The Synthesis & Properties of Chiral Binaphthalenes as Nematic Liquid Crystal Dopants

Chris Schubert

This thesis is submitted in fulfilment of the requirements of the degree of Doctor of Philosophy at the University of East Anglia, UK.

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Preface

The research described within this thesis is, to the best of my knowledge, original and my own work, except where due reference has been made.

Chris Schubert

Norwich, October 2009

Abstract

Research into chiral nematic dopants has increased substantially due to the lure of potential application. Two avenues of research are generally adopted: the development of high twist nematic dopants and determination of the mechanism by which chirality is transferred to the host liquid crystal, and the development of switchable (bistable) dopants for liquid crystal phase control.

The work described in this thesis (Chapter 2.1) concerns the design and development of a range of high twist nematic dopants based on the chiral binaphthalene skeleton. Transition of the molecular shape, through structural elongation of the binaphthalene 2,2' and 6,6'-positions was successful in producing dopants that are among the most effective in the literature. In addition, the substituent effects were catalogued, providing an insight into the mechanism of chiral induction. Linear extension was found to generally induce higher helical twisting powers, whilst extension of the binaphthalene core with linear aromatic substitutents proved effective at inducing helical twisting powers up to 239 μm^{-1}. A large disparity in helical twisting power between linear and non-linearly extended dopants, led to the proposal of an alternate mechanism of chiral induction.

The disparity in helical twisting power, between linear and non-linearly extended binaphthalene dopants, was exploited to develop a novel switchable dopant (Chapter 2.2). Initial efforts attempted the synthesis of an azobenzene based derivative, which ultimately proved unsuitable for application. The successful development of a conceptually similar stilbene derivative induced substantial effects on the chiral nematic phase upon irradiation. In addition, further evidence for an alternate mechanism of chiral induction was obtained.

A study into the feasibility of a switchable dopant, based on the switching between enantiomeric states upon irradiation with circularly polarised light, was conducted (Chapter 2.3). The study utilised the chiral binaphthalene base structure, employing strategic placement of donor and acceptor substituents to induce a helical conjugation pathway, which would induce effective switching. The preliminary data (CD, UV) failed to provide evidence for the helical conjugation pathway, with a limited photoresolution of less than 0.1% calculated. A second dopant design, based on a 1-phenyl-naphthalene parent structure, led to the discovery of an unexpected chemical reaction of a naphthalene boronic acid. Further investigation determined the product to be the result of a boronic acid oxidation to the corresponding naphthol and subsequent dimerisation. The stoichiometric conversion of electron-rich naphthalene boronic acids was consistently observed, under catalyst free conditions, in alkali reaction media. Electron rich benzene boronic acids were also found to be susceptible to oxidation, although to a lesser extent.

Acknowledgements

I would first and foremost like to thank my supervisor, Dr Andy Cammidge, for providing me with the opportunity to conduct this research, and for all his invaluable support, advice and encouragement throughout my studies. It has been a pleasure to work for you Andy. I am also indebted to both Dr Rob Stockman and Dr Chris Richards for providing me with a home within their respective groups, for which I am eternally grateful.

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Last but not least, I would like to thank everyone in my family for their contributions, in particular my parents, for all the continuing love and support they have shown me throughout my life. Mum, thanks for always being there for me.

Dedicated to

Charles Henry Reynolds

Abbreviations

Å	Angström
Ac	acetyl
aq.	aqueous
Ar	aryl
atm	atmosphere
b.p.	boiling point
BINAM	2,2’-diamino-1,1’-binaphthalene
BINAP	2,2’-bis(diphenylphosphino)-1,1’-binaphthalene
BINOL	1,1’-bi(2-naphthol)
br	broad
β_M	helical twisting power
Bn	benzyl
Bu	butyl
c	concentration
CI	chemical ionisation
conc.	concentrated
CPL	circularly polarised light
Cy	cyclohexane
d	doublet
dd	doublet of doublets
ddd	doublet of doublets of doublets
δ	chemical shift in parts per million (ppm)
Δ	heat
de	diastereomeric excess
dba	dibenzylideneacetone
DCM	dichloromethane

DEG	diethylene glycol
DIPEA	diisopropylethylamine (Hünigs base)
DMAP	4-dimethylaminopyridine
DME	dimethoxyethane
DMF	*N*,*N*-dimethylformamide
DMM	dimethoxymethane
DMSO	dimethylsulphoxide
dppf	1,1'-bis(diphenylphosphino)ferrocene
DPPFA	(+)-(*S*)-*N*,*N*-dimethyl-1-[(*R*)-1',2-bis(diphenylphosphino)-ferrocenyl]ethylamine
dr	diastereomeric ratio
ε	molar extinction coefficient
E7	4-heptyl-4'-cyanobiphenyl/4-pentyl-4'-cyanobiphenyl mixture
ee	enantiomeric excess
EI	electron impact
eq.	equivalent
ES	electrospray
Et	ethyl
g_λ	Kuhn anisotropy factor
hr	hour
HRMS	high resolution mass spectrometry
HTP	helical twisting power
Hz	hertz
IR	infra-red
K15	4-pentyl-4'-cyanobiphenyl
λ	wavelength
L	ligand

LAH	lithium aluminium hydride
LC	liquid crystal
LCD	liquid crystal display
lit.	literature
LPL	linearly polarised light
m	multiplet
M	molar
MBBA	4-methoxybenzylidine-4'-*n*-butylaniline
Me	methyl
min	minute
mol	mole
MOM	methoxymethyl
m.p.	melting point
m/z	mass to charge ratio
n	director
N	nematic phase
N^*	chiral nematic phase (cholesteric phase)
Nap	naphthalene
NAPHOS	2,2'-(diphenylphosphinomethyl)-1,1'-binaphthalene
NBS	*N*-bromosuccinimide
NMP	*N*-methylpyrrolidinone
NMR	nuclear magnetic resonance
NPL	non-polarised light
p	pitch length
Ph	phenyl
PPFA	(*S*)-[(*R*)-1-(5-diphenylphosphino)ferrocenyl]-*N*,*N*-dimethylethanamine

ppm	parts per million
Pr	propyl
Py	pyridine
q	quartet
θ	dihedral angle
R_f	retention factor
rt	room temperature
s	singlet
S	smectic phase
S_A	smectic A phase
S_C	smectic C phase
S_C^*	chiral smectic C phase
sat.	saturated
sept	septet
t	triplet
Tf	trifluoromethanesulphonyl
THF	tetrahydrofuran
Tol	toluene
TLC	thin layer chromatography
Ts	*para*-toluenesulphonyl (tosyl)

Contents

Chapter 1

Introduction

1.1 – Liquid Crystals

1.1.1 – The Mesophase

Liquid crystals constitute a unique state of matter, which exhibit properties between those of a conventional liquid (isotropic liquid) and a crystalline solid (*Figure 1.1*). Occasionally referred to as the *fourth state of matter*, the liquid crystalline phase is more commonly termed the *mesophase*. The mesophase exists due to anisotropy within the phase; all molecular directions are non-equivalent as opposed to a conventional liquid where isotropic distribution is observed. Molecular order within a crystal is typically both positional and orientational, whilst in contrast an isotropic liquid is devoid of molecular order, with random diffusion throughout the sample. In the mesophase, molecules possess a degree of orientational, and occasionally positional, order due to weak anisotropic interactions; however the order is only a fraction of that observed in a crystalline solid, resulting in the observed fluidity. The unique properties of the mesophase have led to vast interest in the fields of chemistry and physics.

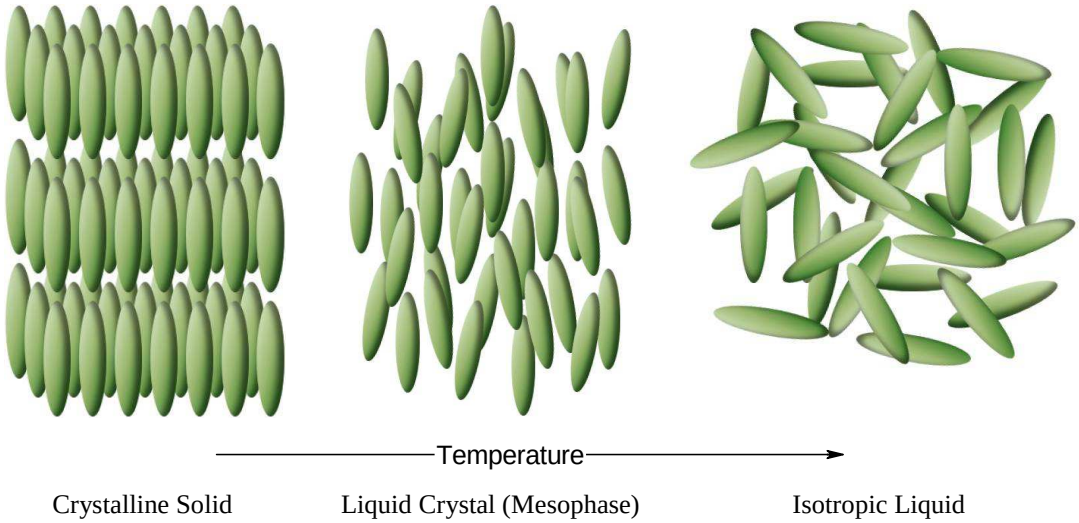


Figure 1.1 – States of matter

1.1.2 – Historical Perspective[1-4]

In 1888 a novel state of matter was discovered by Austrian botanist (biochemist) Friedrich Reinitzer at the German University of Prague. Reinitzer was attempting to determine the chemical formula of cholesterol and noticed some spectacular colour

changes upon the cooling of cholesterol benzoate just above the solidification temperature. A number of previous studies had witnessed similar observations with cholesterol acetate, which Reinitzer himself confirmed.[5-8] Most prominently, Reinitzer observed that cholesterol benzoate appeared to have two melting points; at 145.5 °C the crystalline solid melted to an opaque liquid, which at 178.5 °C became transparent. The phenomenon was also observed to be reversible, and that dramatic colours were apparent near the transition temperatures. Reinitzer sent samples to professor of physics and notorious crystallographer, Otto Lehmann, at the polytechnical School of Aachen, and after some consultation, published the results.[9] Whilst Friedrich Reinitzer's involvement in the field declined, Otto Lehmann conducted extensive research into the observed phenomena. Lehmann postulated that the opaque liquid constituted a unique phase of matter with the properties of both a liquid and a crystal (crystals that flow).[10]

Lehmann discovered further materials which displayed similar properties to cholesteryl benzoate, and materials that exhibited different phases, which he termed *Fliessende Krystalle* (flowing crystals) and *Kristalline Flüssigkeit* (crystalline fluid). Lehmann's proposals were not without scepticism from the scientific community. Gustav Tammann and Walther Nernst proposed that the observed phenomena were a result of a colloidal suspension of one liquid in another. Although now known to be incorrect, the theory formed a plausible explanation of the so far unsolved property of birefringence.

In 1903, Daniel Vorländer, professor of chemistry at the University of Halle began intense research which would propel him to the forefront of the field for the next 30 years. Vorländer determined that liquid crystalline behaviour was a result of molecular shape, with the liquid crystal phase primarily formed by molecules with a *rod-like* structure. His research culminated in the discovery of hundreds of materials with liquid crystalline properties, and revealed that liquid crystalline materials can exhibit more than one liquid crystal phase.

In 1922, Georges Friedel published an article in *Annales de Physique*[11] criticising the terms '*liquid crystal*' and '*crystalline fluid*' proposed by Lehmann, on the basis that the materials were neither true crystals or true liquids and constituted an entirely new phase of matter. The term *mesophase* was proposed to avoid any confusion as to

their nature. Friedel also sought to clarify the terms describing the phases to provide an unambiguous description that omitted the terms 'liquid' and 'crystal'. The terms *smectic* (derived from the Greek word *smectos*, meaning '*soap-like*') for Lehmann's '*flowing crystals*', due to their soap-like texture appearance under a polarising microscope, and *nematic* (derived from the Greek word *nematos*, meaning '*thread-like*') for the '*crystalline fluid*', due to the appearance of thread-like (defect) lines, were introduced.

Research on liquid crystals continued into the 1930s and 1940s, mainly focussing on physical properties. Interest in the field slowly declined following the Second World War as the once vibrant field lacked practical application. Interest in the field was revived in the United States, United Kingdom and Soviet Union during the mid-1950s. US chemist Glenn Brown wrote a review[12] of the current literature and established the Liquid Crystal Institute (LCI) at Kent State University in 1965, now named in his honour.[13]

The 1960s also saw the first display application proposed by Richard Williams and George Heilmeier based on the dynamic scattering mode (DSM) effect.[14, 15] This led to the first practical liquid crystal display (LCD) application[16] which, compared to display devices of the time offered lower voltage and power consumption, smaller scale, and ease of manufacture (*Figure 1.2*). However, the requirement for continuous current flow limited their application in battery operated devices.

