for the preparation of 4-methyl-2-propyloxybenzaldehyde **111a** was employed, using the following quantities:
1,4-dimethyl-2-(3-phenylpropoxy)benzaldehyde **110c**, 8 g, 33 mmol; copper sulfate pentahydrate 8.3 g, 33 mmol; potassium persulfate 26.8 g, 99 mmol, 1:1 acetonitrile/water as solvent, 250 mL.
The desired product **111c** was isolated pure, as a dark red oil, 6.0 g, 72%.

NMR: ^{1}H (300.1 MHz, $CDCl_3$) δ 2.18 (m, 2H, CH_2); 2.38 (s, 3H, CH_3); 2.85 (t, $^{3}J_{H-H}$ 7.5 Hz, 2H, CH_2); 4.07 (t, $^{3}J_{H-H}$ 6.2 Hz, 2H, CH_2O); 6.72 (s, 1H, CH); 6.83 (m, 1H, CH); 7.24. (m, 5H, CH); 7.74 (m, 1H, CH); 10.45 (s, 1H, CHO).
$^{13}C\{1H\}$ (62.9 MHz, $CDCl_3$): δ 22.7 (**C**H_3); 31.0 (**C**H_2); 32.5 (**C**H_2); 67.7 (**C**H_2O); 113.4 (**C**H); 122.2 (**C**H); 123.1 (**C** ipso); 126.5 (**C**H); 128.7 (**C** ipso); 128.9 (**C**H); 141.5 (**C** ipso); 147.8 (**C** ipso); 161.9 (**C** ipso); 189.9 (**C**HO).
MS (EI): Accurate mass: predicted M^+ = 254.3236, measured M^+ = 254.3234
IR: *υ max* (cm^{-1}) 2956 (m, aromatic ring); 1681 (s, CHO); 1605 (s); 1496 (m, aromatic ring); 1453 (m, aromatic ring); 1258 (s); 1163 (s); 1112 (m); 1030 (m); 815 (m); 700 (m).

1,4-Dibutyloxybenzene 112a

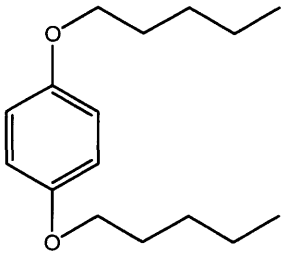


Hydroquinone (20.0 g, 0.18 mol) and potassium carbonate (55.0 g, 0.4 mol) were stirred together in actetonitrile (*ca.* 500 mL) using an overhead stirrer. Bromobutane (38.0 mL, 0.18 mol) was added, and the reaction heated at reflux for 72h. On cooling, the mixture was filtered through Celite and solvent removed from the filtrate *in vacuo*, yielding a dark brown oil

which solidified on standing. This was then recrystallised from hot methanol to give the desired product **112a** as pale beige platelets, 30 g, 75%.

CHN: Calcd. (for $C_{14}H_{22}O_2$) C 75.68%, H 9.91%, found C 75.62%, H 10.01%.
NMR: ^{1}H (300.1 MHz, $CDCl_3$) δ 1.42 (t, $^3J_{H-H}$ 7.3 Hz, 6H, CH_3); 1.92 (m, 4H, CH_2); 2.18 (m, 4H, CH_2); 4.35 (t, $^3J_{H-H}$ 6.5 Hz, 4H, CH_2O); 7.27 (s, 4H, CH).
$^{13}C\{^1H\}$ (75.5 MHz, $CDCl_3$): δ 13.9 (**C**H_3); 19.3 (**C**H_2); 31.5 (**C**H_2); 68.3 (**C**H_2O); 115.4 (**C**H); 115.8 (**C**H); 154.3 (**C** ipso).
MS (EI): M^+ = Accurate mass: predicted M^+ = 222.1620, measured M^+ = 222.1619
MP: 44.2 - 45.7 °C

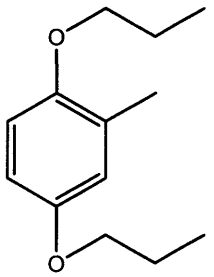
1,4-Dipentyloxybenzene 112b



An identical procedure to that used for the preparation of 1,4-dibutyloxybenzene **112a** was employed, using the following quantities:
Hydroquinone 20.0 g, 0.18 mol; potassium carbonate 74 g, 0.54 mol; bromopentane 67.0 mL, 0.54 mol. Two recrystallisations from hot methanol gave the desired product **112b** as pale beige platelets, 28.4 g, 63%.

CHN: Calcd. C 76.8%, H 10.47%, found C 76.7%, H 10.23%.
NMR: ^{1}H (300.1 MHz, $CDCl_3$) δ 0.94 (t, $^3J_{H-H}$ 7.0 Hz, 6H, CH_3); 1.41(m, 4H, CH_2); 1.77, (pent, $^3J_{H-H}$ 6.7 Hz, 4H, CH_2); 3.91 (t, $^3J_{H-H}$ 6.5 Hz, 4H, CH_2O); 6.83 (s, 4H, CH).
$^{13}C\{^1H\}$ (75.5 MHz, $CDCl_3$): δ 14.4 (**C**H_3), 22.9 (**C**H_2), 28.6 (**C**H_2), 29.5 (**C**H_2), 68.9 (**C**H_2O), 115.7 (**C**H), 153.5 (**C** ipso).
MS (EI): M^+ = 250.
MP: 44.6 – 46.2 °C

2-Methyl-1,4-dipropoxybenzene 113a



Methylhydroquinone (8.0 g, 65 mmol), 1-bromopropane (12.2 mL, 135 mmol) and potassium carbonate (19.1 g, 138 mmol) were stirred together in dimethylformamide (300 mL) and heated at 100°C for 18h. On cooling, water was added (200 mL) and the mixture extracted with dichloromethane (3 x 200 mL). Combined organic fractions were washed with saturated aqueous sodium hydrogen carbonate (2 x 200 mL), dried over magnesium sulfate, filtered

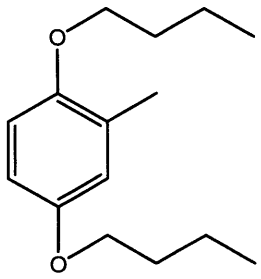
and the solvent removed *in vacuo* to yield a dark oil. This was purified *via* Kügelrohr distillation (1 mmHg / 130°C) to yield the product **113a** as a yellow oil, 9.2 g, 68%.

NMR: ^{1}H (200 MHz, $CDCl_3$): δ 0.94 (t, $^{3}J_{H-H}$ 7.5 Hz, 3H, CH_3); 0.96 (t, $^{3}J_{H-H}$ 7.3 Hz, 3H, CH_3); 1.70 (m, 4H, CH_2); 2.13 (s, 3H, CH_3); 3.77 (t, $^{3}J_{H-H}$ 6.6 Hz, 2H, CH_2O); 3.78 (t, $^{3}J_{H-H}$ 6.4 Hz, 2H, CH_2O); 6.62 (m, 3H, CH).

$^{13}C\{^{1}H\}$ (62.9 MHz, $CDCl_3$): δ 10.9 (**C**H_3); 11.0 (**C**H_3); 16.7 (**C**H_3); 23.1 (**C**H_2); 23.2 (**C**H_2); 70.5 (**C**H_2O); 70.8 (**C**H_2O); 112.0 (**C**H); 112.8 (**C**H); 118.1 (**C**H); 128.6 (**C** ipso); 151.9 (**C** ipso); 153.2 (**C** ipso).

MS (EI): Accurate mass: predicted M^+ = 208.2967, measured M^+ = 208.2964

1,4-Dibutyloxy-2-methylbenzene 113b



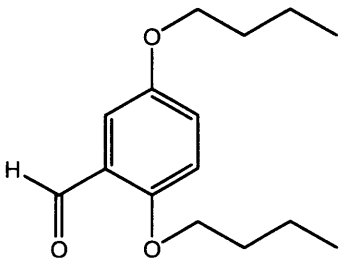
Methylhydroquinone (20 g, 0.16 mol) and potassium carbonate (44.2 g, 0.32 mol) were stirred together in acetonitrile (360 mL) using an overhead stirrer. 1-Bromobutane (34 mL, 0.32 mol) was then added, and the reaction heated to reflux for 72h. The cooled solution was then isolated *via* suction filtration and solvent removed *in vacuo* to give the desired product **113b** as a dark brown oil, 32.5 g, 86%. No further purification was required, as purity was confirmed by accurate mass spectrometry.

NMR: ^{1}H (250.1 MHz, $CDCl_3$) δ 1.00 (t, $^{3}J_{H-H}$ 7.3 Hz, 3H, CH_3); 1.01 (t, $^{3}J_{H-H}$ 7.3 Hz, 3H, CH_3); 1.52 (m, 4H, CH_2); 1.77 (m, 4H, CH_2); 2.24 (s, 3H, CH_3); 3.93 (t, $^{3}J_{H-H}$ 6.4 Hz, 4H, CH_2O); 6.74 (m, 1H, CH); 6.75 (s, 1H, CH); 6.77 (m, 1H, CH).

$^{13}C\{1H\}$ (100 MHz, $CDCl_3$): δ 13.8 (**C**H_3); 16.3 (**C**H_3); 19.3 (**C**H_2); 31.5 (**C**H_2); 31.6 (**C**H_2); 68.3 (**C**H_2O); 68.7 (**C**H_2O); 111.7 (**C**H); 112.4 (**C**H); 117.7 (**C**H); 136.4 (**C** ipso); 151.5 (**C** ipso); 152.9 (**C** ipso).

MS (EI): Accurate mass: predicted M^+ = 236.1776, measured M^+ = 236.1776.

2,5-Dibutyloxybenzaldehyde 114a



N-methyl formanilide (26.0 mL, 211 mmol) was cooled to 0°C in an ice bath and phosphorus oxychloride (19.7 mL, 211 mmol) added slowly. The resulting yellow syrup was allowed to warm to RT and stirred for 15 minutes at this temperature. 2-Methyl-1,4-dipropyloxybenzene **113a** (9.4 g, 42 mmol) was then added, and the mixture heated to 55°C for 16h. On cooling, the dark oil was poured onto ice/water (50 mL) and extracted with dichloromethane (3 x 30 mL), combined organic fractions were washed

with water (3 x 30 mL) and dried over magnesium sulfate. The solution was isolated *via* suction filtration and solvent removed *in vacuo* to yield the desired product **114a** as a dark orange oil, 6.0 g, 57 %. No further purification was required, as purity was confirmed by accurate mass spectrometry.

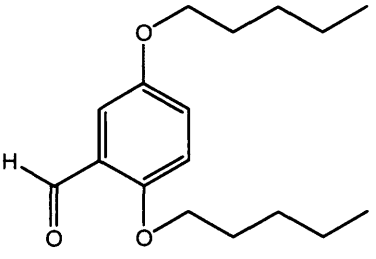
NMR: ^{1}H (250.1 MHz, $CDCl_3$) δ 0.89 (t, $^{3}J_{H-H}$ 7.3 Hz, 3H, CH_3); 0.91 (t, $^{3}J_{H-H}$ 7.2 Hz, 3H, CH_3); 1.40 (sext, $^{3}J_{H-H}$ 7.0 Hz, 2H, CH_2); 1.42 (sext, $^{3}J_{H-H}$ 7.0 Hz, 2H, CH_2); 1.70 (m, 4H, CH_2); 3.90 (t, $^{3}J_{H-H}$ 6.5 Hz, 2H, CH_2O); 3.96 (t, $^{3}J_{H-H}$ 6.5 Hz, 2H, CH_2O); 6.8 (m, 1H, CH); 7.19 (s, 1H, CH); 7.27 (m, 1H, CH); 10.43 (s, 1H, CHO).