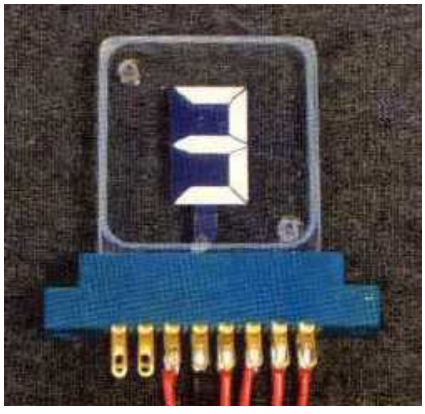


Figure 1.2 – Dynamic scattering liquid crystal display[17]

Pioneering work by George Gray and co-workers at the University of Hull led to the discovery of the cyanobiphenyl class of nematic liquid crystals, which exhibited electrochemically stable nematic phases at ambient temperatures.[18] This enabled the

successful implementation of a new type of liquid crystal display. Independently devised by James Ferguson and co-workers, and Wolfgang Heilfrich and Martin Schadt,[19] the new display was based on the twisted nematic (TN) effect discovered by Charles-Victor Mauguin (*Figure 1.3*).[20] Twisted Nematic liquid crystal displays offered significant advantages over other display technologies of the time, including low power consumption and small size, making them ideal for battery operated, hand-held devices. This has culminated in the global LCD market reportedly surpassing the $90 billion mark in 2008.[21]

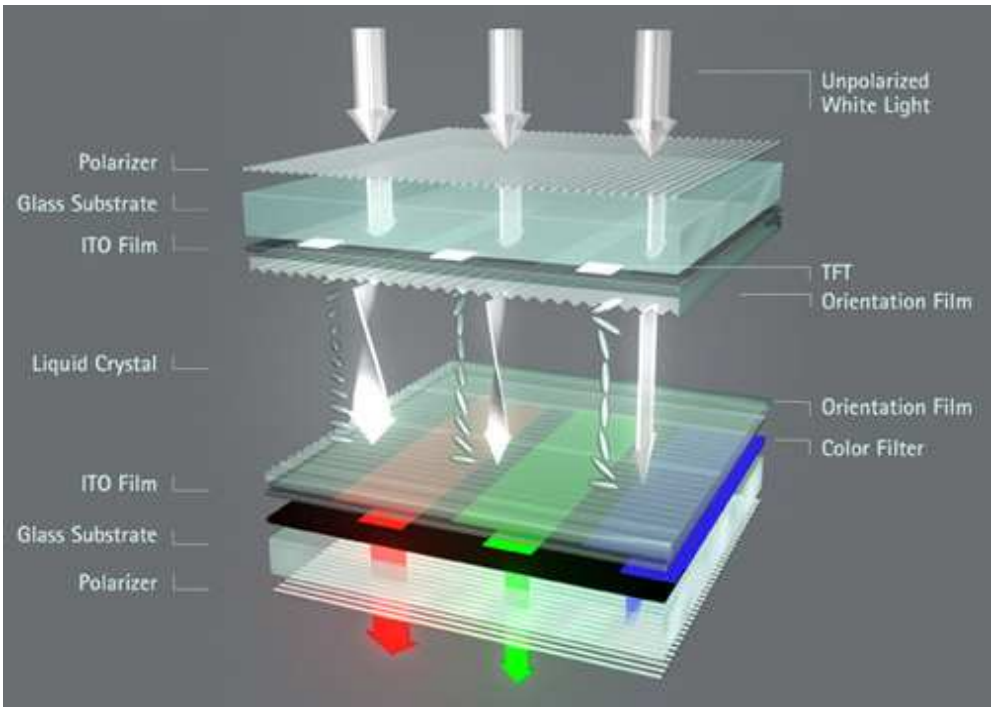


Figure 1.3 – Twisted nematic TFT-LCD[22]

1.1.3 – Classes of Liquid Crystal [1, 4]

Molecules of vastly differing shape and properties are able to form liquid crystal phases; the common feature they share is molecular anisotropy. Essentially the molecules possess one axis vastly different from the others, or exhibit differences in solubility between sections of the molecule. Molecular anisotropy encourages intermolecular interactions, producing a degree of order in the system.

Liquid crystalline materials can be divided into two distinct classes: thermotropic and lyotropic liquid crystals. Thermotropic liquid crystals exhibit phase stability over a specific temperature range. Temperatures above this range (clearing point) result in

thermal motion disrupting the delicate molecular order, with the material reverting to a regular isotropic liquid. At lower temperatures the material returns to a conventional, though anisotropic, crystalline solid. Thermotropic liquid crystals are conventionally divided further into two sub-classes: calamitic and discotic liquid crystals.

Calamitic liquid crystals are the most frequently observed liquid crystalline materials, and are formed by elongated rod-like molecules, such as **1** (one molecular axis longer than the others). Discotic liquid crystals, such as **2**, are conversely formed by molecules possessing one molecular axis shorter than the others (disc-shaped). Lyotropic liquid crystals are distinct from thermotropic liquid crystals in that they form liquid crystal phases upon solvation, with phase stability affected by both concentration and temperature. Anisotropy arises not from molecular shape but from the varying degree of solubility within the molecular structure, generally comprising hydrophilic 'head' groups and hydrophobic 'tail' groups (e.g. **3**). The amphiphillic nature of the molecules promotes a degree of order upon solvation in both polar and non-polar solvents (*Figure 1.4*).

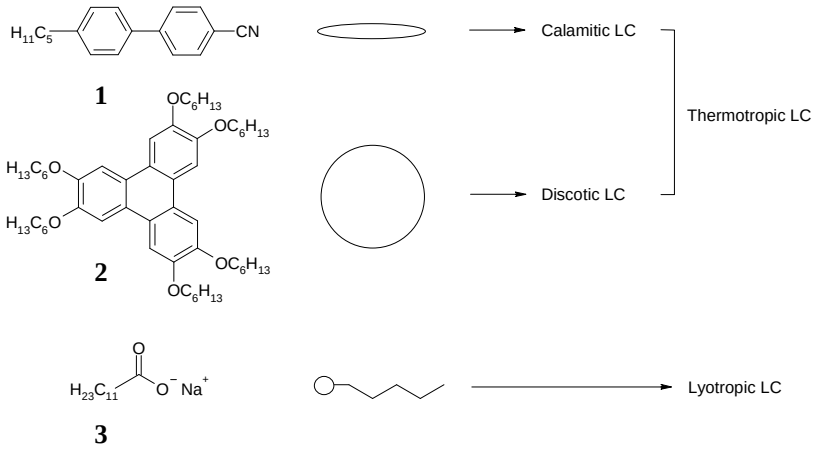


Figure 1.4 – Classes of liquid crystal

Calamitic and discotic mesogens are capable of forming many different liquid crystal phases. The most common of these is the nematic phase, which possesses limited orientational order whilst positional order is absent. Liquid crystal phases which also exhibit a degree of positional order are observed for both calamitic and discotic liquid crystals. The smectic A and smectic C phases are the most common and least ordered of the smectic phases observed for calamitic liquid crystals. The smectic phases possess the orientational order observed for the nematic phase, however they

also possess a degree of positional order producing a layered (lamellar) arrangement. In the smectic A phase the director is, on average, aligned perpendicular to the layers, whilst in the smectic C phase the director is tilted at an angle other than 90° (*Figure 1.5*). It should be noted that no positional order is observed within the individual layers. The increased molecular order of the smectic phases generally results in phase formation at lower temperatures than the nematic phase, with increased viscosity. A number of smectic phases exist with a higher degree of order than the smectic A and C phases, such as the smectic B phase, which forms a hexagonally ordered structure.

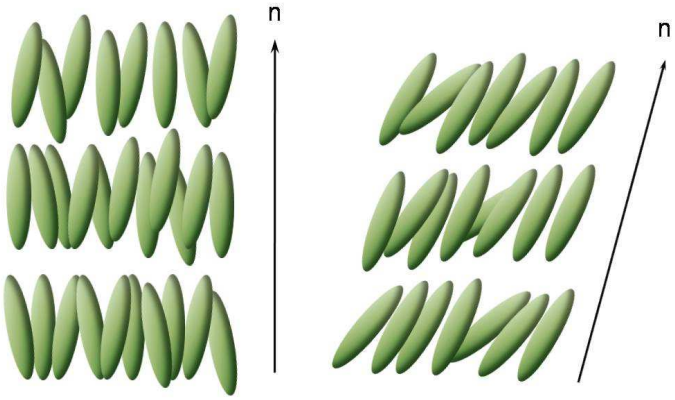


Figure 1.5 – Smectic A and smectic C phases

Positional order in the discotic phase manifests itself through the tendency of the molecules to adopt a columnar molecular arrangement, somewhat analogous to the smectic phases. The columnar arrangement usually adopts a two-directional lattice structure, such as that of a rectangular or hexagonal form (*Figure 1.6*).

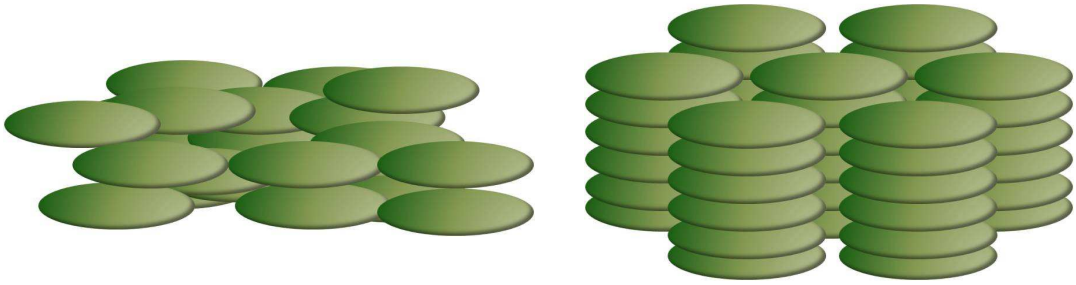
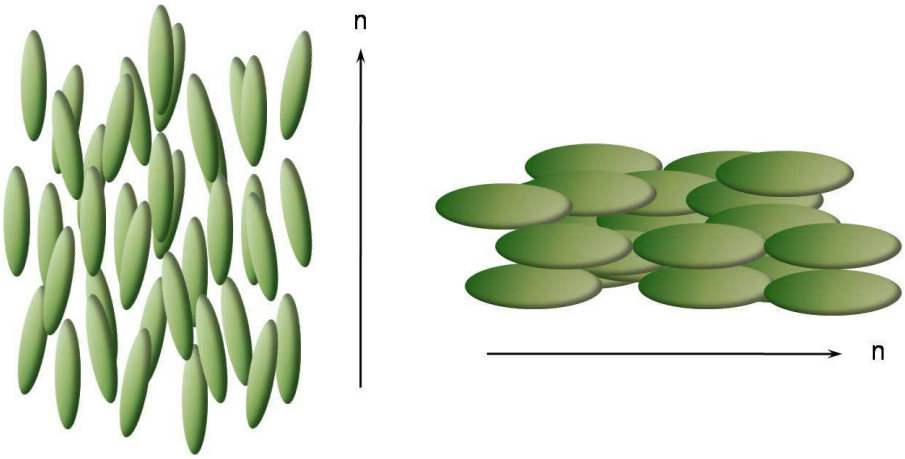


Figure 1.6 – Nematic and columar discotic phases

1.1.4 – Liquid Crystal Phases[1, 4]

1.1.4.1 – The Nematic Phase

The nematic liquid crystal phase (N) is both the simplest liquid crystal phase, in terms of molecular order, and the most common. Unlike an isotropic liquid, where molecular order is absent, the molecules in the nematic phase align with their longest axis orientated in a preferred direction known as the director (n) (*Figure 1.7*). The resultant lack of positional order promotes free molecular diffusion throughout the sample, and a high degree of fluidity.



Nematic Calamitic Nematic Discotic

Figure 1.7 – Molecular order in the nematic phase

The nematic phase can be identified from its characteristic optical texture (*Figure 1.8*). The distinctive dark lines, known as disclination lines, are line defects in the unaligned nematic phase where a director cannot be defined. Both calamitic and discotic liquid crystal mesogens are capable of forming the nematic phase; however the two phases are non-miscible, and therefore non-equivalent.

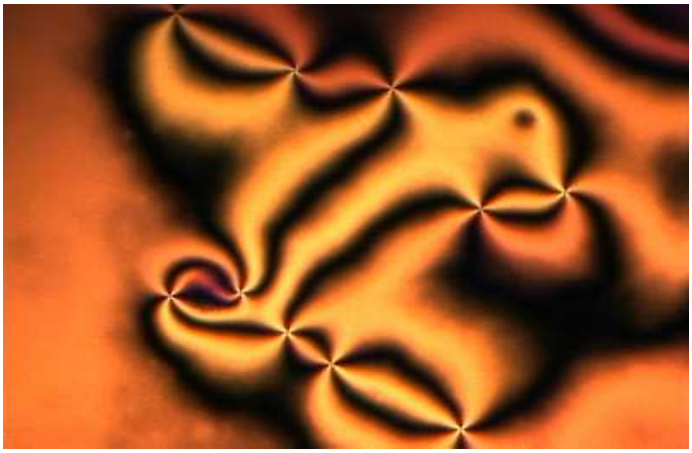


Figure 1.8 – Schlieren texture of the nematic phase

The structural features required to form a liquid crystal capable of exhibiting the nematic phase can be effectively modelled. The tailoring of specific structural features allows for modification of the liquid crystal physical properties. The most essential feature required is a rigid core unit, which maintains shape anisotropy. Typically the core is aromatic in nature (e.g. phenyl **4**, biphenyl **5**, naphthyl **6**), however, non-aromatic (e.g. cyclohexyl **7**) and heterocyclic structures (e.g. pyrimidyl **8)** can also be employed. Molecular axes can be extended through the use of terminal functionalities, which also alter the physical properties of the nematic phase. Linear, flexible functionalities, such as *n*-alkyl and *n*-alkyloxy groups, increase mesophase stability and lower the melting point of the materials, which is essential for ambient temperature applications. The strategic positioning of lateral substituents, either polar (e.g. F **9**, CN, CF_3) or non-polar (e.g. CH_3), located on the core unit or the terminal chains, can be used to modify the physical properties (*Figure 1.9*).

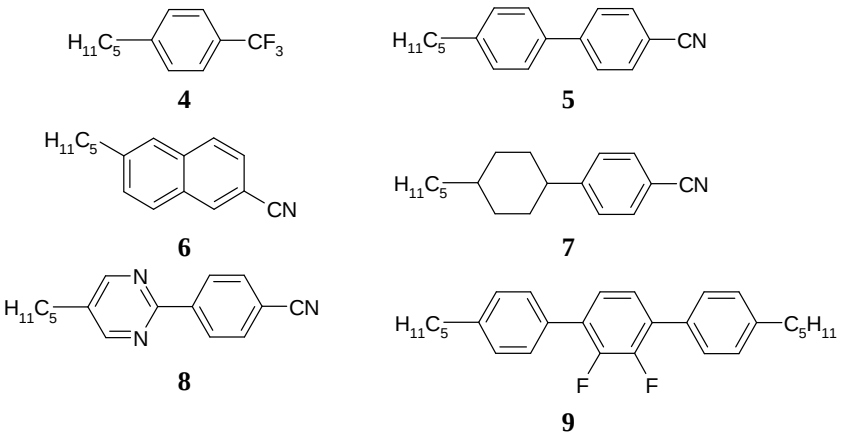


Figure 1.9 – Structural features of typical liquid crystal mesogens

1.1.4.2 – The Chiral Nematic Phase

The chiral nematic phase (N*) is traditionally known as the cholesteric phase, from the cholesterol derivatives from which it was first observed.[9, 10] It is now known that there are many compounds, besides cholesterol derivatives, that exhibit the chiral nematic phase.

Essentially, the chiral nematic phase is a nematic phase, in which molecular asymmetry induces a slight and gradual rotation of the director in a helical fashion, generating a helical supramolecular structure (*Figure 1.10*). The supramolecular structure has both sign (indicated by the direction of helical rotation) and magnitude, which is determined by the pitch length (*p*), with the pitch length being the distance through which a 360° rotation of the director (n) is effected. No layering exists within the phase, with molecular diffusion observed throughout the sample.