$^{13}C\{^{1}H\}$ (75.5 MHz, $CDCl_3$): δ 13.8 (**C**H_3); 19.2 (**C**H_2); 19.3 (**C**H_2); 31.2 (**C**H_2); 31.3 (**C**H_2); 68.3 (**C**H_2O); 68.9 (**C**H_2O); 110.9 (**C**H); 114.4 (**C**H); 124.0 (**C**H); 148.0 (**C** ipso); 153.0 (**C** ipso); 156.3 (**C** ipso); 189.7 (**C**HO).

MS (EI): Accurate mass: predicted M^+ = 250.3334, measured M^+ = 250.3338

IR: *υ max* (cm^{-1}): 2959 (m, aromatic ring); 2934 (m, aromatic ring); 2872 (m, aromatic ring); 1681 (s, CHO); 1494 (s); 1467 (m); 1277 (s); 1212 (s); 1162 (s); 1027 (m); 810 (m).

2,5-dipentyloxybenzaldehyde 114b



An identical procedure to that used for the preparation of 2,5-dibutyloxybenzaldehyde **114a** was employed, using the following quantities:

N-Methyl formanilide 14.3 mL, 115 mmol; phosphoryl chloride 11.2 mL, 120 mmol; 1,4-bis-pentyloxy-benzene **112b** 6.0 g, 24 mmol. was added and the reaction heated at 55°C for 16h. The desired product **114b** was isolated as an orange oil, 4.9 g, 74%. No further purification was required, as purity was confirmed by accurate mass spectrometry.

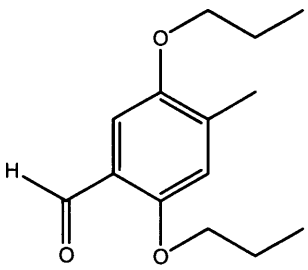
NMR: ^{1}H (300 MHz, $CDCl_3$) δ 0.85 (m, 6H, CH_3); 1.32 (m, 8H, CH_2); 1.70 (m, 4H, CH_2); 3.85 (t, $^{3}J_{H-H}$ 6.4 Hz, 2H, CH_2O); 3.94 (t, $^{3}J_{H-H}$ 6.4 Hz, 2H, CH_2O); 7.01 (m, 1H, CH); 7.19 (s, 1H, CH); 7.23 (m, 1H, CH); 10.39 (s, 1H, CHO).

$^{13}C\{^{1}H\}$ (75.5 MHz, $CDCl_3$): δ 14.4 (**C**H_3); 22.8 (**C**H_2); 28.5 (**C**H_2); 28.6 (**C**H_2); 29.3 (**C**H_2); 29.5 (**C**H_2); 69.0 (**C**H_2O); 69.5 (**C**H_2O): 111.2 (**C**H); 114.7 (**C**H); 115.7 (**C**H); 153.4 (**C** ipso); 156.7 (**C**H); 190.1 (**C**HO).

MS (EI): Accurate mass: predicted M^+ = 278.1882, measured M^+ = 278.1882.

IR: *υ max* (cm^{-1}) 2933 (m, aromatic ring); 1680 (s, CHO); 1495 (s); 1216 (s); 1028 (s); 820 (m).

4-Methyl-2,5-dipropoxybenzaldehyde 115a



An identical procedure to that used for the preparation of 2,5-dibutyloxybenzaldehyde **114a** was employed, using the following quantities:

N-methyl formanilide 5.8 mL, 48 mmol; phosphorus oxychloride 4.45 mL, 48 mmol; 2-methyl-1,4-dipropyloxybenzene **113a** 2 g, 9.6 mmol. The crude product was isolated as a dark oil, which solidified on standing. Recrystallisation from hot methanol yielded the desired product **115a** as greenish brown crystals, 1.3 g, 59%.

CHN: Calcd (for $C_{14}H_{20}O_3$) C 71.19%, H 8.47%, found C 70.33%, H 8.50%.

NMR: ^{1}H (200 MHz, $CDCl_3$) δ 1.04 (t, $^3J_{H-H}$ 7.4 Hz, 3H, CH_3); 1.06 (t, $^3J_{H-H}$ 7.4 Hz, 3H, CH_3); 1.83 (m, 4H, CH_2); 2.28 (s, 3H, CH_3); 3.93 (t, $^3J_{H-H}$ 6.4 Hz, 2H, CH_2O); 3.99 (t, $^3J_{H-H}$ 6.4 Hz, 2H, CH_2O); 6.80 (s, 1H, CH); 7.23 (s, 1H, CH); 10.43 (s, 1H, CHO).

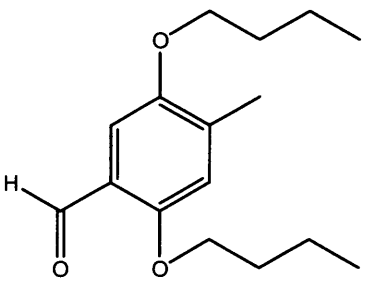
$^{13}C\{^1H\}$ (100.6 MHz, $CDCl_3$): δ 10.6 (**C**H_3); 17.2 (**C**H_3); 22.6 (**C**H_2); 70.0 (**C**H_2O); 70.7 (**C**H_2O); 108.4 (**C**H); 115.7 (**C**H); 123.1 (**C** ipso); 136.8 (**C** ipso); 151.4 (**C** ipso); 156.2 (**C** ipso); 189.4 (**C**HO).

MS (EI): $M^+ = 236$

IR: *υ max* (cm^{-1})*:* 2966 (m, aromatic ring); 2851 (w, aromatic ring); 1671 (s, CHO); 1495 (m); 1474 (m); 1391 (s); 1259 (s); 1212 (s); 1177 (m); 1120 (m); 1024 (s); 907 (m); 880 (m); 762 (s); 706 (s).

MP: 50.3 – 52.2 °C

2,5-Dibutyloxy-4-methylbenzaldehyde 115b



N-Methyl formanilide (26.0 mL, 211 mmol) was cooled to 0°C in an ice bath, and $P(O)Cl_3$ (19.7 mL, 211 mmol) added. The resulting yellow syrup was allowed to warm to RT over 20 minutes during which time it solidified forming a waxy yellow material. 2-Methyl-1,4-dibutoxybenzene (10.0 g, 42.3 mmol) was then added and the mixture heated to 55°C whereupon a dark-coloured syrup was formed. Heating was maintained at this temperature for 36h, after which time the reaction was poured into iced water (200 mL). The brown precipitate thus formed was isolated by vacuum filtration and recrystallised from hot methanol to yield the desired product **115b** as a brown powder. A second crop of solid was obtained following concentration and cooling of the mother liquor; total yield 8.8 g, 79%.

CHN: Calcd. (for $C_{16}H_{24}O_3$) C 72.69 %, H 9.15 %, found C 72.52 %, H 9.22 %.

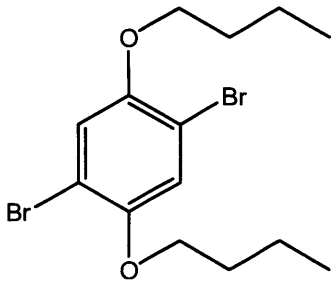
NMR: ^{1}H (200 MHz, $CDCl_3$): δ 1.02 (t, $^{3}J_{H-H}$ 7.2 Hz, 3H, CH_3); 1.03 (t, $^{3}J_{H-H}$ 7.2 Hz, 3H, CH_3); 1.55 (m, 4H, CH_2); 1.84 (m, 4H, CH_2); 2.32 (s, 3H, Ar-CH_3); 4.00 (t, $^{3}J_{H-H}$ 6.4 Hz, 2H, CH_2O); 4.07 (t, $^{3}J_{H-H}$ 6.5 Hz, 2H, CH_2O); 6.84 (s, 1H, CH); 7.27 (s, 1H, CH); 10.46 (s, 1H, CHO).

$^{13}C\{^{1}H\}$ (100 MHz, $CDCl_3$): δ 13.8 (**C**H_3); 13.8 (**C**H_3); 17.2 (**C**H_3); 19.3 (**C**H_2); 19.3 (**C**H_2); 31.3 (**C**H_2); 31.4 (**C**H_2); 68.3 (**C**H_2O); 68.9 (**C**H_2O); 108.3 (**C**H); 115.7 (**C**H); 123.1 (**C** ipso); 136.8 (**C** ipso); 151.4 (**C** ipso); 156.2 (**C** ipso); 189.4 (**C**HO).

MS (EI): $M^+ = 264$

MP: 50.7 – 51.3 °C

1,4-Dibromo-2,5-dibutyloxy benzene 118



1,4-Dibutyloxybenzene **112a** (2.3 g, 10 mmol) was dissolved in acetic acid (*ca.* 40 mL). A solution of bromine (2.1 mL, 41 mmol) in acetic acid (*ca.* 50 mL) was added and the reaction stirred at room temperature for 1h, after which time a white precipitate had formed. This was collected *via* suction filtration and washed with water to remove any remaining acetic acid, then dried *in vacuo* to give the desired product **118** as a white microcrystalline powder, 3.2 g, 81%.

CHN: Calcd. (for $C_{14}H_{20}O_2Br_2$) C 44.35%, H 5.39%, Found C 44.40%, H 5.29%.

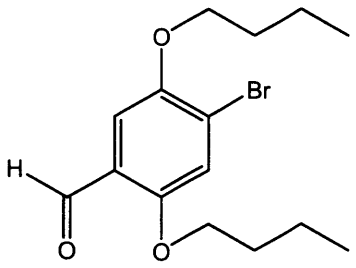
NMR: ^{1}H (200 MHz, $CDCl_3$): δ 0.92 (t, $^{3}J_{H-H}$ 7.4 Hz, 6H, CH_3); 1.46 (m, 4H, CH_2); 1.73 (m, 4H, CH_2); 3.89 (t, $^{3}J_{H-H}$ 6.4 Hz, 4H, CH_2O); 7.03 (s, 2H, CH).

$^{13}C\{^{1}H\}$ (100 MHz, $CDCl_3$): δ 13.8 (**C**H_3); 19.2 (**C**H_2); 31.2 (**C**H_2); 70.0 (**C**H_2O); 111.2 (**C** ipso); 118.5 (**C**H); 150.1 (**C** ipso).

MS (EI): $M^+ = 379$

MP: 72.3 – 73.5 °C

4-Bromo-2,5-dibutoxybenzaldehyde 119

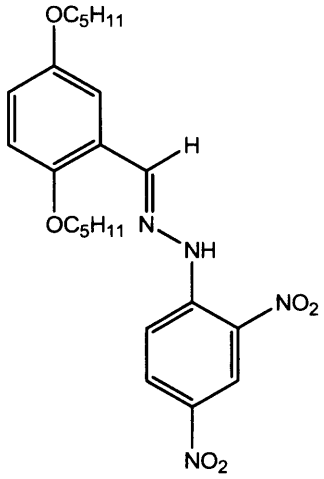


1,4-dibromo-2,5-dibutyloxybenzene **118** (2.0 g, 5 mmol) was dissolved in dry diethyl ether (*ca.* 40 mL) and cooled to -78°C. Butyl lithium (3.3 mL, 1.6 M solution in hexanes, 5 mmol) was added dropwise v*ia* syringe and the reaction stirred at -78°C for 15 minutes. After this time DMF (0.5 mL, 6 mmol) was added, the reaction allowed to warm to room temperature, and stirred for 1h. Quenching with water (30 mL) and extraction with diethyl ether (3 x 30 mL) yielded a yellow solution, which was washed

with water (2 x 30 mL) and saturated brine (2 x 30 mL), dried over magnesium sulfate, isolated by filtration and the solvent removed *in vacuo* to give a yellow solid. This was purified *via* column chromatography on silica gel (25:75 diethyl ether:hexane), yielding a yellow solid, which was then recrystallised from hot methanol to give the desired product **119** as pale yellow needles, 1.4 g, 79%.