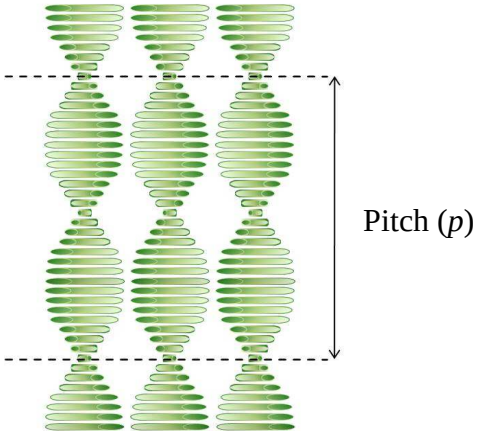
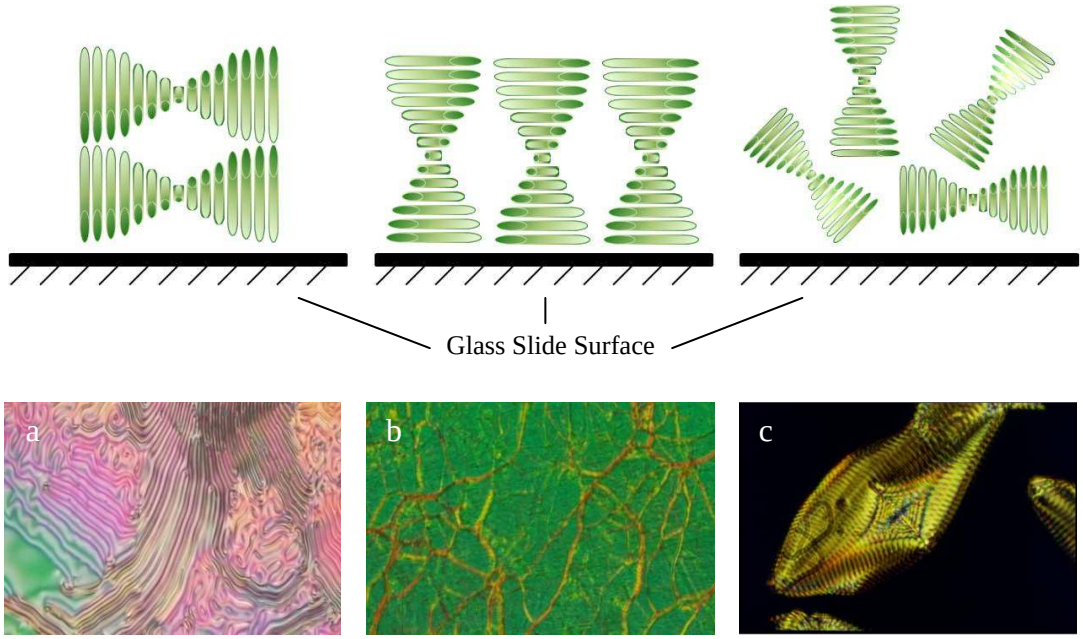


Figure 1.10 – The chiral nematic (cholesteric) phase

Again the chiral nematic phase can be identified from its characteristic optical fingerprint texture (*Figure 1.11*). The distance between dark bands is equal to half the pitch length (180° rotation). The texture observed is, however, dependent on the phase alignment in reference to the propagating light source. Orientation of the helical axes parallel to the slide surface produces the distinctive fingerprint texture; whereas alignment of the helical axes perpendicular to the slide surface produces the planar texture. A third alignment, where alignment of the helical axes is random, produces the focal conic texture.



a) Fingerprint; b) Planar; c) Focal Conic[13]

Figure 1.11 – Structure and optical texture of the chiral nematic (cholesteric) phase

The helical macrostructure possesses the ability to selectively reflect light with wavelengths equal to the pitch length, upon alignment of the helical axes parallel to the direction of the propagated light. The temperature dependence of the pitch length, and therefore the temperature dependence on the reflected light wavelength, forms the basis for the optical technologies that utilise the chiral nematic phase, such as thermo-responsive pigments (*Figure 1.12*).

Figure 1.12 – Thermo-optical liquid crystal applications

The chiral nematic phase can also be induced by solvation of a small quantity of chiral, non-racemic, guest material (dopant) into a nematic liquid crystal host. The

guest material is not itself required to exhibit liquid crystalline properties. The induced chiral nematic phase is highly dependent on the properties of both of the dopant and the nematic liquid crystal host.

The ability of a chiral dopant to induce the chiral nematic phase is expressed as a parameter known as the helical twisting power (β_M), which is intrinsic to every chiral compound. Although similar in nature to the property of optical rotation, the origin of both are inherently different; with optical rotation a consequence of interaction between light and matter, and helical twisting power a result of solute-solvent interactions. The pitch (p) of the induced chiral nematic phase was determined to be inversely proportional to the dopant concentration (c), the helical twisting power (β_M), and the enantiomeric excess (ee):-[23, 24]

$$p = (c.\beta_M.ee)^{-1}$$

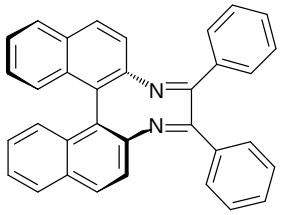
The handedness of the induced chiral nematic phase is labelled as *P* for a right-handed helix and *M* for a left-handed helix. Both the sign and magnitude of the helix are required for a complete quantification of the helical twisting power.

Advantages of the induced chiral nematic phase stem mainly from the ability to selectively tune the pitch length as desired. This can be achieved through alteration of the dopant concentration or enantiomeric excess; the latter being heavily researched as a potential application for optical memories and display devices. The physical properties of the mesophase, such as the clearing point and viscosity, tend to be negatively affected upon the introduction of foreign materials.

1.1.5 – Chiral Nematic Dopants

In 1922, Georges Friedel determined that solvation of a small amount of chiral non-racemic material in a nematic liquid crystal host generated the chiral nematic phase.[11] Despite the significance of the discovery, further research on the subject was not published until the 1960s, when Buckingham reported that irreversible conversion of a nematic phase occurred upon the addition of small quantities of chiral materials, which were themselves not liquid crystalline.[25] Research continued on the induction of the chiral nematic phase, with Stegemeyer inducing the chiral nematic phase with chiral non-liquid crystalline materials,[26] whilst further research into liquid crystalline dopants was conducted by Baessler and Labes.[27]

It was later discovered by Stegemeyer that materials lacking an asymmetric chiral carbon centre, such as the atropisomeric diazocine DDCO **10** (*Figure 1.13*), were able to induce the chiral nematic phase with greater efficiency than any materials studied previously.[28]



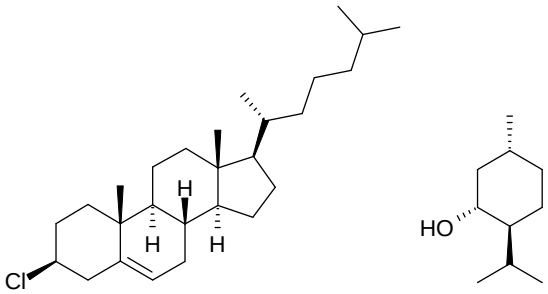
10
DDCO $\beta_M = 32\ \mu m^{-1}$

Figure 1.13 – Chiral induction with an axially chiral material

The potential of the chiral nematic phase, and particularly the induced chiral nematic phase, for application in display devices, dyes, pigments, and optical memory devices, has led to vast interest in chiral liquid crystals and in particular chiral nematic dopants.

1.1.5.1 – Dopants with Chiral Carbon Centres

The first chiral dopants were naturally based on cholesterol derivatives such as **11**[23, 24] due to their liquid crystalline properties. The discovery that non-liquid crystalline materials induced the chiral nematic phase led to research into other centrally chiral materials, commonly based on natural products such as (-)-menthol **12**[26, 29] (*Figure 1.14*).

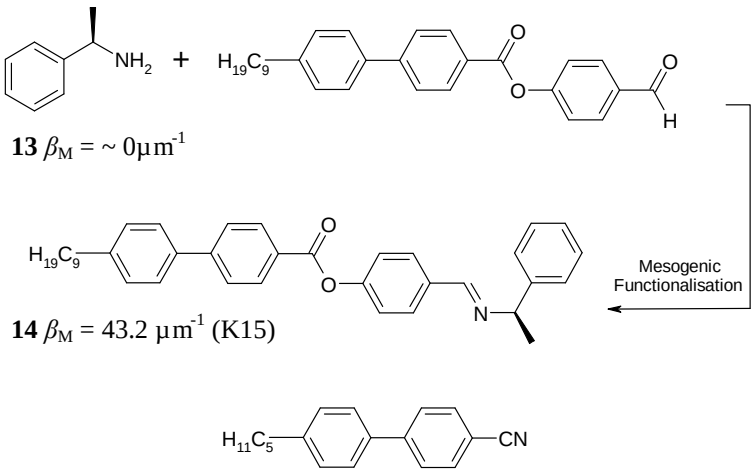


Cholesteryl Chloride - **11** (-)-Menthol - **12**

Figure 1.14 – Natural products as chiral dopants

Aside from the cholesterol derivatives, the majority of chiral natural products possess poor helical twisting powers, and only induce the chiral nematic phase with

long pitch lengths. It has typically been observed that dopants possessing a stereogenic chiral carbon centre exhibit low helical twisting powers, most probably due to the lack of structural similarity between dopant and host. In cases where respectable helical twisting powers have been recorded, structural modification with a group resembling a liquid crystalline material (mesogenic functionalisation) was required to promote interactions with the host nematic (*Scheme 1.1*).



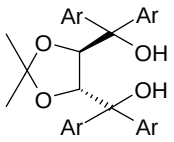
13 β_M = ~ 0 μm^{-1}

14 β_M = 43.2 μm^{-1} (K15)

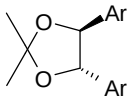
K15 - **15**

Scheme 1.1 – Enhanced helical twisting power via mesogenic functionalisation

An interesting example exists in the case of chiral tartatric acid derivatives such as TADDOLs **16**, and 3,4-diaryl-1,2-dioxolanes **17**, which display chirality as a result of stereogenic carbon centres. TADDOLs in particular have been found to be effective at inducing the chiral nematic phase with helical twisting powers in excess of 100 μm^{-1} and up to 534 μm^{-1}(*Figure 1.15*).[30-32] The mechanism by which chirality is transferred is unproven experimentally, however it has been suggested that chirality may potentially be transferred by a similar mechanism to the more effective, axially chiral dopants discussed in greater detail later in the chapter.



TADDOL - **16**

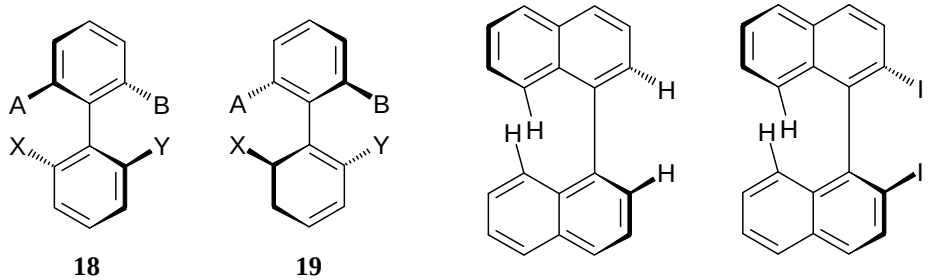


Dioxolane - **17**

Figure 1.15 – Stereogenically chiral dopants possessing high helical twisting powers

1.1.5.2 – Atropisomeric Dopants

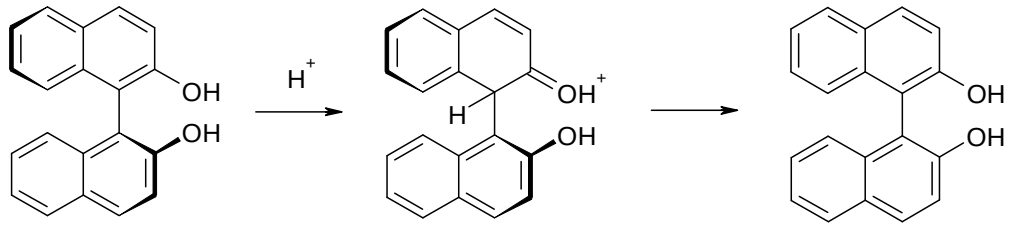
Atropisomeric compounds have been extensively researched due to their unique properties. Their chirality is not based on the presence of an asymmetric chiral carbon centre, but a result of a conformationally and stereogenically restrained axis of rotation. Whilst not all cases are due to restricted rotation about an aryl-aryl bond, chiral biaryls are by far the most utilised axially chiral materials. In the case of biphenyls **18** and **19**, restricted rotation is generated through steric interaction between the *ortho*-substituents on each aryl ring, preventing interconversion of the two isomers. Substituents of sufficient size are required to induce a high energy barrier of rotation, and prevent racemisation. Similarly, axial chirality is also exhibited by 1,1'-binaphthalene **20** (although not at ambient temperatures) through hindered rotation about the pivotal C(1)-C(1') aryl-aryl bond, as a result of steric interactions between the 2,2' and 8,8'-hydrogen atoms (*Figure 1.16*).



18 **19** **20** **21**

Figure 1.16 – Axially chiral biphenyl and binaphthyl compounds

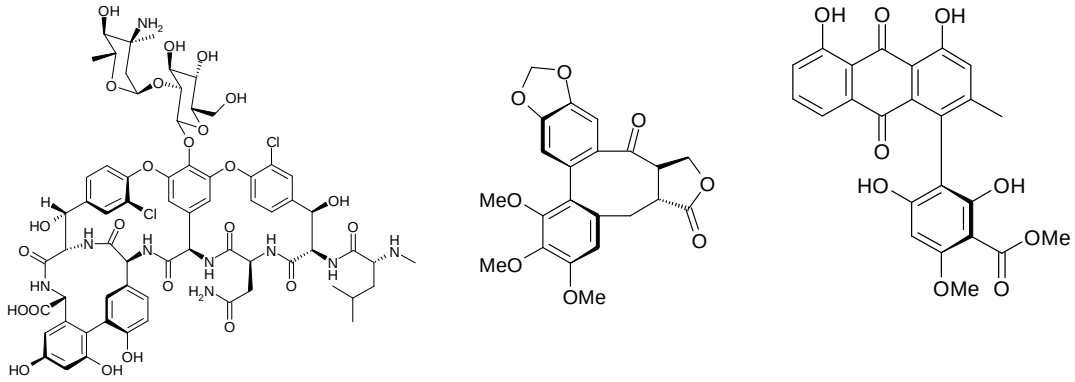
Configurational stability is known to be further increased upon the introduction of substituents in the *meta*-position to the aryl-aryl bond, which prevents sufficient bending of the *ortho*-substituents to induce racemisation. The kinetics of binaphthalene racemisation have been extensively studied with an energy barrier to racemisation of 99.6 kJ mol^{-1} for **20**, and up to 192.5 kJ mol^{-1} for the 2,2'-diiodo derivative **21**.[33] Despite the apparent stability towards racemisation, under certain conditions racemisation can be induced. 1,1'-Bi(2-naphthol) **22** is known to remain stable at temperatures of up to 100 °C for 24 hours in neutral conditions. Lowering the pH of the system induces racemisation of **22** in less than 24 hours via cationic species **23** (*Scheme 1.2*).



(*S*) - **22** **23** (±) - **22**

Scheme 1.2 – Racemisation of 1,1'-bi(2-naphthol) in acidic media

Whilst axially chiral materials have found extensive application in asymmetric synthesis and asymmetric catalysis, nature has also exploited this unique form of chirality. The glycopeptide antibiotic vancomycin **24**,[34-36] anti-leukaemia compound (*S*)-steganone **25**,[37] and anti-tumor compound (*S*)-knipholone **26**,[38] are a select few of many natural products that incorporate axial chirality (*Figure 1.17*).



Vancomycin - **24** (*S*)-Steganone - **25** (*S*)-Knipholone - **26**

Figure 1.17 – Examples of naturally occurring axial chirality

Since Stegemeyer's discovery that atropisomeric materials, lacking an asymmetric chiral carbon centre, were able to induce the chiral nematic phase, research into their respective design and mechanism of chiral induction has escalated rapidly. Motivation for research is driven by the lure of high helical twisting power materials, capable of inducing pitch lengths in the visible wavelength region and their synthetic accessibility.

The mechanism through which chirality is transferred from the dopant to the nematic host solvent has attracted numerous experimental and theoretical studies. It has been accepted that high helical twisting powers are observed for dopants sharing structural similarities with the host nematic (e.g. biphenyl dopants in biphenyl nematic

hosts).[39] The first studies into the induction of chirality by axially chiral materials resulted in a model proposed by Gottarelli and Solladie, whereby chirality was transferred from dopant to host via chiral conformations for dopants and host nematics of similar nature (e.g. biphenyl). In their model the biphenyl host molecules are described as inherently chiral conformers in rapid interconversion. Interaction with the chiral dopant induces stabilisation and the induction of chirality into the system. Chirality is therefore transferred from the guest dopant to the nearest nematic solvent molecule, which in turn transfers chirality to the next producing the helical macrostructure. This mechanism has been observed for both biphenyl and binaphthyl dopants in biphenyl nematic hosts (*Figure 1.18*).[39, 40]

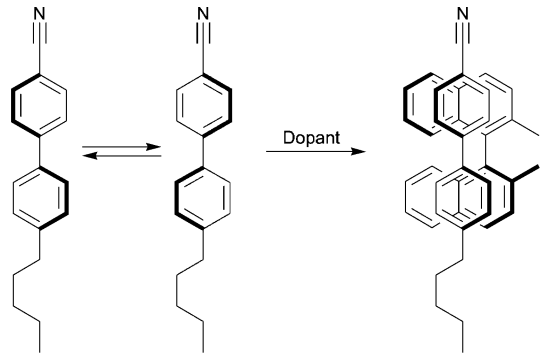
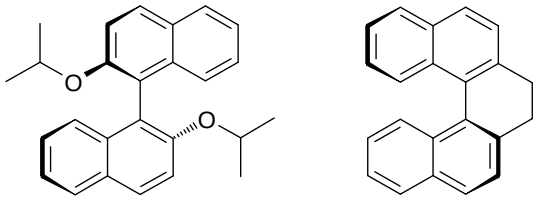


Figure 1.18 – Transfer of chirality by chiral binaphthalene dopants

Spectroscopic evidence of the nematic host molecule's orientation, with respect to the guest dopant, has revealed the alignment of the nematic director to be parallel to the C(1)-C(1') aryl-aryl bond.[39, 41] The transfer of chirality via this mechanism has been determined to be highly dependent on the dihedral angle between the aryl planes, with theoretical predictions suggesting angles of θ = 45° and 135° equate to maximum helical twisting powers, with a value of zero at θ = 90°.[42, 43]

Control of the dihedral angle is therefore considered essential for the design of biaryl dopants of high helical twisting power. Efforts to induce binaphthalenes with optimum angles have led to specific structural designs, either through the incorporation of substituents that maintain an optimum angle via hydrogen bonding, steric repulsion **27**, or more effectively, via covalent bonding of the two aryl planes into a fixed geometry **28** (*Figure 1.19*).



Sterically Hindered - **27** Bridged - **28**

Figure 1.19 – Structural methods of dihedral angle control

Recent research has primarily focused on the complex interactions between solute and solvent, often using theoretical simulations to attempt accurate predictions of helical twisting powers and the sign of helicity; a complete understanding remains elusive.[44] Significant progress has, however, been made in the attempts to generate materials capable of high twist induction. Most prominently this has been achieved using the aforementioned chiral TADDOL and 1,3-dioxolane compounds, which display a 'pseudo-axial' chirality.

Despite the chirality in such compounds not being atropisomeric in nature, in specific cases it has been predicted that their mechanism of chirality transfer is of similar origin. The dioxolane and TADDOL derivatives that display impressive helical twisting powers are highly functionalised with large aromatic substituents, whose steric bulk is believed to force the molecule to adopt a sterically hindered, helical configuration. The helically orientated aromatic planes are predicted to induce chirality through chiral conformations, via π-π stacking interactions in biphenyl liquid crystal hosts, similar in nature to that of the axially chiral dopants (*Figure 1.20*). It remains to be seen if the true nature of chirality transfer is via this proposed mechanism.

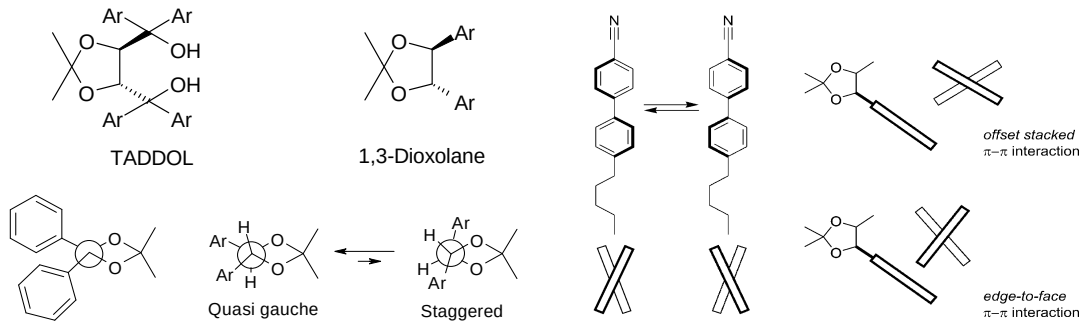


Figure 1.20 – TADDOL / 4,5-diaryl-1,3-dioxolane helical configuration and transfer of chirality[45]

1.1.6 – Bistable Dopants[45-47]

The development of nanotechnology and molecular machinery has attracted significant attention in recent years.[45] One essential component of such technologies is the molecular switch. The molecular switch comprises a molecule capable of existing in one of two or more stable states (bistability), with access to individual states by means of physical stimuli. Numerous systems have been developed which display bistability and meet the specific requirements of a molecular switch; these include azobenzenes, sterically overcrowded alkenes, fulgides, diarylethenes, spiropyrans and stilbenes.[46] In certain systems chirality is inherent to their structure, in others it can be incorporated, rendering them theoretically applicable as chiral nematic dopants. Whilst switching is possible using various external stimuli such as heat, magnetic and electric fields, pH and pressure, in a liquid crystal environment light offers the most potential due to its non-destructive nature and tuneable wavelength (chiroptical switch).

The development of molecular switching systems requires certain factors to be addressed. Primarily, it is required that two or more stable molecular states exist, and that non-destructive access to the individual states is achievable. Thermal stability over the entire applied temperature range, and fatigue resistance through many switching cycles are also of critical importance. The application of molecular switches as chiral nematic dopants also requires the consideration of liquid crystal compatibility, in order to induce sufficient changes to the helical macrostructure upon switching.

Chiroptical molecular switches can be classified into three distinct classes: Type 1 molecular switching concerns that between enantiomeric states; Type 2 switching is between diastereomeric states; and in Type 3 switches the switchable unit is remote from what is essentially a chiral auxiliary coupled to a switchable functionality (*Figure 1.21*).

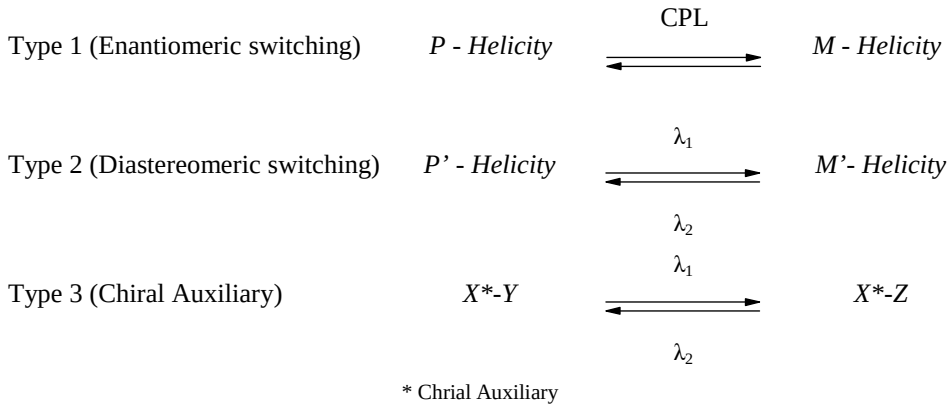


Figure 1.21 – Classes of chiroptical molecular switch

1.1.6.1 – The Switching of Enantiomers (Type 1 Switches)

The bistable states of a Type 1 switch are enantiomeric in nature, with interconversion between the individual states through the action of circularly polarised light (CPL). Irradiation of a racemic Type 1 bistable compound with circularly polarised light, of a certain handedness, can induce a partial photoresolution through preferential excitation of one enantiomer over another. The degree of photoresolution is dependent on the Kuhn anisotropy factor g_λ where $\Delta\varepsilon$ is the ratio of the circular dichromism, and ε the extinction coefficient:

$$ee_{\mathrm{PSS}} = \frac{g_\lambda}{2} = \frac{\Delta\varepsilon}{2\varepsilon}$$

The magnitude of g_λ typically does not exceed 1%, producing a small degree of photoresolution and enantiomeric excesses that rarely surpass 0.5%.[48] The ee generated is sufficient enough, however, to induce a nematic to chiral nematic phase transition. Linear (LPL) or unpolarised (UPL) light can be used to regenerate the racemate and therefore permit switching between the nematic and chiral nematic phases, as well as between phases of different handedness. To produce materials capable of enantiomeric switching, a number of factors must initially be addressed. Fundamentally the materials must possess bistability upon irradiation, with a sufficient Kuhn anisotropy factor to induce the desired enantiomeric excess. The materials must also exhibit thermal stability and fatigue resistance. In their application as chiral nematic dopants, it is also required that adequately high helical twisting powers are obtained, to induce the chiral nematic phase at such low enantiomeric excess.

The concept of enantiomeric switching was experimentally proven by Feringa and co-workers for sterically overcrowded alkenes.[49] The upper segment of the molecule consists of an unsymmetrical unit, generally a phenanthracene, naphthopyran or naphtho(thio)pyran, linked to a lower symmetrical unit, commonly a xanthene, thioxanthene or fluorene. The two units are connected by a stilbene type alkene bond, producing both a *cis* and *trans* configuration within the same molecule. Axial molecular chirality is generated through structural distortion as a result of steric interactions, similar in nature to that of 1,1'-binaphthalenes.[49] The steric bulk of the upper section is sufficient to prevent rapid racemisation, whilst retaining a degree of conformational flexibility to inhibit excessive distortion, which would also result in racemisation. At selected wavelengths, the alkenes undergo a *cis-trans* isomerism similar in nature to that of stilbenes, with photocyclisation prevented by careful structural design.[47]

The switching of enantiomeric overcrowded alkenes represents a three-stage switch. Irradiation of racemate **29**, with circularly polarised light of either handedness, produced the *P*-**29** or *M*-**29** enantiomer in excess. Conversion between the two enantiomers was shown to be possible upon irradiation with left or right-handed circularly polarised light, with enantiomeric excesses of 0.07% generated for each enantiomer. Racemic **29** was regenerated by irradiation with linear polarised light (*Figure 1.22*). Despite the feasible nature of the system, the low Kuhn anisotropy factor and prolonged irradiation times were problematic. Their application as liquid crystal dopants also proved disappointing, with low helical twisting powers of 0.1 μm^{-1} producing only large pitch lengths at 0.07% enantiomeric excess. Despite the low ee, coupled with the low helical twisting power, the system proved sufficient to induce nematic to chiral nematic phase transitions.

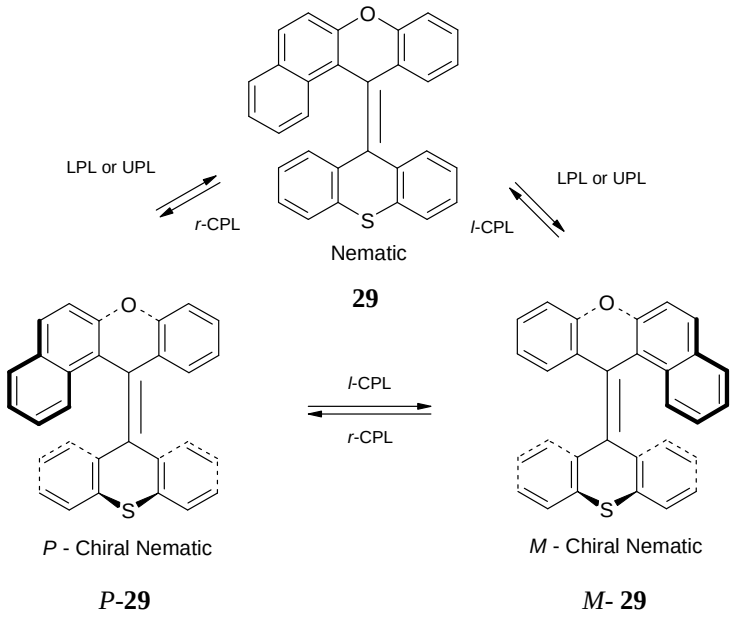


Figure 1.22 – Sterically overcrowded alkenes as switchable dopants

A second class of enantiomeric switches were developed by Schuster and co-workers based on cycloalkenones, intended for liquid crystal application (*Figure 1.23*).[50-53] Again axial chirality is generated through helical distortion of the structure. Incorporation of a styrene or acrylic ester functionality induces racemisation of the material upon irradiation induced isomerism. Again large Kuhn anisotropy factors were necessary to induce sufficient enantiomeric excesses.