CHN: Calcd. (for $C_{15}H_{21}O_3Br$) C 54.71%, H 6.38%, Found C 54.75%, H 6.48%.
NMR: ^1H (200 MHz, $CDCl_3$): δ 0.99 (t, $^3J_{H-H}$ 7.3 Hz, 3H, CH_3); 1.00 (t, $^3J_{H-H}$ 7.3 Hz, 3H, CH_3); 1.53 (pentet, $^3J_{H-H}$ 7.4 Hz, 2H, CH_2); 1.54 (pentet, $^3J_{H-H}$ 7.3 Hz, 2H, CH_2); 4.03 (t, $^3J_{H-H}$ 6.4 Hz, 2H, CH_2O); 4.04 (t, $^3J_{H-H}$ 6.3 Hz, 2H, CH_2O); 7.24 (s, 1H, CH); 7.32 (s, 1H, CH); 10.42 (s, 1H, CHO).
$^{13}C\{^1H\}$ (100 MHz, $CDCl_3$): δ 13.7 (**C**H_3); 13.8 (**C**H_3); 19.2 (**C**H_2); 31.1 (**C**H_2); 69.2 (**C**H_2O); 69.6 (**C**H_2O); 110.7 (**C**H); 118.5 (**C**H); 120.9 (**C** ipso); 124.4 (**C** ipso); 149.9 (**C** ipso); 155.8 (**C** ipso); 188.9 (**C** ipso).
MS (EI): $M^+ = 328.07$
MP: 73.8 – 75.8 °C

_N_-(2,5-dipentyloxybenzylidene)-_N'_-(2,4-dinitrophenyl) hydrazine 120



2,5-dipentyloxybenzaldehyde **114b** (1.0 g, 3.5 mmol) was dissolved in absolute ethanol (25 mL), and water (5 mL) added. To this solution was added dinitrophenyl hydrazine (0.7 g, 3.6 mmol) in absolute ethanol (20 mL). The reaction was stirred at RT for 30 minutes, and filtered to yield an orange solid. This was recrystallised from hot methanol (*ca.* 10 mL) to yield the product **120** as an orange powder, 0.6 g, 35%.

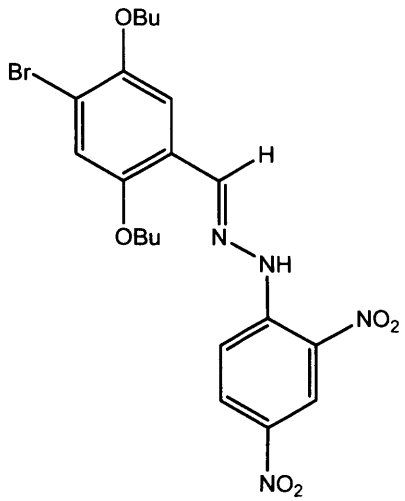
CHN: Calcd (for $C_{21}H_{26}O_6N_4$) C 60.83%, H 6.60%, N 12.20%, found C 60.16%, H 6.25%, N 11.83%.
NMR: ^1H (300.1 MHz, $CDCl_3$) δ 0.96, (t, $^3J_{H-H}$ 7.2 Hz, 3H, CH_3); 0.97, (t, $^3J_{H-H}$ 7.2 Hz, 3H, CH_3); 1.45 (m, 8H, CH_2); 1.84 (m, 4H, CH_2); 3.99, (t, $^3J_{H-H}$ 6.7 Hz, 2H, CH_2O); 4.01 (t, $^3J_{H-H}$ 6.4 Hz, 2H, CH_2O); 6.95 (m, 2H, CH); 7.51, (m, 1H, CH); 8.10 (m, 1H, CH); 8.36, (m, 1H, CH); 8.50 (s, 1H, HC=N); 9.15 (m, 1H, CH), 11.23 (s, 1H, CHN).
$^{13}C\{^1H\}$ (75.5 MHz, $CDCl_3$) δ 14.5 (**C**H_3); 22.8 (**C**H_2); 22.9 (**C**H_2); 28.7 (**C**H_2); 29.4 (**C**H_2); 29.5 (**C**H_2); 69.0 (**C**H_2O); 69.6 (**C**H_2O); 111.7 (**C**H); 114.0 (**C**H); 117.2 (**C**H);

119.3 (**C**H); 122.5 (**C** ipso); 124.0 (**C**H); 129.5 (**C** ipso); 130.4 (**C**H); 138.4 (**C** ipso); 144.5 (**C**HN); 145.2 (**C** ipso); 152.8 (**C** ipso); 153.3 (C ipso).

MS (EI): $M^+ = 459$

IR: *υ max* (cm^{-1}): 3287 (w, br, N-H); 2391 (w, aromatic ring); 2858 (w, aromatic ring); 1616 (s, C=N); 1495 (s); 1325 (s); 1221 (s); 1134 (s); 1013 (s); 824 (s); 740 (s).

_N_-(4-bromo-2,5-dibutyloxybenzylidene)-_N'_-(2,4-dinitrophenyl)hydrazine 121



To water (10 mL) was added potassium bromide (1.0 g, 9 mmol) and bromine (0.50 g, 3 mmol). *N*-(2,5-di-butyloxy-benzylidene)-*N'*-(2,4-dinitrophenyl)-hydrazine **120** (0.5 g, 1 mmol) was then added, and the resulting orange mixture stirred at room temperature for 72h. After this time, an orange precipitate had formed which was collected using suction filtration and recrystallised from hot toluene to yield the desired product **121** as an orange powder, 0.3 g, 64%.

CHN: Calcd. (for $C_{21}H_{25}O_6N_4Br$) C 49.52%, H 4.95%, N 11.00%, found C 49.28%, H 4.89%, N 11.37%.

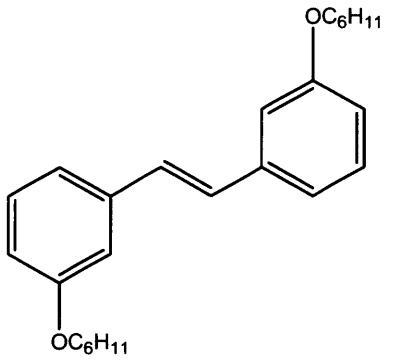
NMR: ^1H (300.1 MHz, $CDCl_3$) δ 1.03 (t, $^3J_{H-H}$ 7.0 Hz, 3H, CH_3); 1.04 (t, $^3J_{H-H}$ 7.2 Hz, 3H, CH_3); 1.53 (sext, $^3J_{H-H}$ 7.5 Hz, 2H, CH_2); 1.58 (sext, $^3J_{H-H}$ 7.5 Hz, 2H, CH_2); 1.85 (m, 4H, CH_2); 4.01 (t, $^3J_{H-H}$ 6.5 Hz, 2H, CH_2O); 4.10 (t, $^3J_{H-H}$ 6.2 Hz, 2H, CH_2O); 7.17 (s, 1H, CH); 7.50 (s, 1H, CH); 8.06 (m, 1H, CH); 8.38 (m, 1H, CH); 8.45 (s, 1H, HC=N); 9.17 (m,1H, CH); 11.35 (s, 1H, CHN).

$^{13}C\{^1H\}$ (100 MHz, $CDCl_3$) δ 13.8 (**C**H_3); 13.9 (**C**H_3); 19.3 (**C**H_2); 31.2 (**C**H_2); 31.3 (**C**H_2); 69.3 (**C**H_2O); 69.9 (**C**H_2O); 110.2 (**C**H); 116.6 (**C**H); 117.9 (**C**H); 121.3 (**C** ipso); 123.6 (**C**H); 129.3 (**C** ipso); 129.9 (**C**H); 138.2 (**C** ipso); 143.5 (**C**HN); 144.7 (**C** ipso); 150.0 (**C** ipso); 152.4 (**C** ipso).

MS (EI): $M^+ = 510$

MP: 192.8 – 194.9 °C

3,3'-Dihexyloxy-*trans*-stilbene 122a



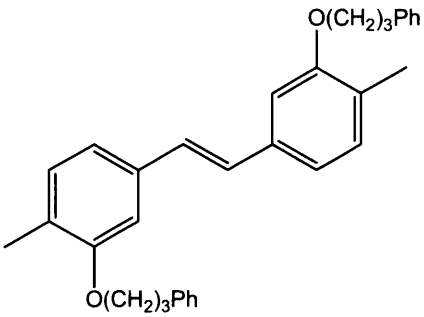
To a stirred suspension of zinc-copper couple (6.4 g, 98.6 mmol) in dry THF (50 mL) was added titanium tetrachloride (7.4 g, 39.1 mmol) slowly at -10°C, under an atmosphere of N_2. The dark green mixture was

subsequently heated to 70°C and a solution of 3-hexoxy benzaldehyde **109c** (3 g, 14.5 mmol) in dry THF (200 mL) added dropwise. Stirring was continued at reflux for 18h. The cooled solution was hydrolysed by dropwise addition of sodium hydrogen carbonate solution (10%, 250 mL) Extraction with diethyl ether (3 x 50 mL) gave a yellow solution, which was dried over magnesium sulfate and yielded a yellow solid after removal of all volatile components under reduced pressure. Recrystallisation from hot ethanol gave the product **122a** as white needles. (1.34g, 24%)

CHN: Calcd. (for $C_{26}H_{36}O2$) C 82.06 %, H 9.53 %, found C 82.17 %, H 9.55 %.
NMR: ^{1}H (250 MHz, $CDCl_3$): δ 0.90 (t, $^3J_{H-H}$ 7.0 Hz, 6H, CH_3); 1.35 (m, 8H, CH_2); 1.45 (m, 4H, CH_2); δ 1.80 (m, 4H, CH_2); 4.01 (t, $^3J_{H-H}$ 6.3 Hz, 4H, CH_2O); 6.81 (s, 2H HC=CH); 7.13 (m, 6H, CH); 7.25 (m, 2H, CH).
$^{13}C\{^1H\}$(62.9 MHz, $CDCl_3$): δ 14.4 (**C**H_3); δ 23.0 (**C**H_2); δ 26.1 (**C**H_2); δ 29.7 (**C**H_2); δ 32.0 (**C**H_2); δ 68.4 (**C**H_2O); δ 112.7 (**C**H); δ 114.3 (=**C**HPh); δ 119.5, (**C**H); δ 129.2 (**C**H); δ 129.9 (**C**H).
MS (EI): $M^+ = 380$

4,4'-Dimethyl-3,3'-di(3-phenylpropoxy)-*trans*-stilbene

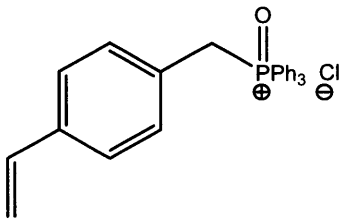
122b.



An identical procedure to that used for the preparation of 3,3'-dihexoxy-*trans*-stilbene **122a** was employed, using the following quantities: 4-methyl-2-(3-phenylpropoxy) benzaldehyde **111c** 6.95 g, 27 mmol, zinc-copper couple 11.1 g, 171 mmol, titanium tetrachloride 7.5 mL, 69 mmol.
The desired product was obtained as a dark brown oil. Recrystallisation from hot petroleum ether yielded the product **122b** as yellow crystals, 1.3 g, 21 %.

CHN: Calcd. (for $C_{32}H_{32}O_2$) C 85.68 %, H 7.19 %, found C 85.79 %, H 7.25 %.
NMR: ^{1}H (300.1 MHz, $CDCl_3$) δ 2.02 (m, 4H, CH_2); 2.74 (t, $^3J_{H-H}$ 7.2 Hz, 4H, CH_2); 3.84 (t, $^3J_{H-H}$ 6.1 Hz, 4H, CH_2); 6.50 (s, 2H, CH); 6.57 (m, 2H, CH); 6.76 (s, 2H HC=CH); 6.92 (m, 2H, CH); 7.15 (m, 10H, CH).
$^{13}C\{^1H\}$(62.9 MHz, $CDCl_3$): 31.6 (**C**H_2); 32.8 (**C**H_2); 67.1 (**C**H_2); δ 114.3 (**HC=CH**); 121.2 (**C**H); 124.1 (**C**H); 126.4 (**C**H); 126.7 (**C**H); 128.9 (**C**H); 129.1 (**C**H); 130.9 (**C**H); 137.0 (**C** ipso); 157.5 (**C** ipso).
MS (EI): $M^+ = 448$

4-Vinylphenyltriphenylphosphonium chloride 126



Triphenylphosphine (12.8 g, 49 mmol) was dissolved in dichloromethane (*ca.* 100 mL), and 4-vinyl benzyl chloride (3.7 mL, 25 mmol) added *via* syringe. The reaction was then heated to reflux for 48h. On cooling, the solvent was reduced in volume using a rotary evaporator, and a white precipitate formed. This was isolated *via* suction filtration and dried *in vacuo* to give the desired product **126** as a white powder, 7.6 g, 74%.