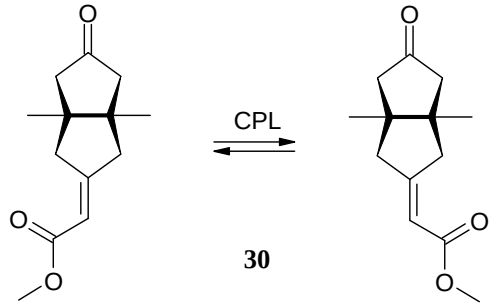
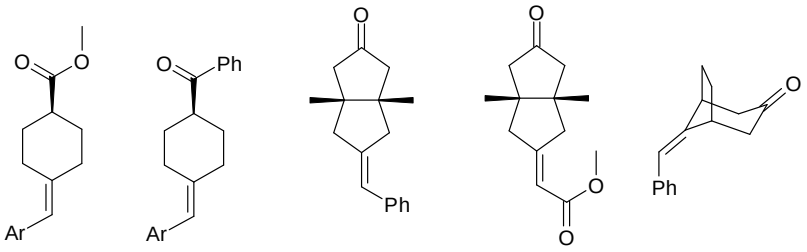


Figure 1.23 – Axially chiral cycloalkenones as chiroptical switches

Initial efforts with methyl ester **31** led to rapid racemisation; however, both styrene compounds **31** and **32** were found to undergo competing photodegredation, as well as possessing low Kuhn anisotropy values.[51] The design features were improved by Schuster with derivatives **30** and **33**, through separation of the light-absorbing and photoisomerisation units. High Kuhn anisotropy values were also generated through

positioning of a ketone with forbidden n-π^* transitions. Photoresolution of **30** was successful in producing an enantiomeric excess of 0.4%, with switching between enantiomeric states also possible. Substantially higher enantiomeric excesses were reported for compound **34**; however photoresolution proved excessively slow (*Figure 1.24*).[53]



31 **32** **33** **30** **34**

Figure 1.24 – Axially chiral cycloalkenone molecular switches

Despite the potential of the cycloalkenones towards liquid crystal application, their success has been limited. Nematic to chiral nematic phase transitions were observed, but reversible switching to regenerate the nematic phase was not. The issue of liquid crystal compatibility, producing poor helical twisting powers (β_M = 5.5 μm^{-1} for **30**), again proved a limiting factor in their application as a switchable dopant system.[54, 55]

1.1.6.2 – The Switching of Diastereomers (Type 2 Switches)

The concept of diastereomeric switching is again based on the sterically overcrowded alkene class of compound, similar in structure to the overcrowded alkenes previously detailed. Irradiation produces a stilbene type *cis-trans* isomerism and a resultant change in helix handedness, whilst protecting against photocyclisation through careful structural design (*Figure 1.25*).[46] Barriers to racemisation are readily optimised through the alteration of the bridged groups, namely the X and Y heteroatoms. The diastereomeric nature is produced by the additional functionalities incorporated into the overall structure. The near mirror-image isomers, however, display closely matched circular dichromism spectra, and so they are considered *pseudo*-enantiomeric in nature. The nature of the substituents presents the opportunity to selectively tune the wavelength of absorption, for increased control over the switching process. Once again the application to liquid crystal systems is limited by the low helical twisting powers observed. However,

mesogenic functionalisation of the structure, whilst maintaining the optimal properties of the switch, may potentially lead to increased compatibility with the nematic host and improve the switching system.

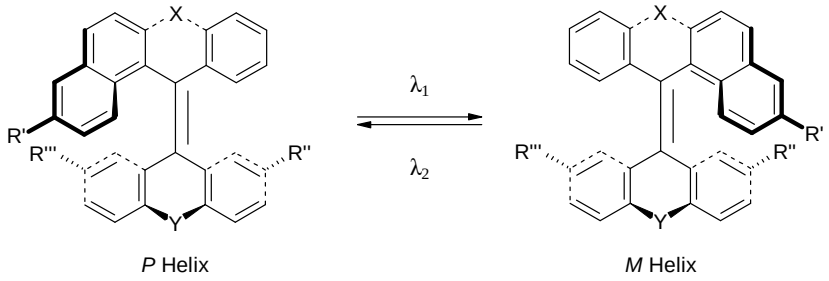
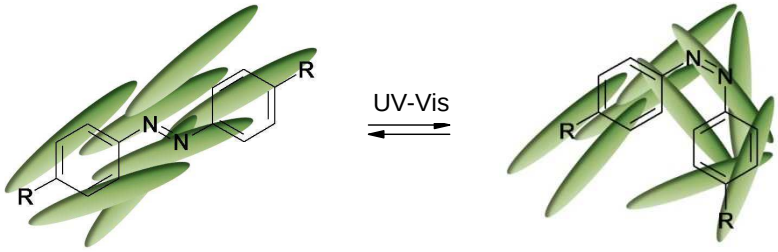


Figure 1.25 – Overcrowded alkenes as diastereomeric molecular switches.

1.1.6.3 – Type 3 Switches

The previously detailed switching systems have involved control of the molecular chirality. In contrast, Type 3 switches are formed from a combination of a chiral auxiliary and a switchable unit. This results in any switching process excluding the chiral auxiliary itself, and instead inducing change in the molecular structure, and therefore the chiral properties of the entire molecule.[56-60]

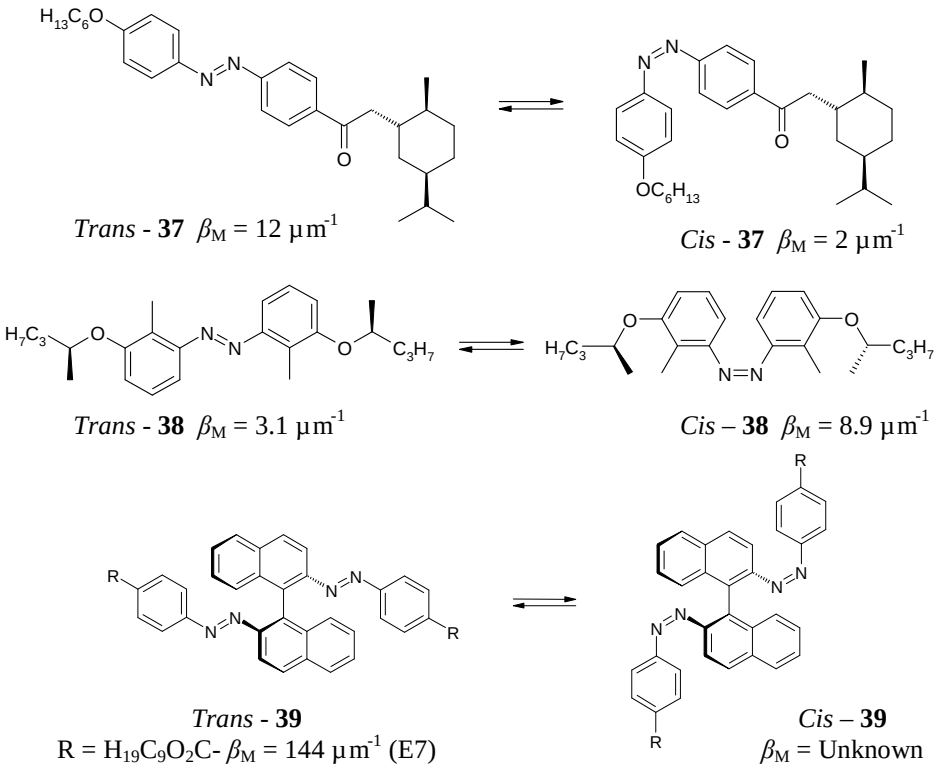
Azobenzenes form the majority of Type 3 switches that are commonly encountered. Large changes in molecular shape are associated with the *cis-trans* (*E-Z*) isomerisation of azobenzenes upon irradiation with selective wavelengths of light. The sensitivity of liquid crystal systems to changes in molecular structure means that the Type 3 switches are ideally suited to liquid crystal application, either as liquid crystal mesogens themselves, or as chiral nematic dopants. The *trans*-azobenzene isomer **35** is rod-like in its structure, and as such is capable itself of forming a nematic phase, or stabilising the nematic phase as a guest material. In contrast the *cis*-isomer **36** has a bent conformation, which serves to destabilise the nematic phase through the generated disorder (*Figure 1.26*). Switching between isomers therefore presents an effective mechanism for control of the liquid crystal system.



Trans-**35** *Cis*-**36**

Figure 1.26 – Effects of cis-trans isomerism on liquid crystal phase

Chiral nematic dopants comprising a chiral auxiliary and switchable azobenzene functionality have shown great promise in their use as chiroptical nematic dopants. As with the previously discussed axial and centrally chiral dopants, the azobenzene dopants also exhibit modest helical twisting powers, when incorporating an asymmetrical chiral carbon centre **37**, in comparison to their axially chiral counterparts **39** (*Figure 1.27*).[61-64] Whilst disruption of the liquid crystal phase is observed for the *cis*-4,4'-substituted azobenzenes, altering the substitution pattern by introducing 3,3'-substituents reverses the trend, as in the case of compound **38**, where the *cis* isomer exhibits a higher twisting power due to its more rod-like molecular shape.[65, 66]



Trans - **37** β_M = 12 µm^{-1}

Cis - **37** β_M = 2 µm^{-1}

Trans - **38** β_M = 3.1 µm^{-1}

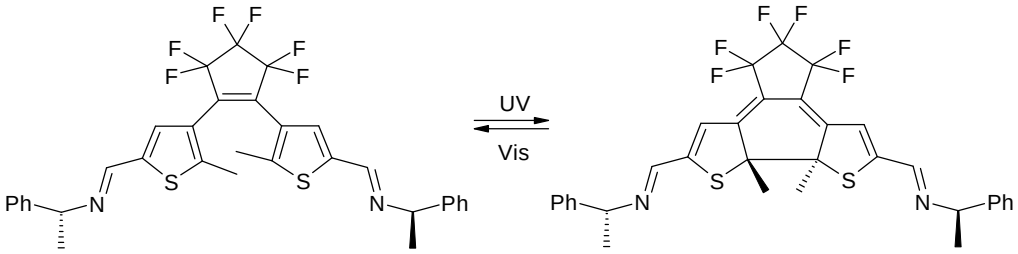
Cis – **38** β_M = 8.9 µm^{-1}

Trans - **39**
R = $H_{19}C_9O_2C$- β_M = 144 µm^{-1} (E7)

Cis – **39**
β_M = Unknown

Figure 1.27 – Bistable azobenzene based chiral nematic dopants

Despite the development of numerous switching systems in the literature, only the diarylethene and fulgide classes of compound exhibit the essential property of thermal stability at elevated temperatures (~100 °C). Upon irradiation, diarylethenes undergo a reversible ring closing cyclisation, resulting in distinct changes in molecular structure. Diarylethenes also display enhanced fatigue resistance, maintaining satisfactory performance for ring closing/opening cycles of up to 10^4. The change in molecular structure permits their application as chiral nematic dopants upon the incorporation of chiral substituents. Liquid crystal phase switching is based on either the open or closed structure producing a higher helical twisting power than the other. A chiral nematic to nematic phase change was observed for compound **40** upon irradiation with UV light, as a result of the extremely low helical twisting power of the ring-closed form being insufficient to induce chirality. Irradiation with visible light reversed the process, regenerating the chiral nematic phase. Deterioration of the liquid crystal phase was observed after six switching cycles (*Figure 1.28*).[67]



Ring Open – **40** β_M 13 μm^{-1} (K15) Ring Closed – **40** β_M ~0 μm^{-1} (K15)

Figure 1.28 – Diarylethene employed as a chiral nematic dopant

The conceptually similar fulgide family of compounds were first synthesised by Stobbe.[46] Heller introduced structural measures to limit the thermal reversibility of ring closure. The overcrowded structural features generate an axially chiral helical configuration, which is lost upon irradiation to form the centrally chiral ring cyclised product (*Figure 1.29*).[68] In the case of **41**, the *P*-**41** and *M*-**41** axially chiral compounds generate the *S*-**41** and *R*-**41** enantiomers respectively.

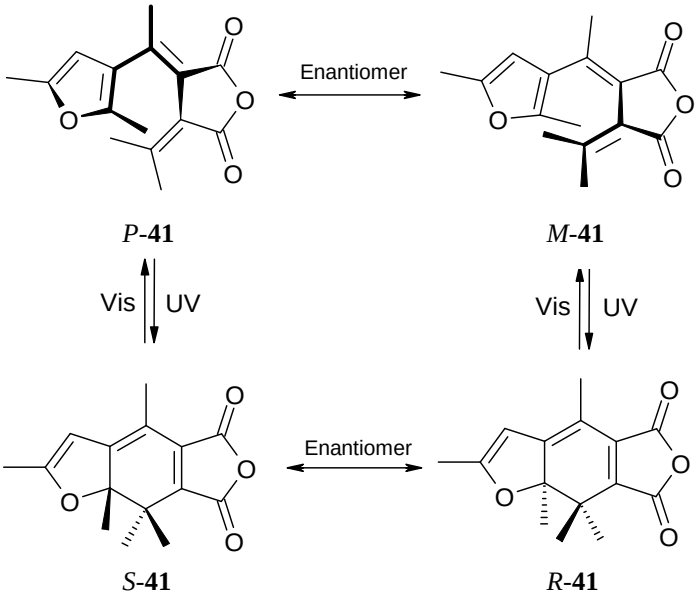


Figure 1.29– Chiroptical switching of fulgides

In their application as chiral nematic dopants, changes in chiral nematic pitch lengths have been reported independently by the groups of Schuster and Yokoyama. Schuster reported the use of fulgide **42** as a co-dopant, with binaphthalene **43** in K15, with reversible switching producing changes in pitch length up to 12 μm^{-1}.[69] Yokoyama employed binaphthol fulgide derivative **44**, achieving a change in pitch length from 15.8 μm^{-1} to 2.6 μm^{-1} (*Figure 1.30*).[70]

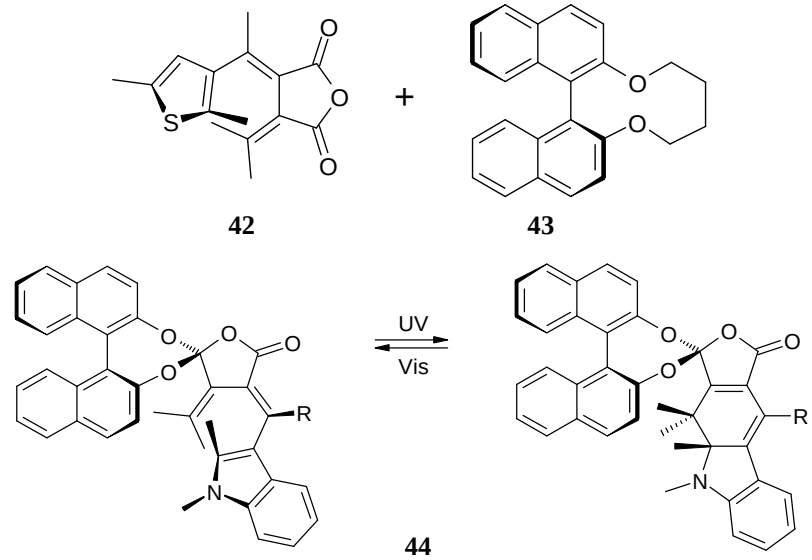


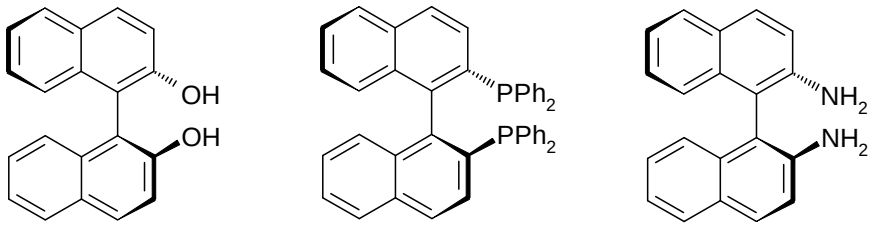
Figure 1.30 – Fulgides as chiral nematic dopants

The development of compounds capable of switching on the molecular level is currently in its infancy. Despite some significant advances in the field, problems

with thermal stability, fatigue resistance, and other key aspects need to be addressed. In addition to the immense efforts required, the production of materials capable of simple molecular switching is complicated further by the additional requirements for the successful switching of liquid crystal systems.