CHN: Calcd. (for $C_{27}H_{24}ClOP$) C 75.26 %, H 5.61 %, found C 75.39 %, H 5.68 %.

NMR: ^{1}H (400 MHz, $CDCl_3$): δ 5.21 (dd, $^{2}J_{H-H}$ ~0 Hz*, $^{3}J_{H-H}$ 11.2 Hz, 1H, H_2C=CH); 5.47 (d, $^{2}J_{H-P}$ 43.2 Hz, 2H, CH_2P); 5.66 (dd, $^{2}J_{H-H}$ ~0 Hz*, $^{3}J_{H-H}$ 17.6 Hz, 1H, H_2C=CH); 6.77 (dd, $^{2}J_{H-H}$ 17.6 Hz, $^{3}J_{H-H}$ 10.8 Hz, 1H, H_2C=C*H*); 7.12 (m, 4H, CH); 7.683 (m, 10H, CH).

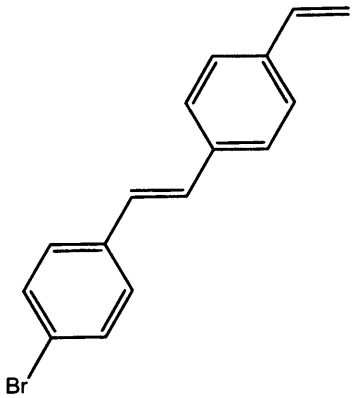
^{31}P {^{1}H} (90 MHz, $CDCl_3$): δ 23.8.

^{13}C {^{1}H} (100.6 MHz, $CDCl_3$): δ 30.4 (d, $^{1}J_{C-P}$ 46.0 Hz, **C**H_2P); 114.7 (C=**C**H_2); 117.8 (d, $^{1}J_{C-P}$ 85.1 Hz, **C**-P); 126.4 (d, $^{3}J_{C-P}$ 2.9 Hz, **C**H); 126.7 (d, $^{2}J_{C-P}$ 8.7 Hz, **C** ipso); 130.1 (d, $^{2}J_{C-P}$ 12.3 Hz, **C**H); 131.7 (d, $^{4}J_{C-P}$ 5.9 Hz, **C**H); 134.3 (d, $^{3}J_{C-P}$ 9.6 Hz, **C**H); 134.9 (d, $^{4}J_{C-P}$ 2.9 Hz, **C**H); 135.9 (d, $^{6}J_{C-P}$ 2.9 Hz, H**C**=CH_2); 137.4 (d, $^{5}J_{C-P}$ 4.4 Hz, **C** ipso).

MS (EI): $M^+ = 430$

*Accurate values for the extremely small geminal coupling constants could not be determined.

4-Vinyl-4'-bromostilbene 127



To an aqueous solution (50 mL) of sodium hydroxide (10 g, 0.4 mol) was added a solution of 4-vinyl triphenylphosphonium chloride **76** (4 g, 8 mmol) and 4-bromo benzaldehyde **75** (1.8 g, 8 mmol) in dichloromethane (20 mL). The reaction mixture was stirred vigorously at room temperature for 30 minutes after which time water (50 mL) was added. The solution was then extracted with dichloromethane (3 x 30 mL) and combined organic fractions dried over magnesium sulfate. TLC analysis showed three spots at R_f values of 0.15, 0.68 and 0.75. Purification *via* column chromatography (90:10 hexane/diethyl ether) yielded the desired product **127** as a white solid, 0.9 g, 35%.

CHN: Calcd. (for $C_{16}H_{13}Br$) C 67.39 %, H 4.59 %, found C 67.43 %, H 4.57 %

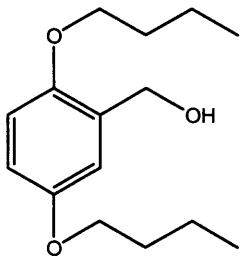
NMR: ^1H (250.1 MHz, $CDCl_3$): δ 5.18 (dd, $^3J_{H-H}$ 10.8 Hz, $^2J_{H-H}$ 0.7 Hz, 1H, CH); 5.69 (dd, $^3J_{H-H}$ 18.3 Hz, $^2J_{H-H}$ 0.6 Hz, 1H, CH); 6.64 (m, 1H, CH); 6.97 (m, 2H, CH); 7.43 (m, 8H, CH).

$^{13}C\{^1H\}$ (100 MHz, $CDCl_3$): δ 112.91 (**CH_2**=CH); 125.59 (**C**H); 125.72 (**C**H); 126.3 (**C**=**C**); 126.94 (**C**H); 127.98 (**C**=**C**); 128.025 (**C**=**C**); 130.39 (**C**H); 130.79 (**C**H); 131.06 (**C** ipso); 131.16 (**C** ipso); 136.21 (**C** ipso).

MS (EI): $M^+ = 280$

IR: *υ max* (cm^{-1})*:* 3017 (w, aromatic ring); 1484 (m); 1407 (m); 1071 (m); 970 (s); 835 (s).

2,5-Dibutyloxy benzyl alcohol 128a.



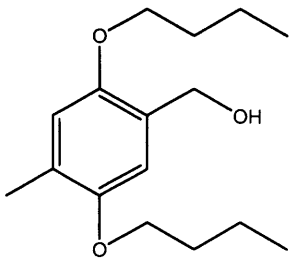
2,5-Dibutyloxybenzaldehyde **114a** (4 g, 16 mmol) was dissolved in dry diethyl ether (*ca.* 100 mL), and cooled to 0°C. Lithium aluminium hydride (16 mL, 1M solution in diethyl ether, 16 mmol) was then added slowly *via* syringe, the reaction allowed to warm to RT and stirred for 18h at this temperature. The reaction was quenched with dilute aqueous hydrochloric acid, and extracted with diethyl ether (3 x 50 mL). Combined organic fraction were washed with water and dried over magnesium sulfate. Isolation of the solution *via* suction filtration and removal of the solvent *in vacuo* yielded the desired product **128a** as a pale yellow oil, 2.5 g, 61%. No further purification was required, as purity was confirmed by accurate mass spectrometry.

NMR: ^1H (400 MHz, $CDCl_3$): δ 0.89 (t, $^3J_{H-H}$ 7.4 Hz, 3H, CH_3); 0.90 (t, $^3J_{H-H}$ 7.6 Hz, 3H, CH_3); 1.40 (pent, $^3J_{H-H}$ 7.6 Hz, 2H, CH_2); 1.41 (pent, $^3J_{H-H}$ 7.6 Hz, 2H, CH_2); 1.66 (sext, $^3J_{H-H}$ 6.4 Hz, 2H, CH_2); 1.68 (sext, $^3J_{H-H}$ 6.4 Hz, 2H. CH_2); 2.39 (br $\upsilon_{½}$ 50.8 Hz, 1H, OH); 3.84 (t, $^3J_{H-H}$ 6.6 Hz, 2H, CH_2O); 3.89 (t, $^3J_{H-H}$ 6.4 Hz, 2H, CH_2O); 4.58 (s, 2H, CH_2OH); 6.69 (m, 1H, CH); 6.74 (s, 1H, CH); 6.79 (m, 1H, CH).

$^{13}C\{^1H\}$ (100.6 MHz, $CDCl_3$): δ 13.8 (**CH_3**); 19.3 (**CH_2**); 31.5 (**CH_2**); 62.4 (**CH_2**OH); 68.4 (**CH_2**O); 112.2 (**C**H); 113.9 (**C**H); 115.4 (**C**H); 130.2 (**C** ipso); 151.0 (**C** ipso); 153.1 (**C** ipso).

MS (EI): Accurate mass: predicted M^+ =252.3493, measured M^+ = 252.3494

2,5-Dibutyloxy-4-methyl benzyl alcohol 128b



An identical procedure to that used for the preparation of 2,5-dibutyloxy benzyl alcohol **128a** was employed, using the following quantities: 4-methyl-2,5-dibutyloxybenzaldehyde **115b** 3.7 g, 14 mmol; lithium aluminium hydride 14.0 mL 1M solution in diethyl ether, 14 mmol. Following removal of solvent *in vacuo*, the product **128b** was obtained as a white powder, 2.3 g, 62%.

CHN: Calcd. (for $C_{16}H_{26}O_3$) C 72.18%, H 9.77%, found C 72.05%, H 9.85 %.

NMR: ^{1}H (200 MHz, $CDCl_3$): δ 0.98 (t, $^3J_{H-H}$ 7.4 Hz, 3H, CH_3); 0.99 (t, $^3J_{H-H}$ 7.4 Hz, 3H, CH_3); 2.0 (m, 4H, CH_2); 1.77 (m, 4H, CH_2); 2.23 (s, 3H, CH_3); 2.24 (broad s, 1H, OH); 3.93 (t, $^3J_{H-H}$ 6.3 Hz, 2H, CH_2O); 3.97 (t, $^3J_{H-H}$ 6.4 Hz, 2H, CH_2O); 4.65 (s, 2H, CH_2-OH); 6.70 (s, 1H, CH); 6.78 (s, 1H, CH).

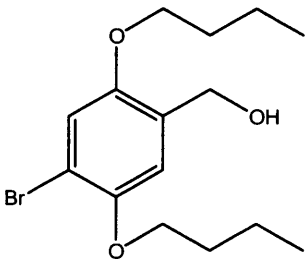
^{13}C{1H} (100 MHz, $CDCl_3$): δ 13.8 (**C**H_3); 13.9 (**C**H_3); 16.3 (**C**H_3); 19.3 (**C**H_2); 19.4 (**C**H_2); 31.5 (**C**H_2); 31.6 (**C**H_2); 62.3 (**C**H_2O); 112.8 (**C**H); 114.6 (**C**H); 127.0 (**C** ipso); 150.5 (**C** ipso); 151.1 (**C** ipso).

MS (EI): $M^+ = 266$

IR: *υ max* (cm^{-1}): 3264 (br, w, -OH); 2958 (m, aromatic ring); 2936 (m, aromatic ring); 2863 (m, aromatic ring); 1508 (m); 1391 (m); 1203 (s); 1044 (s); 1013 (s); 850 (m).

MP: 55.8 – 57.3 °C

4-Bromo-2,5-dibutyloxy benzyl alcohol 128c



4-bromo-2,5-dibutyloxybenzaldehyde **119** (0.5 g, 1.5 mmol) was dissolved in tetrahydrofuran (*ca.* 50 mL), and sodium borohydride (0.04 g, 1.5 mmol) added. The reaction was stirred at room temperature for 30 minutes after which time water (20 mL) was added. The solution was extracted with diethyl ether (3 x 20 mL) and combined organic fractions washed with brine (3 x 20 mL) and dried over magnesium sulfate. The solution was isolated *via* suction filtration and solvent removed *in vacuo* to yield the desired product **128c** as a colourless oil, 0.4g, 78%. No further purification was required, as purity was confirmed by accurate mass spectrometry.

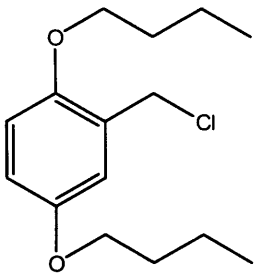
NMR: ^{1}H (300 MHz, $CDCl_3$): δ 1.16 (t, $^3J_{H-H}$ 7.3 Hz, 6H, CH_3); 1.69 (m, 4H, CH_2); 1.94 (pent, $^3J_{H-H}$ 6.3 Hz, 2H, CH_2); 1.97 (pent, $^3J_{H-H}$ 6.6 Hz, 2H, CH_2); 2.26 (br $\upsilon_{½}$ 27.4 Hz, 1H,

OH); 4.13 (t, $^{3}J_{H-H}$ 6.3 Hz, 2H, CH_2O); 4.16 (t, $^{3}J_{H-H}$ 6.4 Hz, 2H, CH_2O); 4.81, (s, 2H, CH_2OH); 7.09 (s, 1H, CH); 7.23 (s, 1H, CH).

$^{13}C\{1H\}$ (100.6 MHz, $CDCl_3$): δ 13.9 (**C**H_3); 19.4 (**C**H_2); 31.6 (**C**H_2); 41.4 (**C**H_2); 64.6 (**C**H_2OH); 68.6 (**C**H_2O); 113.0 (**C** ipso); 115.9 (**C**H); 117.5 (**C**H); 125.9 (**C** ipso); 149.8 (**C** ipso); 151.1 (**C** ipso).

MS (EI): Accurate mass: predicted M^+ = 331.2453 measured M^+ = 331.2456

2,5-Dibutyloxy benzyl chloride 129a



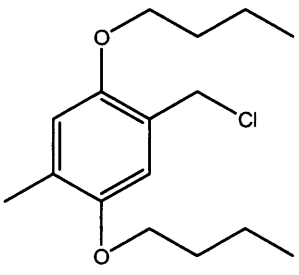
2,5-Dibutyloxy benzyl alcohol **128a** (2.5 g, 10 mmol) was dissolved in trimethylsilyl chloride (2.5 mL, 10 mmol), and dimethylsulfoxide (0.14 mL, 2 mmol) added. The reaction was stirred at room temperature for 18h, followed by removal of volatiles *in vacuo* yielding a yellow oil. This was dissolved in dichloromethane (*ca.* 20 mL), and washed with water (5 x 20 mL) to remove residual dimethylsulfoxide. The solution was then dried over magnesium sulfate, isolated *via* suction filtration and solvent removed *in vacuo* to give the desired product **129a** as a yellow oil, 2.0 g, 74 %.

NMR: ^{1}H (400 MHz, $CDCl_3$): δ 0.99 (t, $^{3}J_{H-H}$ 7.3 Hz, 3H, CH_3); 1.00 (t, $^{3}J_{H-H}$ 7.5 Hz, 3H, CH_3); 1.51 (m, 4H, CH_2); 1.78 (m, 4H, CH_2); 3.93 (t, $^{3}J_{H-H}$ 6.4 Hz, 2H, CH_2O); 3.98 (t, $^{3}J_{H-H}$ 6.4 Hz, 2H, CH_2O); 4.65 (s, 2H, CH_2Cl); 6.81 (s, 1H, CH); 6.82 (s, 1H, CH); 6.84 (s, 1H, CH).

$^{13}C\{^{1}H\}$ (100.6 MHz, $CDCl_3$): δ 13.9 (**C**H_3); 19.3 (**C**H_2); 31.5 (**C**H_2); 41.6 (**C**H_2Cl); 68.4 (**C**H_2O); 68.7 (**C**H_2O); 113.1 (**C**H); 115.4 (**C**H); 116.8 (**C**H); 126.9 (**C** ipso); 150.9 (**C** ipso); 153.0 (**C** ipso).

MS (EI): Accurate mass: predicted M^+ =270.7949, measured M^+ = 270.7952.

4-Methyl-2,5-dibutyloxy benzyl chloride 129b.



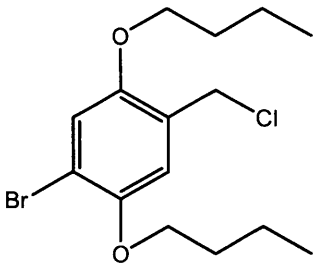
An identical procedure to that used for the preparation of 2,5-dibutyloxy benzyl chloride **129a** was employed, using the following quantities:

2,5-dibutyloxy-4-methyl benzyl alcohol **128b** 2.3 g, 9 mmol; trimethylsilyl chloride 2.2 mL, 17 mmol; dimethyl sulfoxide 0.14 mL, 2 mmol.

The desired product **129b** was isolated as a brown waxy solid, 1.6 g, 66%.

NMR: ^{1}H (200 MHz, $CDCl_3$): δ 0.99 (t, $^3J_{H-H}$ 7.4 Hz, 6H, CH_3); 1.40 (m, 4H, CH_2); 1.68 (m, 4H, CH_2); 2.14 (s, 3H, CH_3); 3.94 (t, $^3J_{H-H}$ 6.3 Hz, 2H, CH_2O); 3.98 (t, $^3J_{H-H}$ 6.3 Hz, 2H, CH_2O); 4.66 (s, 2H, CH_2Cl); 6.72 (s, 1H, CH); 6.84 (s, 1H, CH).
$^{13}C\{^1H\}$ (100.6 MHz, $CDCl_3$): δ 12.9 (**C**H_3); 15.4 (**C**H_3); 19.4 (**C**H_2); 30.6 (**C**H_2); 61.3 (**C**H_2Cl); 67.6 (**C**H_2O); 113.9 (**C**H); 114.4 (**C**H); 127.7 (**C** ipso); 149.5 (**C** ipso); 150.1 (**C** ipso).
MS (EI): Accurate mass: predicted M^+ = 284.1543, measured M^+ = 284.1543.

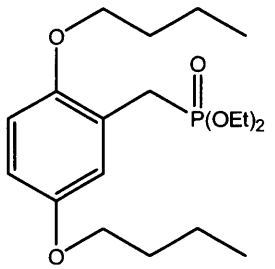
4-Bromo-2,5-Dibutyloxy benzyl chloride 129c



An identical procedure to that used for the preparation of 2,5-dibutyloxy benzyl chloride **129a** was employed, using the following quantities:
4-Bromo-2,5-dibutyloxy benzyl alcohol **128c** 0.39 g, 1.17 mmol; trimethylsilyl chloride 0.30 mL, 2.35 mmol; dimethyl sulfoxide 0.02 mL, 0.26 mmol.
The product **129c** was isolated as a yellow oil, 0.34 g, 83%.

NMR: ^{1}H (200 MHz, $CDCl_3$): δ 1.00 (t, $^3J_{H-H}$ 7.2 Hz, 6H, CH_3); 1.50 (m, 4H, CH_2); 1.79 (m, 4H, CH_2); 3.96 (t, $^3J_{H-H}$ 6.2 Hz, 2H, CH_2O); 4.00 (t, $^3J_{H-H}$ 6.3 Hz, 2H, CH_2O); 4.60 (s, 2H, CH_2Cl); 6.94 (s, 1H, CH); 7.08 (s, 1H, CH).
$^{13}C\{^1H\}$ (100.6 MHz, $CDCl_3$): δ 13.8 (**C**H_3); 19.2 (**C**H_2); 31.3 (**C**H_2); 41.2 (**C**H_2); 68.7 (**C**H_2O); 70.0 (**C**H_2Cl); 112.9 (**C** ipso); 115.9 (**C**H); 117.3 (**C**H); 125.9 (**C** ipso); 149.6 (**C** ipso); 151.1 (**C** ipso).
MS (EI): Accurate mass: predicted M^+ = 349.6910, measured M^+ = 350.0492.

(2,5-Dibutoxybenzyl)phosphonic acid diethyl ester 130a.



2,5-dibutyloxy benzyl chloride **129a** (1.9 g, 7 mmol) and triethyl phosphite (1.2 mL, 7 mmol) were heated together at 150°C for 24h. On cooling, the crude oil was purified *via* Kügelrohr distillation to yield the desired product **130a** as a pale yellow oil, 2.3 g, 86%.

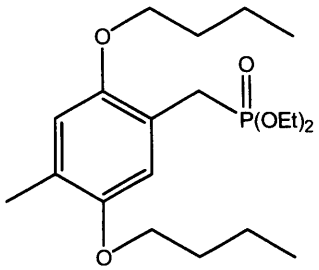
NMR: ^{1}H (400 MHz, $CDCl_3$): δ 0.96 (t, $^3J_{H-H}$ 7.4 Hz, 3H, CH_3); 0.97 (t, $^3J_{H-H}$ 7.6 Hz, 3H, CH_3); 1.25 (t, $^3J_{H-H}$ 7.0 Hz, 6H, CH_3); 1.43 (m, 4H, CH_2); 1.64 (m, 4H, CH_2); 3.23 (d, $^2J_{H-P}$ 22.0 Hz, 2H, CH_2P); 3.91 (dq, $^3J_{H-H}$ 6.4 Hz, $^3J_{P-H}$ 1.1 Hz, 4H, CH_2OP); 4.01 (t, $^3J_{H-H}$ 7.6 Hz, 2H, CH_2O); 4.05 (t, $^3J_{H-H}$ 7.2 Hz, 2H, CH_2O); 7.04 (m, 1H, CH); 7.10 (s, 1H, CH).

$^{13}C\{^1H\}$(100.6 MHz, $CDCl_3$): δ 13.8 (**C**H_3); 16.3 (**C**H_3); 19.2 (**C**H_2); 31.3 (**C**H_2); 33.2 (d, $^1J_{C\text{-}P}$ 132 Hz, **C**H_2P); 41.2 (**C**H_2); 62.1 (d, $^2J_{C\text{-}P}$ 7.9 Hz, **C**H_2O); 68.7 (**C**H_2O); 129.2 (d, $^3J_{C\text{-}P}$ 6.2Hz, **C**H); 129.6 (d, $^4J_{C\text{-}P}$ 5.3 Hz, **C**H); 130.5 (d, $^5J_{C\text{-}P}$ 3.1 Hz, **C**H); 137.4 (d, $^4J_{C\text{-}P}$ 4.4 Hz, **C** ipso); 137.9 (d, $^3J_{C\text{-}P}$ 5.9 Hz, **C** ipso); 150.3 (d, $^2J_{C\text{-}P}$ 7.9 Hz, **C** ipso).

$^{31}P\{^1H\}$ (90 MHz, C_6D_6): δ 28.21 (s)

MS (EI): Accurate mass: predicted M^+ = 372.4361, measured M^+ = 372.4374.

(2,5-Dibutoxy-4-methylbenzyl)phosphonic acid diethyl ester 130b.



An identical procedure to that used for the preparation of (2,5-dibutoxybenzyl)phosphonic acid diethyl ester **130a** was employed, using the following quantities:

2,5-dibutyloxy-4-methyl benzyl chloride **129b** 1.8 g, 7 mmol, triethyl phosphite 1.7 mL, 10 mmol.

Purification *via* Kügelrohr distillation (180°C, 0.5 mmHg) yielded the desired product **130b** as a yellow oil, 2.1 g, 84%.

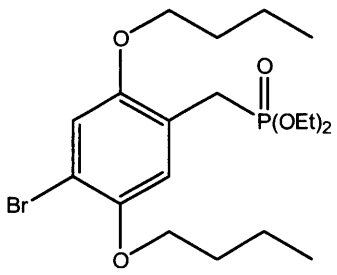
NMR: ^1H (200 MHz, $CDCl_3$): δ 0.97 (t, $^3J_{H\text{-}H}$ 7.0 Hz, 6H, CH_3); 1.25 (t, $^3J_{H\text{-}H}$ 7.0 Hz, 6H, CH_3); 1.47 (m, 4H, CH_2); 1.75 (m, 4H, CH_2); 2.18 (s, 3H, CH_3); 3.22 (d, $^2J_{H\text{-}P}$ 21.6 Hz, 2H, CH_2P); 3.91 (m, 4H, CH_2O); 4.03 (t, $^3J_{H\text{-}H}$ 7.3 Hz, 2H, CH_2O); 4.11 (t, $^3J_{H\text{-}H}$ 7.3 Hz, 2H, CH_2O); 7.00 (m, 1H, CH); 7.03 (s, 1H, CH).