1.2 – Chiral Biaryls[71, 72]

It is clear that chiral biaryls, and chiral binaphthalenes in particular, are of immense importance in the fields of natural products, asymmetric synthesis, asymmetric catalysis and liquid crystals. It is therefore no surprise that the synthesis of axially chiral materials has received a great deal of attention.



45 **46** **47**

Figure 1.31 – Commercially available chiral binaphthalenes

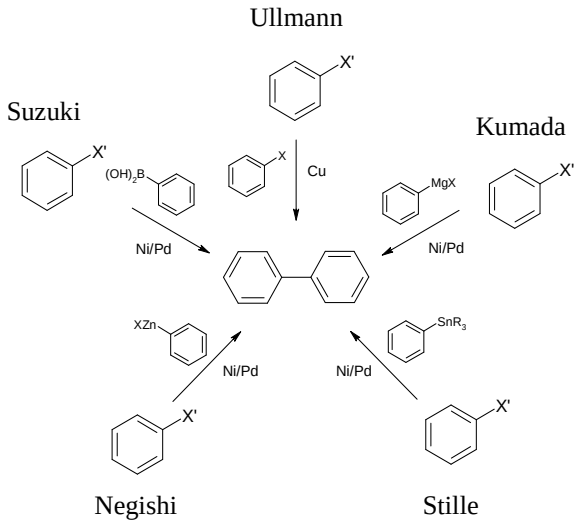
The synthesis of axially chiral compounds presents similar challenges to that of compounds containing an asymmetric chiral carbon centre. However, an additional challenge is the absence of an axial equivalent of the 'chiral pool'.[72] Chiral resolution has therefore remained an essential tool, despite the increased access via chiral aryl-aryl bond forming reactions.

Two approaches to chiral biaryl synthesis can be adopted. The classical method involves synthesis of the racemic compound, followed by subsequent chiral resolution to afford the individual isomers. This method, whilst involving a less complicated synthetic process, usually requires stoichiometric quantities of, generally expensive, chiral resolving agents, and is limited to the recovery of a maximum 50% of each individual isomer. The second method involves construction of the aryl-aryl axis in tandem with the induction of molecular asymmetry. Attempts to induce chirality directly have extended to the use of chiral auxiliaries, chiral starting materials and chiral catalysis. It is to be noted that the synthesis of biaryls is generally a sterically hindered process, which requires forcing conditions to achieve

respectable yields. However, the use of harsh reaction conditions can result in poor chiral selectivity, requiring a fine balance to couple yield with stereoselectivity.

1.2.1 – Racemic Synthesis & Chiral Resolution

The traditional method of aryl-aryl bond formation was via the Ullmann coupling of two aryl halides in the presence of copper metal. Whilst a number of biaryl structures have been produced via this method, the progress of nickel and palladium catalysed aryl-aryl bond forming reactions have led to the Ullmann coupling, whilst remaining effective in certain cases, becoming somewhat obsolete. The nickel/palladium catalysed methods, including the renowned Kumada,[73] Stille,[74] Negishi[75] and Suzuki[76] coupling reactions (*Figure 1.32)*, offer distinct advantages over the Ullmann coupling, such as effective unsymmetrical biaryl synthesis, mild reaction conditions and, in certain cases, enhanced functional group tolerance.

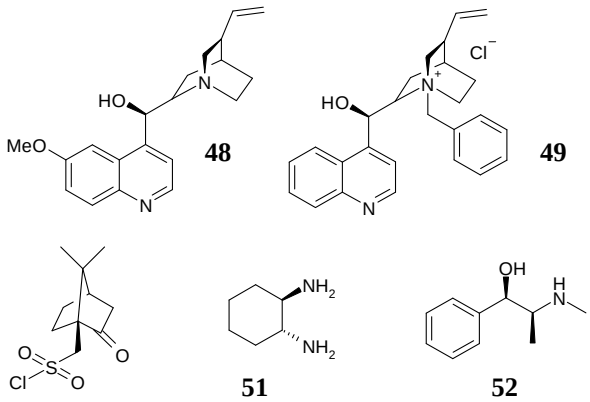


X = Cl, Br, I; X’ = Br, I, OTf

Figure 1.32 – Commonly applied aryl-aryl bond forming reactions

Whilst racemic couplings have proved effective, the recovery of optically pure materials is ultimately dependent on the process of chiral resolution. As such, various methods of chiral resolution have been devised, utilising a diverse range of reagents such as **48-52** (*Figure 1.33*). The formation of diastereomeric complexes, producing different solubility properties, can present the opportunity for recrystallisation of one complex preferentially over the other. Similarly the formation of diastereomers via covalent bonding of a chiral auxiliary offers the

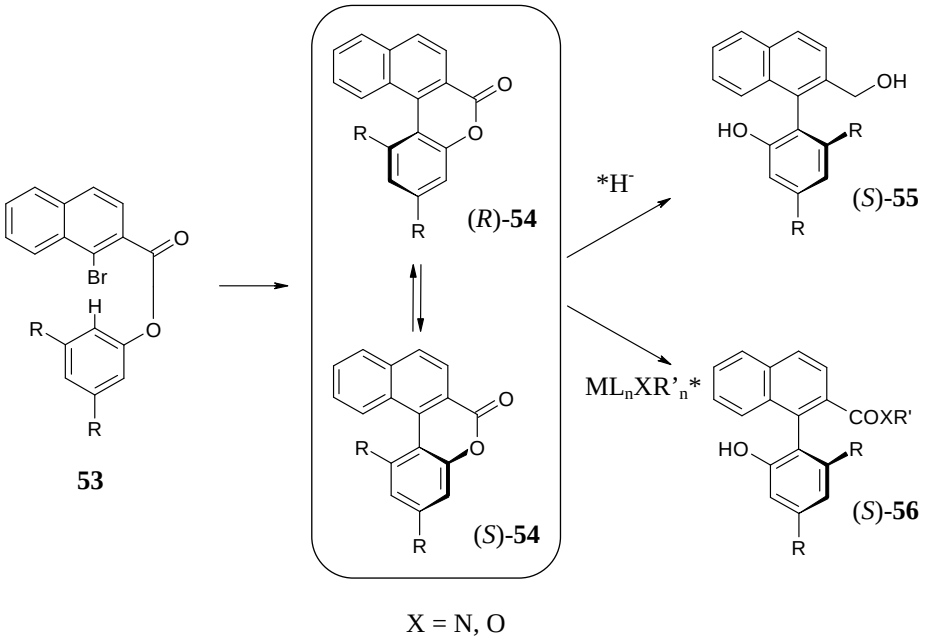
prospect of separation, either through the recrystallisation of diastereomers with different solubility properties, or through chromatographic separation, provided that sufficiently different retention factors are observed. Despite the recovery of materials in decent yield and enantiomeric excess, the procedure is limited by the stoichiometric quantities of often expensive chiral resolving agents.



48 Quinine;[77] **49** (*R*)-*N*-Benzylcinchodinium chloride;[78-80] **50** (*S*)-Camphor-10-sulphonyl chloride;[81, 82] **51** (1*R*,2*R*)-diaminocyclohexane;[83] **52** Ephedrine[84]

Figure 1.33 – Commonly employed chiral resolving agents

Whilst not strictly considered a racemic coupling and chiral resolution strategy, an efficient method of biaryl synthesis was developed by Bringmann *et al.* based on the chiral cleavage of a bridging lactone.[85-87] Formation of the biaryl is achieved in a non-stereoselective manner from a preformed arylbromide ester, such as compound **53**, via a standard transition metal catalysed coupling reaction. The bridging lactone **54** permits rapid interconversion of the enantiomers, in comparison to the ring opened form, via a lowering of the racemisation barrier. The method of asymmetric cleavage of the lactone bridge determines the resultant product as a chiral biaryl ester or amine **56**, or alcohol **55**, with reported yields of up to 97% in up to 90% de (*Scheme 1.3*). The lactone method of biaryl synthesis has successfully been applied to the total synthesis of natural products including knipholone, korupensamine A and steganone among others.[71]



* Chiral Reagent = $*H^-$ e.g. BINAL-H; HXR_n* e.g. 1-phenylethylamine or menthol

Scheme 1.3 – Stereoselective lactone approach to biaryl synthesis

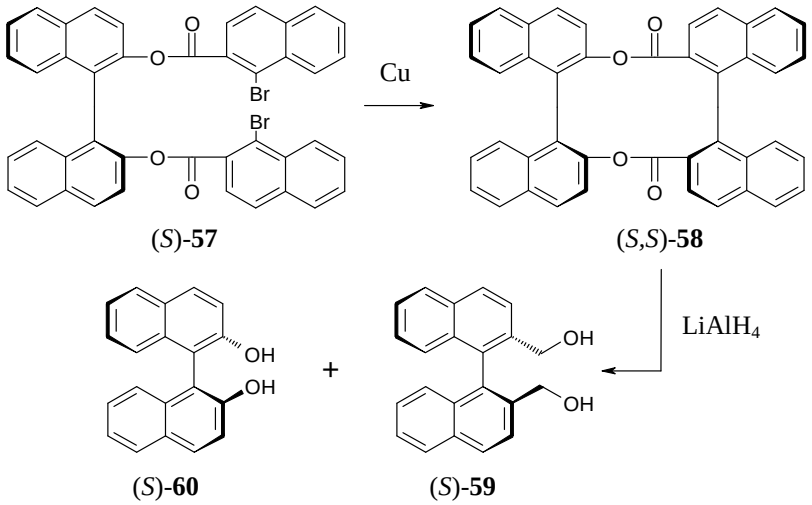
1.2.2 – Asymmetric Aryl-Aryl Couplings

Asymmetric aryl-aryl couplings can be broadly grouped into two categories: diastereoselective and enantioselective. Diastereoselective methods typically involve the use of a chiral bridge, often sourced from the chiral pool, which pre-links the substituents, through which an intramolecular coupling is achieved in the desired fashion. Enantioselective methods utilise chiral leaving groups, stoichiometric or catalytic oxidative dimerisations, and transition metal based catalytic couplings employing catalytic quantities of chiral ligands.

The application of chiral auxiliaries in asymmetric synthesis has been well documented since their introduction by Corey in 1975.[90] Their application in biaryl synthesis is advantageous in that on occasion only one coupling partner requires chiral modification, presenting a sterically less hindered coupling process that utilises less potentially costly chiral material.

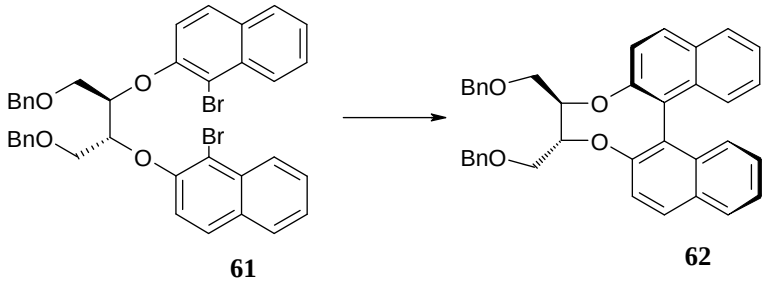
The application of chiral bridges for asymmetric biaryl synthesis was first introduced by Miyano *et al.*, who employed chiral diesters in an intramolecular Ullmann-type coupling to produce biaryls in respectable yields, with excellent stereocontrol of up to 100% de. Cleavage of the diester, via hydrolysis, afforded the desired biaryl and

the subsequent recovery of the chiral bridge, somewhat mitigating the requirement for stoichiometric quantities of chiral starting material (*Scheme 1.4*).[88]



Scheme 1.4 – Application of chiral starting material in chiral biaryl synthesis

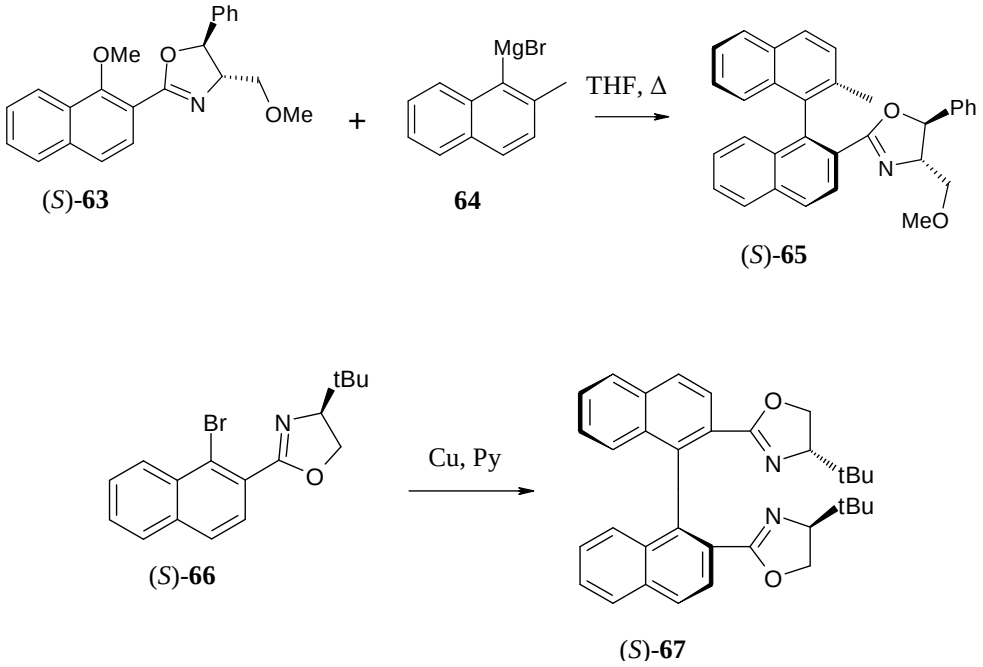
Superior couplings were reported by Lipshutz using functionalised chiral tartrate tethers with yields up to 78% and 100% de (*Scheme 1.5*).[89] Despite the excellent stereoselectivity of the protocol the recovered yields are often moderate, with further synthetic steps required to introduce and remove the chiral bridges using potentially harsh reaction conditions.



Scheme 1.5 – Asymmetric coupling employing chiral tartrate tether

Meyers developed an efficient strategy based on the nucleophilic aromatic substitution (S_NAr) of a methoxy group **63** with an aryl Grignard coupling partner **64** (*Scheme 1.6*).[91] The *ortho*-chiral oxazoline facilitated displacement of the methoxy group through stabilisation of the resulting negative charge, permitting convenient access to unsymmetrical biaryl **65**. Inconveniences of the protocol include the requirement for post-reaction manipulation of the chiral oxazoline functionality, which introduces extra reaction steps, and the limited functional group tolerance of the Grignard coupling partner. Meyers also developed a procedure to produce

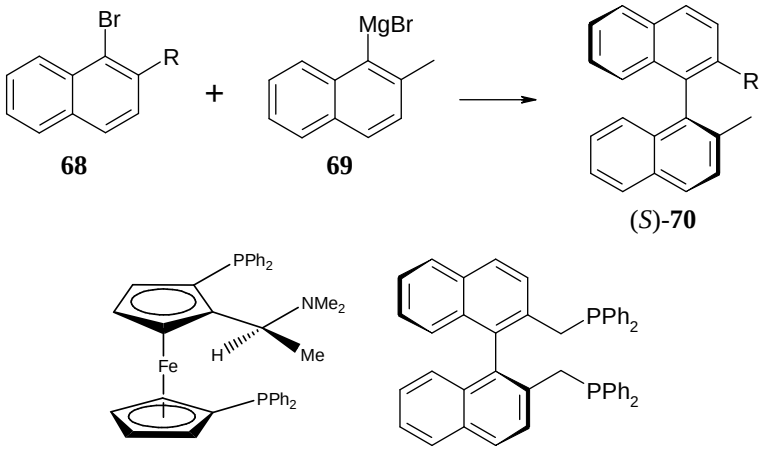
symmetrical biaryl **67** via the intermolecular Ullmann coupling of **66**. Diastereoselectivity was found to be dependent on the steric bulk of the oxazoline substituent, with up to 94% de recorded in 77% yield, using a *tert*-butyl substituent. The procedure again suffers economically, due to the requirement for stoichiometric quantities of chiral oxazoline starting material (*Scheme 1.6*).



Scheme 1.6 – Chiral biaryl synthesis utilising chiral auxiliaries

The increasing exploitation of asymmetric catalysis has led to significant advances in the field since its initial conception. Catalytic syntheses offer significant advantages over the previously described strategies, due to the mild reaction conditions, the ability to tailor individual coupling partners to meet structural requirements, the relatively easy access to unsymmetrical biaryls, and the catalytic quantities of chiral reagents.

Kumada *et al.* reported the first successful nickel catalysed asymmetric coupling between aryl halide **68** and aryl Grignard reagent **69**, using the chiral ligands (*S*)-(*R*)-DPPFA **71**[92] and (*S*)-NAPHOS **72**.[93, 94] The obtained yields proved respectable in tandem with enantiomeric excesses up to 95% (*Scheme 1.7*). Whilst a limited number of reported syntheses utilise this method, the nature of the catalyst system has been shown to produce variable results, with functional group tolerance limited by the use of a Grignard reagent.[95]

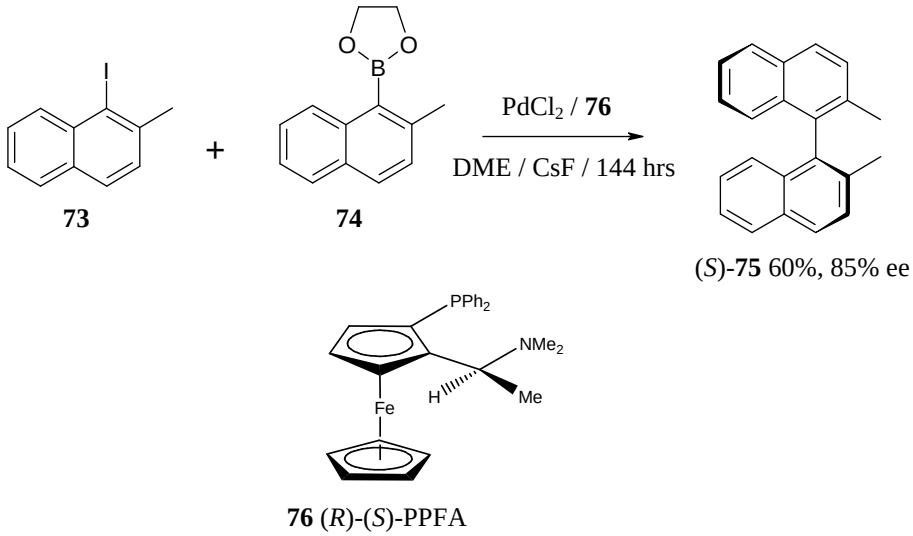


68 **69** (*S*)-**70**

71 (*S*)-(*R*)-DPPFA **72** (*S*)-NAPHOS

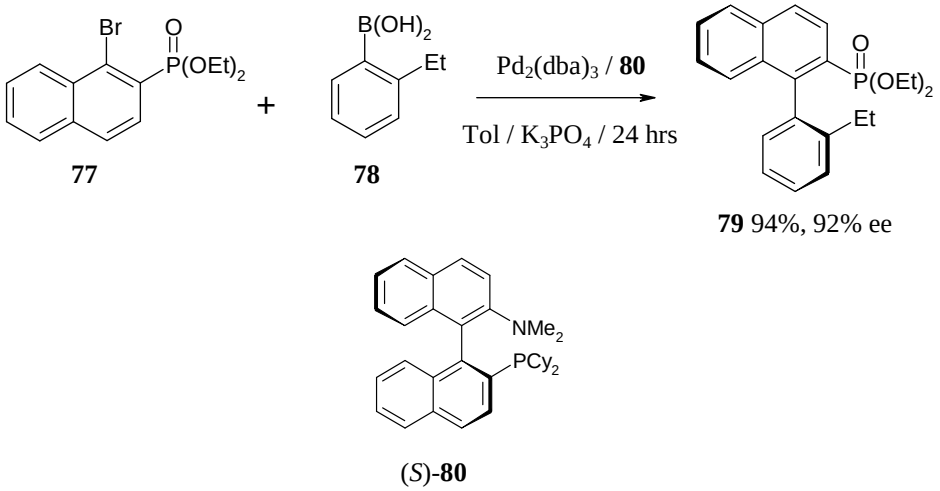
Scheme 1.7 – Asymmetric Kumada coupling reaction

The lack of functional group tolerance associated with the Kumada coupling has led to the development of milder catalytic cross-coupling reactions. The considerable advantages of the Suzuki-Miyaura cross-coupling reaction – including milder reaction conditions, non-toxic reagents and high functional group tolerance – has led to its increased importance and application as a method of aryl-aryl bond forming.[76] Uemura and co-workers reported the use of planar-chiral aryl halides as an effective method of chiral biaryl synthesis under Suzuki-Miyaura conditions.[96] The first investigations into asymmetric Suzuki-Miyaura syntheses using achiral reagents were reported by Cammidge and Crépy. Iodonaphthalene **73** and boronic ester **74** were employed as model substrates, with $PdCl_2$ and a number of chiral binaphthalene and ferrocenyl ligands as the catalyst system. Variable yields and enantiomeric excesses were returned, with chiral ligand **76** inducing the most successful coupling, in 60% yield and 85% ee (*Scheme 1.8*).[95, 97]



Scheme 1.8 – First asymmetric Suzuki-Miyaura cross-coupling

Buchwald *et al.* also reported their investigations into the asymmetric Suzuki-Miyaura coupling reaction, utilising chiral binaphthalene ligand **80** (*Scheme 1.9*). The coupling of naphthyl phosphate **77** with boronic acid **78** afforded biaryl phosphate **79** in excellent yield (94%) and stereoselectivity (92% ee), representing the most successful asymmetric Suzuki-Miyaura coupling to date.[98]



Scheme 1.9 – Asymmetric Suzuki-Miyaura coupling by Buchwald

The significant advances and efforts in biaryl syntheses highlight the importance of axially chiral materials in fields such as asymmetric catalysis, asymmetric synthesis, natural products, and liquid crystal chemistry. Despite substantial progress and

diverse synthetic strategies towards biaryl synthesis, a complete approach, addressing each of the key requirements, remains elusive. Methods such as the lactone synthesis have proved successful in the total synthesis of some natural products; however, it is catalytic procedures which offer the greatest opportunity for the mild, efficient, and economic syntheses of biaryl structures. Despite the obvious advantages of asymmetric catalytic couplings, examples utilising other transition metals (e.g. zinc/Negishi, tin/Stille) have yet to be realised. The asymmetric Suzuki-Miyaura coupling has proved effective at introducing high stereoselectivities in tandem with good yield in selected cases, but the variable nature has limited the application to date. It remains to be seen whether the potential of asymmetric catalysis will be fully realised in the synthesis of chiral biaryls.

1.3 – Project Outline

The induced chiral nematic phase has attracted substantial interest due to potential applications in displays, optical storage, lasers, dyes and pigments. The process of inducing chirality, through the solvation of a chiral non-racemic dopant into an achiral nematic host, has its disadvantages. To achieve sufficient pitch lengths (visible light wavelength) for particular applications, high dopant concentrations may be required, which may affect the clearing point, optical properties (birefringence), viscosity. In addition, crystallisation from the host nematic may be observed at increasing concentrations. These potential problems can be abated through the careful design of dopants with elevated helical twisting powers, which can accomplish the required pitch lengths at low concentrations. In this approach, chiral binaphthalenes have shown considerable promise in their application as high twist nematic dopants.

Significant research has also been undertaken to determine the mechanism of chirality induction from biaryl dopants to the host nematic liquid crystal, either via practical experimentation or via theoretical studies. However, whilst a few general predictions of the dopants' structural effects on helical twisting power have been reported (e.g. dihedral angle, mesogenic functionalisation, substituent location), no detailed observations on the effects of specific functional groups have been noted.

Therefore, the main objective of this research was to design and synthesise a range of high twist nematic dopants based on the axially chiral 1,1'-binaphthalene

skeleton, and to assess the effects of substitution on helical twisting power. Strategic substituent placement and nature was expected to produce elevated helical twisting powers through mesogenic functionalisation and increasing liquid crystal host compatibility. The designed synthetic routes to such derivatives were expected to produce optically pure materials, and to be accessible over a minimal number of steps to enhance the yield and ease of synthesis. In addition, assessment of the individual substituent effects on helical twisting power were to be catalogued, to provide a detailed analysis.

A secondary sub-project was to be based on a proof of concept approach to the design of a Type 1 chiroptical molecular switch, based on the chiral binaphthalene skeleton. The project was to involve the development and synthesis of optically pure materials, with potential for chiroptical switching upon irradiation with circularly polarised light (CPL). Whilst the switching process requires only racemic materials in order to generate an enantiomeric excess, the optically pure materials were required for property analysis and concept feasibility.

Chapter 2

Results & Discussion

2.1 – High Twist Nematic Dopants

2.1.1 – The Induction of Chirality

The lure of potential applications has led to significant interest into the induced chiral nematic phase, with the general focus of research divided into two distinct objectives. The first concerns a design-based approach to produce high twist nematic dopants, and an understanding of the complex dopant-host interactions that generate the chiral nematic phase. The second concerns the development of dopants possessing switchable (bistable) properties for potential control over the properties of the chiral nematic phase.[45] The latter of the two will be discussed in greater detail later in the chapter.

It is clear that in order to design dopants capable of inducing a high degree of twist, an understanding of the complex interactions between the dopant and nematic host are of vital importance. Whilst it is recognised that the magnitude and sign of the helical twist is strongly dependent on factors such as temperature, the nature of the nematic host, and the origin of the dopant material's chirality,[99-104] a detailed understanding of the mechanism by which chirality is transferred to the nematic host remains elusive.

To date, numerous theoretical simulation techniques[5, 105] and proposed models have attempted to determine the origin of the induced chirality, to enable the prediction of the sign and magnitude of the helical twisting power for a given dopant structure. The work of Nordio and Ferrarini has found some success in predicting helical twisting power, based on theoretical mean field calculations of the interaction between chiral dopant and nematic liquid crystal host.[106-108] Other simulations based on a number of complex factors such as dopant-host chiral anisotropic interactions[109, 110] and dopant shape and solvent macroscopic properties[111, 112] have found varying degrees of success.