$^{13}C\{^1H\}$ (100.6 MHz, $CDCl_3$): δ 13.4 (**C**H_3); 16.6 (d, $^6J_{C\text{-}P}$ 1.2 Hz, **C**H_3); 18.5 (**C**H_3); 20.2 (**C**H_2); 32.5 (**C**H_2); 32.9 (d, $^1J_{C\text{-}P}$ 137 Hz, **C**H_2P); 41.8 (**C**H_2); 61.8 (d, $^2J_{C\text{-}P}$ 6.1 Hz, **C**H_2O); 68.4 (**C**H_2O); 130.1 (d, $^3J_{C\text{-}P}$ 4.2 Hz, **C**H); 130.6 (d, $^4J_{C\text{-}P}$ 3.9 Hz, **C**H); 135.6 (d, $^3J_{C\text{-}P}$ 5.6 Hz, **C** ipso); 135.9 (d, $^4J_{C\text{-}P}$ 4.2 Hz, **C** ipso); 146.3 (d, $^5J_{C\text{-}P}$ 2.5 Hz, **C** ipso); 152.3 (d, $^2J_{C\text{-}P}$ 5.8 Hz, **C** ipso).

$^{31}P\{^1H\}$ (90 MHz, C_6D_6): δ 28.30 (s).

MS (EI): Accurate mass: predicted M^+ = 386.4627, measured M^+ = 386.4682

(4-Bromo-2,5-dibutoxybenzyl)phosphonic acid diethyl ester 130c.

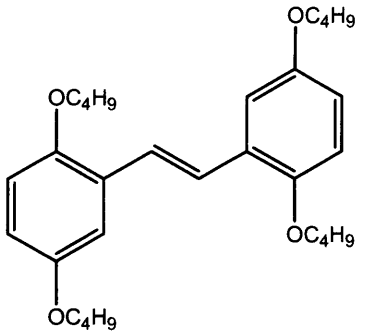


An identical procedure to that used for the preparation of (2,5-dibutoxybenzyl)phosphonic acid diethyl ester **130a** was employed, using the following quantities:

4-bromo-2,5-dibutyloxy benzyl chloride **129c** 0.84 g, 2.39 mmol; triethyl phosphite 0.4 mL, 2.39 mmol. The crude oil was purified *via* Kügelrohr distillation to yield the desired product **130c** as a pale yellow oil, 0.9 g, 83%.

NMR: ^{1}H (200 MHz, $CDCl_3$): 1.04 (t, $^{3}J_{H-H}$ 7.3 Hz, 6H, CH_3); 1.35 (t, $^{3}J_{H-H}$ 7.1 Hz, 6H, CH_3); 1.57 (m, 4H, CH_2); 1.62 (m, 4H, CH_2); 3.24 (d, $^{2}J_{H-P}$ 21.8 Hz, 2H, CH_2P); 4.01 (m, 8H, CH_2O); 7.11 (m, 1H, CH); 7.19 (s, 1H, CH).
$^{13}C\{^{1}H\}$ (100.6 MHz, $CDCl_3$): δ 12.8 (**C**H_3); 16.2 (**C**H_3); 20.7 (**C**H_2); 32.5 (**C**H_2); 32.9 (d, $^{1}J_{C-P}$ 142 Hz, **C**H_2P); 40.2 (**C**H_2); 62.3(d, $^{2}J_{C-P}$ 5.7 Hz, **C**H_2O); 67.1 (**C**H_2O); 129.3 (d, $^{4}J_{C-P}$ 2.6 Hz, 1H, **C**H); 131.1 (d, $^{3}J_{C-P}$ 4.9 Hz, 1H, **C**H); 134.5 (d, $^{3}J_{C-P}$ 5.3 Hz, **C** ipso); 136.3(d, $^{4}J_{C-P}$ 2.9 Hz, **C** ipso); 146.3 (d, $^{5}J_{C-P}$ 2.6 Hz, **C** ipso); 152.3 (d, $^{2}J_{C-P}$ 7.1 Hz, **C** ipso).
$^{31}P\{^{1}H\}$ (90 MHz, C_6D_6): δ 28.76 (s)
MS (EI): Accurate mass: predicted M^+ = 451.3321, measured M^+ = 451.3548.

2,5,2',5'-Tetrabutyloxy-*trans*-stilbene 131a



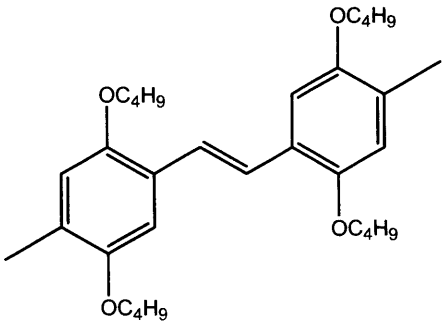
2,5-(Dibutyloxybenzyl)phosphonic acid diethyl ester **130a** (2.4 g, 7 mmol) was dissolved in dry THF (*ca.* 100 mL), and 2,5-dibutyloxybenzaldehyde **114a** (1.7 g, 7 mmol) added. To the stirred solution was added potassium *tert*-butoxide (0.98 g, 8.04 mmol) and 18-crown-6 (0.18 g, 0.67 mmol). The reaction was stirred at room temperature for 18h. Quenching with water (50 mL) and extraction with dichloromethane (3 x 50 mL) yielded a yellow solution, which was subsequently washed with brine, dried over magnesium sulfate, filtered and solvent removed *in vacuo* to give an orange solid. This was recrystallised from hot methanol to yield the desired product **131a** as yellow needles, 1.0 g, 33%.

CHN: Calcd (for $C_{30}H_{44}O_4$) C 76.92%, H 9.40%, found C 76.22%, H 9.36%.
NMR: ^{1}H (200 MHz, $CDCl_3$): δ 1.00 (t, $^{3}J_{H-H}$ 7.3 Hz, 12H, CH_3); 1.53 (m, 8H, CH_2); 1.79 (m, 8H, CH_2); 3.99 (t, $^{3}J_{H-H}$ 6.4 Hz, 8H, CH_2O); 6.79 (m, 2H, CH); 6.82 (s, 2H, CH); 7.12 (m, 2H, CH); 7.46 (s, 2H, CH).
$^{13}C\{^{1}H\}$ (75.5 MHz, $CDCl_3$): δ 13.9 (**C**H_3); 19.3 (**C**H_2); 19.4 (CH_2); 31.5 (**C**H_2); 31.6 (**C**H_2); 68.3 (**C**H_2O); 69.3 (**C**H_2O); 112.3 (**C**H); 113.9 (**C**H); 114.5 (**C**H); 129.9 (**C=C**); 128.2 (**C** ipso); 150.9 (**C** ipso); 153.3 (**C** ipso).
MS (EI): M^+ = 468

IR: *v max* (cm^{-1}): 2953 (m, aromatic ring); 2865 (m, aromatic ring); 1605 (w, C=C); 1499 (s); 1431 (m); 1215 (s); 974 (m); 808 (m).

MP: 89.9 – 92.0 °C

4,4'-Dimethyl-2,5,2',5'-tetrabutyloxy-*trans*-stilbene 131b



An identical procedure to that used for the preparation of 2,5,2',5'-tetrabutyloxy-*trans*-stilbene 81a was employed, using the following quantities: (2,5-Dibutoxy-4-methylbenzyl)phosphonic acid diethyl ester **130b** 1.5 g, 4 mmol; 2,5-dibutyloxy-4-methylbenzaldehyde **115b** 1.1 g, 4 mmol, potassium *tert*-butoxide 0.56 g, 5.05 mmol; and 18-crown-6 (0.1 g, 0.34 mmol). The crude product was recrystallised from hot methanol to yield the desired product **131b** as yellow needles, 1.0 g, 33%.

CHN: Calcd (for $C_{32}H_{48}O_4$) C 77.38%, H 9.74%, found C 77.46%, H 9.71%.

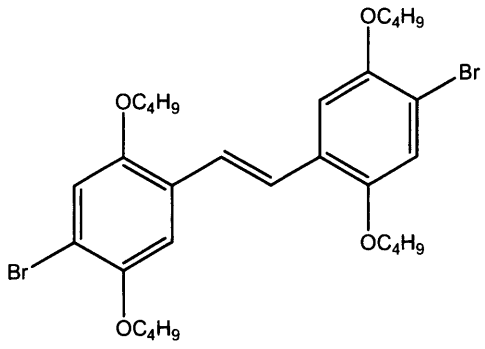
NMR: ^1H (200 MHz, $CDCl_3$): δ 0.97 (t, $^3J_{H-H}$ 7.2 Hz, 12H, CH_3); 1.27 (s, 3H, CH_3); 1.51 (m, 8H, CH_2); 1.84 (m, 8H, CH_2); 4.05 (t, $^3J_{H-H}$ 6.2 Hz, 8H, CH_2O); 7.12 (d, 2H, CH); 6.87 (s, 2H, CH); 6.98 (d, 2H, CH); 7.52 (s, 2H, CH).

$^{13}C\{1H\}$ (75.5 MHz, $CDCl_3$): δ 12.3 (**C**H_3); 16.4 (**C**H_3); 18.2 (**C**H_2); 20.1 (CH_2); 32.1 (**C**H_2); 32.6 (**C**H_2); 65.3 (**C**H_2O); 69.9 (**C**H_2O); 113.7 (**C**H); 114.2 (**C**H); 114.8 (**C**H); 130.2 (**C**=**C**); 132.1 (**C** ipso); 153.9 (**C** ipso); 155.7 (**C** ipso).

MS (EI): $M^+ = 496$.

MP: 97.2 – 97.5 °C.

4,4'-Dibromo-2,5,2',5'-tetrabutyloxy-*trans*-stilbene 131c.

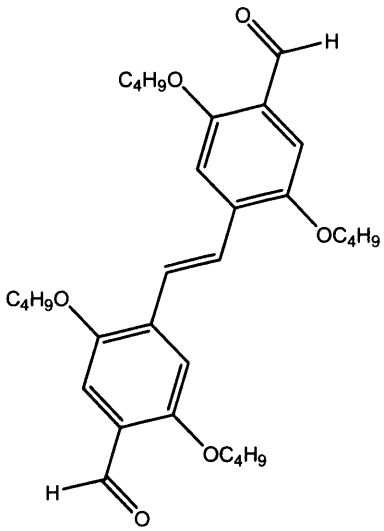


An identical procedure to that used for the preparation of 2,5,2',5'-tetrabutyloxy-*trans*-stilbene **131a** was employed, using the following quantities: (4-bromo-2,5-dibutoxybenzyl)phosphonic acid diethyl ester 0.32 g, 0.76 mmol; 4-bromo-2,5-dibutyloxybenzaldehyde 0.23 g, 0.76 mmol; potassium *tert*-butoxide 0.10 g, 0.91 mmol; 18-crown-6 (one crystal) as phase transfer catalyst.

The product **131c** was obtained after recrystallisation from hot methanol, as extremely small yellow needles, 0.11 g, 22%.

CHN: Calcd. (for $C_{30}H_{42}Br_2O_4$) C 57.52%, H 6.76%, found C 56.82%, H 6.88%.*
NMR: ^1H (400 MHz, $CDCl_3$): δ 1.00 (t, $^3J_{H-H}$ 7.2 Hz, 6H, CH_3); 1.01 (t, $^3J_{H-H}$ 7.4 Hz, 6H, CH_3); 1.56 (m, 8H, CH_2); 1.83 (m, 8H, CH_2); 3.98 (t, $^3J_{H-H}$ 6.2 Hz, 4H, CH_2O); 4.04 (t, $^3J_{H-H}$ 6.4 Hz, 4H, CH_2O); 7.09 (s, 2H, CH); 7.14 (s, 2H, CH); 7.37 (s, 2H, C=C).
$^{13}C\{^1H\}$ (100.6 MHz, $CDCl_3$): δ 12.9 (**C**H_3); 18.3 (**C**H_2); 30.4 (**C**H_2); 68.3 (**C**H_2O); 68.9 (**C**H_2O); 110.8 (**C**H); 116.9 (**C**H); 122.7 (**C**=**C**); 126.0 (**C** ipso); 148.9 (**C** ipso); 150.1 (**C** ipso).
*Despite repeated attempts, correct elemental analysis for carbon could not be obtained. This can be attributed to the compound probably having co-crystallised with 1 equivalent of methanol. A crystal structure could not be obtained as the crystals were of low quality.
MS (EI): $M^+ = 626$
MP: 102.1 – 104.1 °C

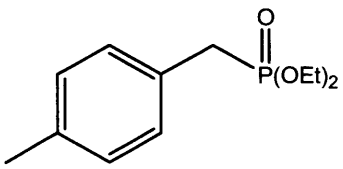
2,5,2',5'-Tetrabutyloxy-4,4'-diformyl–*trans*-stilbene 143



An identical procedure to that used for the preparation of 4-methyl-2,5-dipropyloxybenzaldehyde **115a** was employed, using the following quantities:
N-methyl formanilide 0.67 mL, 5.4 mmol; phosphorus oxychloride 0.50 mL, 5.4 mmol; 2,5,2',5'-tetrabutyloxy-*trans*-stilbene **131a** 0.50 g, 1.1 mmol.
Recrystallisation from hot methanol yielded the desired product **143** as a brown powder, 0.34 g, 61%.

CHN: Calcd. (for $C_{32}H_{44}O_6$): C 73.25 %, H 8.45 %, found C 72.88 %, H 8.34 %.
NMR: ^1H (200 MHz, $CDCl_3$) δ 0.93 (t, $^3J_{H-H}$ 7.3 Hz, 12H, CH_3); 1.49 (sext, $^3J_{H-H}$ 7.3 Hz, 8H, CH_2); 1.77 (pent, $^3J_{H-H}$ 6.5 Hz, 8H, CH_2); 3.98 (t, $^3J_{H-H}$ 6.5 Hz, 4H, CH_2O); 4.05 (t, $^3J_{H-H}$ 6.5 Hz, 4H, CH_2O); 7.21 (s, 2H, CH); 7.35 (s, 2H, CH); 7.60 (s, 2H, HC=CH); 10.46 (s, 2H, CHO).
$^{13}C\{^1H\}$ (75.5 MHz, $CDCl_3$): δ 13.8 (**C**H_3); 13.9 (**C**H_3); 19.3 (**C**H_2); 19.4 (**C**H_2); 31.3 (**C**H_2); 68.9 (**C**H_2O); 110.3 (**C**H); 110.9 (**C**=**C**); 124.8 (**C** ipso); 126.4 (**C**H); 134.1 (**C** ipso); 151.0 (**C** ipso); 156.1 (**C** ipso); 189.1 (**C**HO).
MS (EI): $M^+ = 524$

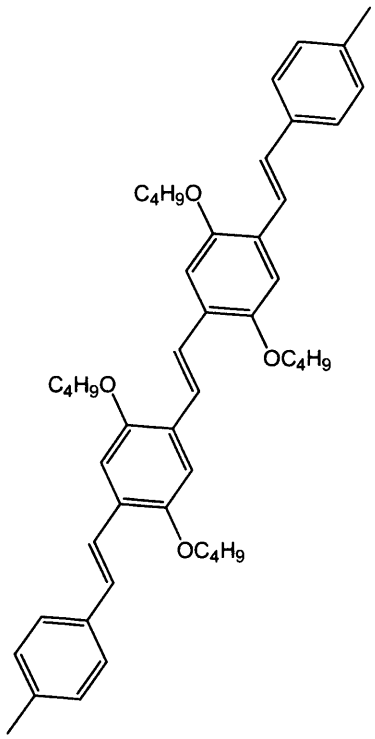
4-Methylphosphonicacid diethyl ester 144



α-Bromo-*para*-xylene (4.0 g, 22 mmol) was dissolved in dry DMF (100 mL), and triethylphosphite (3.7 mL, 22 mmol) added *via* syringe. The solution was then heated to reflux for 5h. On cooling, solvent was removed *in vacuo* to yield a cloudy, colourless oil, which was purified using flash chromatography on alumina (hexane, followed by methanol) to give the desired product **144** as a clear oil, 3.4 g, 65%.

NMR: ^{1}H (200 MHz, $CDCl_3$): δ 1.34 (t, $^{3}J_{H-H}$ 7.1 Hz, 6H, CH_3); 2.4 (s, 3H, CH_3); 3.21 (d, $^{3}J_{H-P}$ 21.4 Hz, 2H, CH_2P); 4.11 (m, 4H, CH_2); 7.21 (m, 2H, CH); 7.29 (m, 1H, CH).
$^{13}C\{^{1}H\}$ (100.6 MHz, $CDCl_3$): δ 16.3 (d, $^{6}J_{C-P}$ 5.8 Hz, **C**H_3); 21.1 (**C**H_3); 33.2 (d, $^{1}J_{C-P}$ 137 Hz, **C**H_2P); 62.1 (d, $^{2}J_{C-P}$ 7.2 Hz, **C**H_2O); 129.2 (d, $^{4}J_{C-P}$ 2.9 Hz, 1H, **C**H); 129.6 (d, $^{3}J_{C-P}$ 6.6 Hz, 1H, **C**H); 149.2 (d, $^{5}J_{C-P}$ 2.4 Hz, **C** ipso); 153.2 (d, $^{2}J_{C-P}$ 8.2 Hz, **C** ipso).
$^{31}P\ \{^{1}H\}$ (90 MHz, $CDCl_3$): δ 27.80 (s).
MS (EI): Accurate mass: predicted M^+ = 242.2512, measured M^+ = 242.2514

Oligomeric PPV 145



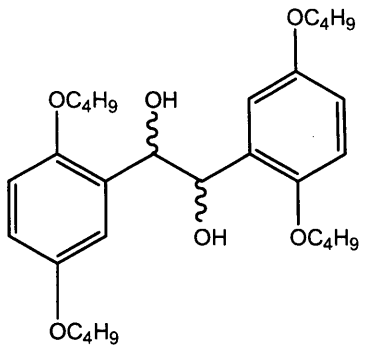
An identical procedure to that used for the preparation of 2,5,2',5'-tetrabutyloxy-*trans*-stilbene **131a** was employed, using the following quantities:
2,5,2',5'-tetrabutyloxy-4,4'-diformyl-*trans*-stilbene **143** 0.5 g, 0.9 mmol; 4-methyl phosphonic acid diethyl ester **88** 0.4 g, 0.2 mmol; potassium *tert*-butoxide 0.03 g, 0.2 mmol, 18-crown-6 (one crystal) as phase transfer catalyst.
The desired product **145** was obtained after recrystallisation from hot methanol as a yellow powder, 0.3 g, 47%.

CHN: Calcd.(for $C_{48}H_{60}O_4$) C 82.24 %, H 8.63 %, found C 81.55 % H 8.41 %.
NMR: ^{1}H (500 MHz, $CDCl_3$) δ 1.04 (t, $^{3}J_{H-H}$ 7.0 Hz 6H, CH_3); 1.60 (m, 4H, CH_2); 1.88, (pent, $^{3}J_{H-H}$ 6.5 Hz, 4H, CH_2); 2.30 (s, 3H, CH_3); 4.08 (t, $^{3}J_{H-H}$ 6.5 Hz, 2H, CH_2O); 4.09 (t, $^{3}J_{H-H}$ 6.5 Hz, 2H, CH_2O); 7.14 (s, 2H, CH); 7.15 (m, 2H, HC=C); 7.18 (s, 2H, CH); 7.20 (m, 2H, HC=C); 7.43 (m, 4H, CH); 7.46 (m, 4H, CH); 7.50 (s, 2H, HC=CH).

$^{13}C\{^1H\}$ (125 MHz, $CDCl_3$) δ 12.9 (**C**H_3); 16.3 (**C**H_3); 18.5 (**C**H_2); 30.6 (**C**H_2); 68.3 (**C**H_2O); 109.5 (**C**H); 109.7 (**C**H); 121.6 (**C**H); 122.2 (H**C**=CH); 125.4 (**C**H); 125.9 (**C** ipso); 126.5 (**C** ipso); 127.6 (H**C**=CH); 128.3 (HC=**C**H); 134.6 (**C** ipso); 136.2 (**C** ipso); 150.1 (**C** ipso).

MS (EI): $M^+ = 700$.

1,2-Di-(2,5-dibutoxyphenyl)ethane-1,2-diol 156a



2,5,2',5'-Tetrabutoxy-stilbene **131a** (0.3 g, 0.7 mmol) was dissolved in THF (3.5 mL). To the stirred solution was added AD-Mix β (0.9 g), methanesulfonamide (0.06 g, 0.7 mmol), *t*-butanol (3.5 mL) and water (3.5 mL). The yellow two-phase reaction was then stirred at room temperature for 24h. After this time dichloromethane (20 mL) was added and the mixture washed with water (3 x 20 mL) and saturated brine (2 x 20 mL). Combined organic fractions were dried over magnesium sulfate, the solution isolated by filtration and solvent removed *in vacuo* yielding a yellow waxy solid. This was purified by recrystallisation from warm pentane to give the desired diol **156a** as a white powder, 0.05 g, 15%.

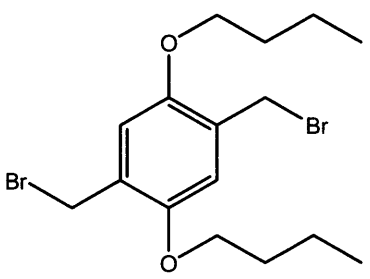
CHN: Calcd. (for $C_{30}H_{46}O_6$) C 71.71 %, H 9.16 %, found C 71.25 %, H 9.10 %.

NMR: ^1H (200 MHz, $CDCl_3$): δ0.95 (t, $^3J_{H\text{-}H}$ 7.3 Hz, 6H, CH_3); 0.97 (t, $^3J_{H\text{-}H}$ 7.2 Hz, 6H, CH_3); 1.41-1.51, (m, 8H, CH_2); 1.65-1.70 (m, 8H, CH_2O); 3.79 (m, 8H, CH_2); 4.99 (d, $^3J_{H\text{-}H}$ 2.0 Hz, 2H, CHOH), 6.68 (s, 4H, CH); 6.70 (s, 1H, CH); 6.71 (s, 1H, CH).

$^{13}C\{^1H\}$ (100 MHz, $CDCl_3$): δ 14.1 (**C**H_3); 14.1 (**C**H_3); 19.4 (**C**H_2); 19.6 (**C**H_2); 31.6 (**C**H_2); 31.7 (**C**H_2); 68.5 (**C**H_2O); 68.5 (**C**H_2O); 75.2 (**C**HOH); 112.4 (**C**H); 114.5 (**C**H); 115.1 (**C**H); 129.4 (**C** ipso); 150.8 (**C** ipso); 153.1 (**C** ipso).

MS (EI): M – 18 = 484 (consistent with loss of water from parent molecule. Molecular ion not observed.

1,4-Dibromomethyl-2,5-dibutyloxy benzene 164a

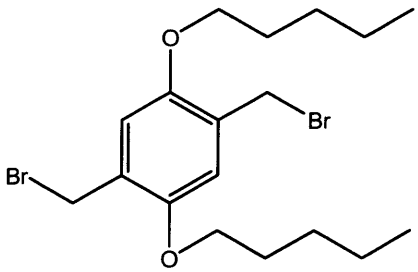


Dibutyloxybenzene **112a** (5.0 g, 22 mmol) and paraformaldehyde (1.1 g) were dissolved in acetic acid (50 mL), and HBr in acetic acid (11.0 mL of 30% w/w HBr solution) added *via* syringe. The reaction mixture was stirred

at 70°C for 2h, cooled, and poured into iced water (50 mL). The resulting precipitate was isolated by vacuum filtration and dried *in vacuo* to yield the product **164a** as a beige powder, 4.8 g, 53%.

CHN: Calcd. (for $C_{16}H_{24}Br_2O_2$) C 47.08 %, H 5.93 %, found C 47.15 %, H 5.99 %.
NMR: ^1H (200 MHz, $CDCl_3$): δ 0.97 (t, $^3J_{H-H}$ 7.3 Hz, 6H, CH_3); 1.49 (sext, $^3J_{H-H}$ 7.3 Hz, 4H, CH_2); 1.75 (pent, $^3J_{H-H}$ 6.2 Hz, 4H, CH_2); 3.96 (t, $^3J_{H-H}$ 6.4 Hz, 4H, CH_2O); 4.50 (s, 2H, CH_2Br); 6.92 (s, 2H, CH).
$^{13}C\{^1H\}$ (100 MHz, $CDCl_3$): δ 14.1 (**C**H_3); 19.6 (**C**H_2); 31.8 (**C**H_2); 58.5 (**C**H_2Br); 68.9 (**C**H_2O); 69.4 (**C**H_2O); 112.6 (**C**H); 127.0 (**C** ipso); 150.7 (**C** ipso).
MP: 55.8 – 57.2 °C

1,4-Dibromomethyl-2,5-dipentyloxy benzene 164b



An identical procedure to that used for the preparation of 1,4-dibromomethyl-2,5-dibutoxy benzene **164a** was employed, using the following quantities:
Dipentyloxy benzene **112b** 6.0 g, 25 mmol; paraformaldehyde 1.3 g; HBr (30 % w/w in acetic acid) 9.0 mL.
The product **164b** was isolated as a pale beige powder, 8.2 g, 78 %.

CHN: Calcd. (for $C_{18}H_{28}O_2Br_2$) C 49.56 %, H 6.47 %, found C 49.50, H 6.41.
NMR: ^1H (300 MHz, $CDCl_3$): δ 0.87 (t, $^3J_{H-H}$ 7.2 Hz, 6H, CH_3); 1.36 (m, 8H, CH_2); 1.72 (m, 4H, CH_2); 3.91 (t, $^3J_{H-H}$ 6.4 Hz, 4H, CH_2O); 4,45 (s, 4H, CH_2Br); 6.78 (s, 1H, CH); 7.18 (s, 1H, CH).
$^{13}C\{^1H\}$ (100 MHz, $CDCl_3$): δ 13.3 (**C**H_3); 21.7 (**C**H_2); 27.5 (**C**H_2); 28.3 (**C**H_2); 68.2 (**C**H_2O); 76.5 (**C**H_2Br); 113.9 (**C**H); 126.7 (**C** ipso); 149.9 (**C** ipso).
MS (EI): $M^+ = 434$.
MP: 80.2 – 82.5 °C .

APPENDICES

Appendix A: Additional Activities

APG Training

Demonstration Training

18 / 9 / 01 Pre-Session Demonstrator Training

Induction

24 / 9 / 01 Departmental Induction

25 / 9 / 01 Introduction to Key Techniques and Equipment

26 / 9 / 01 Graduate School Induction

27 / 9 / 01 Faculty Induction

Information Skills

17 / 10 / 01 Information Skills for Chemists Session 1 - An Introduction to Chemical Information Databases

24 / 10 / 01 Information Skills for Chemists Session 2 – Advanced Searching in *Crossfire*

5 / 12 / 01 Developing a Personal Skills Portfolio – *Royal Society of Chemistry*

12 / 6 / 02 Advanced Scientific Writing for Chemists

12 / 6 / 02 Applications of *Endnote*

Module CH501

31 / 10 / 01 1D-NMR Spectroscopy

28 / 11 / 01 2D-NMR Spectroscopy

30 / 1 / 02 The *nOe* Effect

5 / 6 / 02 Presentation of NMR data

6 / 3 / 02 *Chemdraw*, *Molecular Modelling* and *Powerpoint*

Study, Writing and Presentation Skills

4 / 3 / 02 and 11 / 3 / 02 Study Skills - Effective Management, Reading and Note Making Skills

6 / 2 / 02 and 13 / 2 / 02 Writing Skills

1 / 5 / 02 Presentation Skills – Powerful Spoken and Poster Presentations

Career Skills

29 / 5 / 02 Developing Skills for a Future Career

Intellectual Property Rights

13 / 5 / 02 IPR, Patent Protection and Commercialisation

Research Seminars

University of Leicester, July 2001 – December 2003

4 / 10 / 01 Royal *Society of Chemistry Lecture*

Dr Peter O'Brien – University of York

'Basic Instinct: New Synthetic Adventures with Chiral Bases'

10 / 10 / 01 Dr Didier Bourrissou – Universitié Paul Sabatier, Toulouse

'Stable Carbenes and Diradicals: New Stabilisation and Bonding Modes'

22 / 10 / 02 *Royal Society of Chemistry Student Chemical Society Lecture*

Dr Anthony Hooper – Institute of Arable Crops, Rothamstead

'Sex, Bugs and Rock and Roll: Identification and Synthesis of Semiochemicals and Exploitation of the Ecological Interactions they Regulate as an Approach to Pest Management'

14 / 11 / 01 *Royal Society of Chemistry Joseph Chatt Lecture*

Professor Vernon C. Gibson – Imperial College, London

'Designing Catalysts for Polymer Synthesis'

10 / 12 / 01 Dr Jonathan McMaster – University of Nottingham

'The Electronic Structure of the Active Sites of Molybdenzymes'

14 / 12 / 02 Professor Peter Flecker – Johannes Gutenberg University, Mainz

'Dissecting Intramolecular versus Intermolecular Protein Recognition'

28 / 1 / 02 Professor Judith Howard – University of Durham

'The Application of Very Low Temperature Crystallography to Chemical Problems'

11 / 2 / 02 Dr Robin Bedford – University of Exeter

'High Activity Catalysts for C-C Bond Formation'

25 / 2 / 02 Professor John Nixon – University of Sussex

'The New World of Phospha-Organometallic Chemistry'

4 / 3 / 02 Dr Holger Braunschweig – Imperial College, London

'Compounds with Novel Boron Containing Ligands: Transition Metal Complexes of Boron and [1] Bora – Metallocenophanes'

6 / 3 / 02 Dr Richard Shutt – ExxonMobil, Belgium

'Supercritical Phase Phenomena in Ethylene Polymerisation and Polymer Separation'

8 / 5 / 02 Dr Nick Long – Imperial College, London

'Ferrocene – Ligand Design'

20 / 5 / 02 Dr Martyn Coles – University of Sussex

'Anionic and Neutral Guanidine – based Ligands in Coordination Chemistry and Catalysis'

28 / 10 / 02 Dr Clive Metcalfe – University of Leicester

'Transition Metal Complexes and their Interaction with DNA'

18 / 11 / 02 Dr Mike Turner – University of Sheffield

'Synthesis of Conjugated Polymers for Polarised Electroluminescence and Polymer Electronics'

9 / 12 / 02 Prof. Todd Marder – University of Durham

'The Role of Transition Metal Boryl Complexes in Catalysed Borylations including Rhodium Catalysed C-H Bond Functionalisation'

17 / 2 / 03 Prof. V. McKee – University of Loughborough

'Manipulating Metal Arrays within Macrocycles'

10 / 3 / 03 Prof. Duncan Bruce – University of Exeter

'Metallomesogens by Design'

28 / 4 / 03 Prof. Kingsley Cavell – University of Cardiff

'Reactions of Heterocyclic Carbene Complexes: Important Ramifications for their Application in Catalysis'

30 / 5 / 03 Dr Carine Aubrey – University of Leicester

'Synthèse, Analyse Stucturale et Activité Biologique d'analogues Rigides d'un Antagoniste de l'octadecaneuropeptide (ODN)'

2 / 6 / 03 Dr Sarah Heath – University of Manchester

'Shedding Light on Biological Systems: the Development of Dinuclear Lanthanide Probes'

Inaugural Lecture

3 / 6 / 03 Prof. Jonathan Percy – Appointed as Professor of Chemistry at the University of Leicester

'Against Nature: Unnatural Products in the Service of Humanity'

9 / 6 / 03 Dr Alan Spivey – Imperial College, London

'Catalytic Asymmetric Acylation – Studies towards the Total Synthesis of Polyol Sesquiterpenes'

29 / 9 / 03 Dr Ze Pikramenou – University of Birmingham

'Luminescent Supramolecular Architectures: from Shape to Function'

6 / 10 / 03 Dr Chris Richards – Queen Mary, University of London

'Palladium and Platinum Metallacycles for Organic Synthesis'

The Second Tim Norwood Memorial Lecture

8 / 10 / 03 Prof. Ian Campbell – University of Oxford

'NMR and Proteins'

20 / 10 / 03 Dr Sandie Dann – University of Loughborough

'Something Old, Something New Something Borrowed and Something Blue: Complex Oxides and Sulfides'

27 / 10 / 03 Dr Chris Hayes – University of Nottingham

'Natural and non-Natural Products: Total Synthesis and Biological Applications'

3 / 11 / 03 Prof. Helen Fielding – University College London

'Controlling Electrons and Molecules using Light'

17 / 11 / 03 Prof. Chris Binns – Department of Physics University of Leicester

'Building High-Performance Magnetic Materials by Assembling Nanoclusters'

1 / 12 / 03 Prof. Richard Winpenny – University of Manchester

'Synthetic Studies of Metal Wheels and other Cages'

8 / 12 / 03 Prof. Peter Hore – University of Oxford

University of Durham, January – August 2004.

21/01/04 Prof. M. Bradley – University of Southampton

"Combinatorial Chemistry and Arrays"

28/02/01 Dr. L. Yellowlees – University of Edinburgh

"Electrochemical and Spectroelectrochemical Studies of Transition Metal Complexes"

04/02/04 Prof. P. O'Brien – University of Manchester

"Quantum Dots"

11/02/04 Prof. D. Parker – University of Durham

"Chiral Lanthanide Complexes: Structure, Dynamics, and Function"

10/04/04 Prof. T. Fehlner – University of Notre Dame

"*Molecular Expression of Quantum Cellular Automata: Surface Bound Mixed Valence Complexes as Switchable Charge Containers"*

14/06/04 Prof. S. Collins – University of Akron

"Anion Effects in Olefin Polymerisation"

Appendix B: Crystal Data for Compound 122b

Identification code	2072	
Empirical formula	C34 H36 O2	
Formula weight	476.63	
Temperature	150(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	a = 7.707(5) Å	α = 73.163(10)°.
	b = 13.345(8) Å	β = 80.737(10)°.
	c = 13.891(9) Å	γ = 88.889(9)°.
Volume	1349.0(15) $Å^3$	
Z	2	
Density (calculated)	1.173 Mg/m^3	
Absorption coefficient	0.071 mm^{-1}	
F(000)	512	
Crystal size	0.33 x 0.22 x 0.08 mm^3	
Theta range for data collection	1.59 to 25.00°.	
Index ranges	-9 ≤ h ≤ 9, -15 ≤ k ≤ 15, -16 ≤ l ≤ 16	
Reflections collected	9548	
Independent reflections	4669 [R(int) = 0.1460]	
Completeness to theta = 25.00°	98.2 %	
Absorption correction	None	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4669 / 0 / 328	
Goodness-of-fit on F^2	0.932	
Final R indices [I>2sigma(I)]	R1 = 0.1254, wR2 = 0.3072	
R indices (all data)	R1 = 0.2500, wR2 = 0.3650	
Extinction coefficient	0.040(11)	
Largest diff. peak and hole	0.346 and -0.296 $e.Å^{-3}$	