Gottarelli and Spada attempted to justify the high helical twisting powers observed in their *trans*-stilbene oxide derivative systems through a proposed model.[41] Their model suggested that chirality is transferred from the chiral guest molecules to the nematic host via chiral conformations. The nematic solvent molecules were described as existing in chiral enantiomorphic conformations in rapid

interconversion, which were stabilised upon interaction with a dopant molecule. Chirality is then transferred throughout the system through each chiral solvent molecule acting as a template for its nearest neighbour, and so forth, inducing the chiral macrostructure. The model was subsequently applied, with a high degree of success, to chiral binaphthalene derivatives in biaryl nematic solvents. It was later determined, in such systems, that the binaphthalene two-fold symmetry axis aligns perpendicular to the nematic director, inducing a homochiral stabilisation of the mesogens and deracemisation of the bulk solvent (*Figure 2.1*).[39]

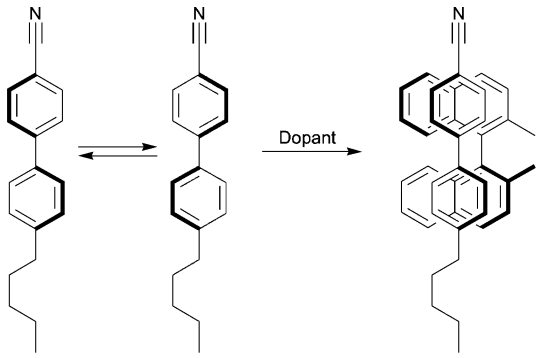


Figure 2.1 - Mechanism of chiral induction

The transfer of chirality via this mechanism, and ultimately the helical twisting power, is highly dependent on the dihedral angle θ between the naphthyl planes.[107, 113, 114] The dihedral angle itself is dictated by the nature and position of ring substituents, most notably the 2,2'-substituents. Sterically large and unlinked substituents are known to induce dihedral angles of $90° < \theta < 180°$ and a transoid conformation. In contrast, covalently linked or hydrogen bonded substituents result in dihedral angles of $0° < \theta < 90°$ and a cisoid conformation (*Figure 2.2*). Theoretical calculations predict maximum helical twisting powers for dihedral angles of $\theta = 45°$ or 135°, with a zero value at 90°, where an effectively racemic system exists.[42, 43] Chiral induction is known to be more effective for cisoid conformations than for transoid conformations, with large helical twisting powers observed. These predictions are experimentally observed for bridged binaphthalene dopants, where dihedral angles close to the optimum produce high helical twisting powers. In contrast, small, unlinked 2,2'-substituents are observed to produce low helical twisting powers, potentially as a result of a dihedral angle close to the 90° zero value.[115]

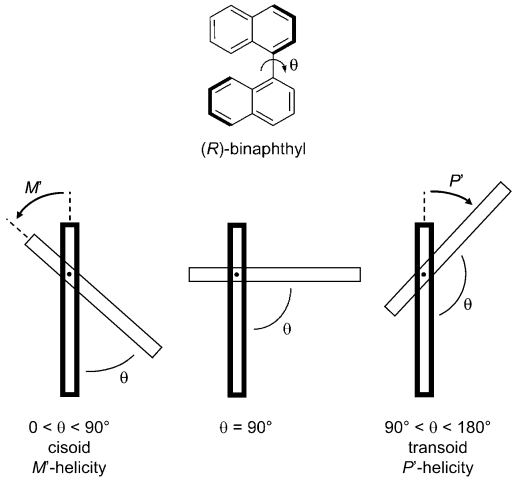
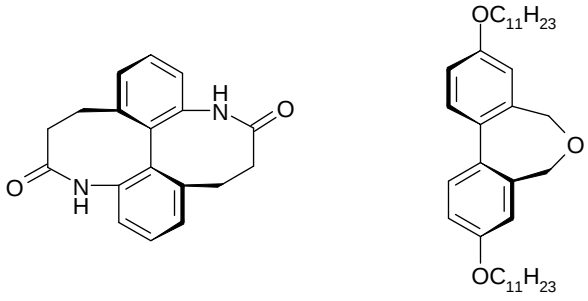


Figure 2.2 – Binaphthalene conformations[45]

In the case of chiral biphenyls, conformity with the model is not consistently observed, despite their structural analogy to binaphthalene compounds.[116, 117] It has recently been proposed by Ferrarini *et al.* that the orientation of the biphenyl guest molecules in relation to the host nematic director is shape dependent.[118] Substituted biphenyl derivatives with 2,2' and 6,6'-substituents possess a disc-like molecular shape, and preferentially align the molecular plane perpendicular to the nematic director. The inclusion of 4,4'-substituents induces a more rod-like molecular shape, which displays a tendency to align the long molecular axis parallel to the nematic director (*Figure 2.3*). This may inevitably induce differences in the mechanism of chiral induction.



81 **82**

Figure 2.3 – Chiral biphenyl derivatives with disc and rod molecular structure

In the binaphthalene model proposed by Gottarelli and Spada, it is clear that the transfer of chirality, via chiral conformations, is highly dependent on the orientation of the dopant molecules with respect to the nematic director. It is therefore predictable that unsubstituted binaphthalenes, or derivatives with small 2,2'-

substituents, will conform to the proposed model and align with the two-fold symmetry axis perpendicular to the nematic director. It is also reasonable to assume that structural modification of the binaphthalene core, to a more rod-like molecular shape, may induce an alternate orientation with respect to the nematic director (*Figure 2.4*).

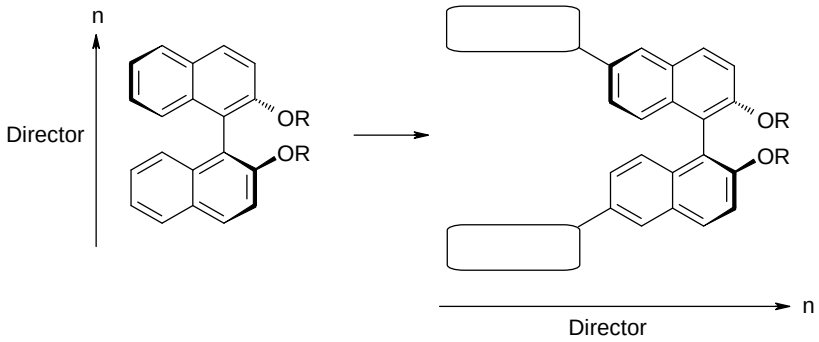
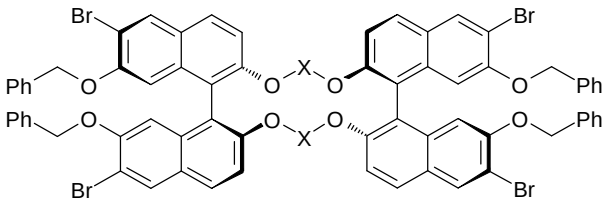


Figure 2.4 Proposed alignment of nematic director from a disc-like to rod-like molecular shape transition

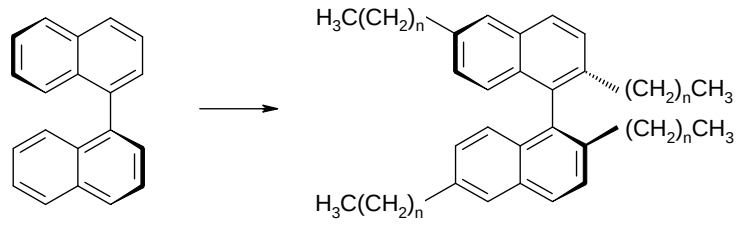
Deviation of molecular orientation from that of the Gottarelli-Spada model prevents the transfer of chirality via chiral conformations. Whilst generalised predictions of the structural effects on helical twisting power may be predicted for the current model (e.g. effects of dihedral angle), an alternate mechanism of chiral induction may not adhere to such observations, and may represent a more efficient mechanism of chirality transfer. This is supported by the experimentally observed helical twisting power of the 1,1'-bi(2-naphthol) based dimer **83**, reported by Diederich and Spada (*Figure 2.5*). The helical twisting power of 242.3 μm^{-1} is far higher than the expected additive sum of the two individual binaphthalene monomers.[102] It is possible that the increased helical twisting power observed is a direct result of the disc to rod-like molecular shape transitions, representing a more efficient mechanism of chirality transfer. Deussen and Shibaev also reported similar increases in helical twisting power with their 6,6'-vinyl and styryl derivatives.[119]



83 X = $CH_2(p\text{-}C_6H_4)CH_2$ β_M = 242.3 μm^{-1} (E7)

Figure 2.5 - Potential effects of molecular elongation on helical twisting power

It was therefore envisaged that alteration of the binaphthalene shape would induce an alternative mechanism for chiral induction, with potential for dopants with enhanced helical twisting powers. To investigate the proposal, a prototype dopant was designed with the primary objective of modifying the molecular shape from that of a disc to an elongated 'dual' rod-like structure. The initial design was expected to remain simplistic in its approach, limiting the extension of the two naphthalene core units in both the 2,2' and 6,6'-positions to linear alkyl chains **84** (*Figure 2.6*).



84

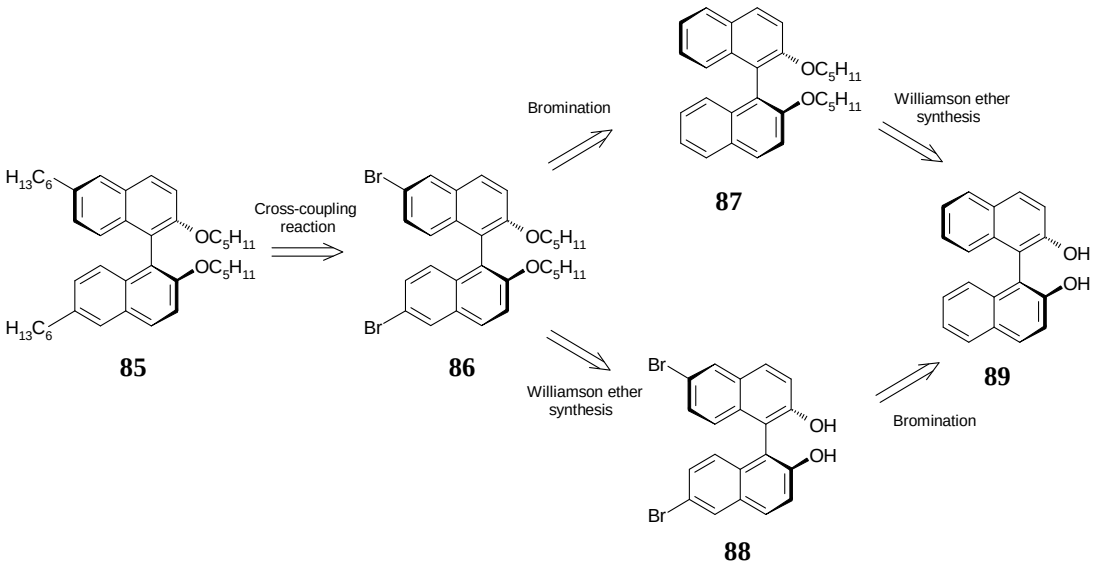
Figure 2.6 - Initial prototype dopant design

2.1.2 – Prototype Dopant Synthesis & Analysis

Our initial synthetic concern was the formation of the binaphthalene skeleton. It was deemed possible to synthesise the desired binaphthalene core structure via an asymmetric cross-coupling reaction, or via a racemic cross-coupling reaction and subsequent optical resolution. Despite abundant experience of such syntheses within the Cammidge group,[95, 97, 120-122] it was decided that the requirement for optically pure materials was essential, and that any potential problems associated with optical resolution be avoided through the use of an optically pure starting material. Optically pure 1,1'-bi(2-naphthol) has been widely utilised as an axially chiral starting material in the synthesis of asymmetric ligands, with various transformations prevalent in the

literature. The relatively low cost and presence of the easily manipulated, ideally placed 2,2'-hydroxyl functionalities made it an ideal candidate for our dopant syntheses.

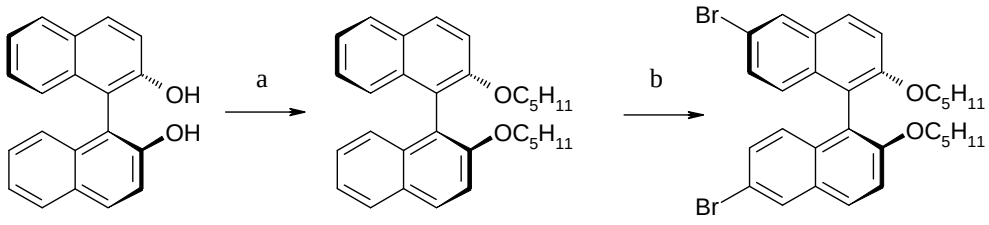
Construction of the dopant was expected to be possible via the retrosynthetic disconnections shown in *Scheme 2.1*. In the event of success with the prototype dopant, successful synthesis of dibromide **86** would provide access to a wide range of structurally similar dopants. In the forward sense, protection of the 2,2'-hydroxyl functionalities under Williamson ether synthesis conditions would produce **87**, which upon regioselective bromination would give **86**. A relatively straightforward Kumada or Suzuki-Miyaura cross-coupling was expected to afford target compound **85**. The introduction of 5 and 6 membered chains were expected to be sufficient to induce a change in molecular shape.



*Scheme 2.1 - Retrosynthetic analysis of the prototype dopant **85***

It was also possible to produce dibromide **86** via initial bromination of 1,1'-bi(2-naphthol) **89** to afford **88,** which would allow for protection of the 2,2'-hydroxyl functionalities with groups of varying nature. Despite the attractiveness of large scale synthesis of **88** providing access to a wide range of protected dibromide intermediates, initial protection of the 2,2'-hydroxyl groups was favoured. This was primarily undertaken to guard against potential loss of optical purity in subsequent reaction steps.[123, 124] It was also noted that monitoring of the reaction progress during the bromination of **89** was limited, resulting in premature termination of the reaction and problems with the resulting product purity.[125]

Protection of the 2,2'-hydroxyl groups was achieved using the non-racemising conditions of Kellogg[126, 127] to afford **87** in 73% isolated yield. Regioselective bromination of the 6,6'-positions was reportedly achievable at ambient temperatures using elemental bromine.[125] However, complete regiocontrol was not observed at such temperatures, with competing thermodynamic bromination of the 3,3'-positions. A reduction in temperature to -10°C was sufficient to achieve complete regiocontrol and afford dibromide **86** in 92% yield (*Scheme 2.2*).

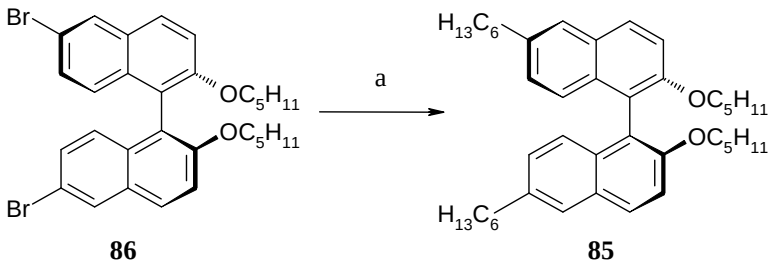


89 **87** **86**

a) *n*-$H_{11}C_5Br$ / K_2CO_3 / Acetone (73%); b) Br_2 / DCM / -10°C / streaming N_2 (92%)

*Scheme 2.2 - Synthesis of dibromide intermediate **86***

The final step to form prototype dopant **85** from dibromide **86** was expected to be readily achievable via a transition metal cross-coupling reaction. A Kumada coupling was expected to provide a more simplistic method of synthesis; however, it was decided to attempt the synthesis via Suzuki-Miyaura coupling due to the enhanced scope for future dopant design. The synthesis of the prototype dopant would offer the opportunity to examine the reaction conditions on a sterically undemanding substrate (*Scheme 2.3*).



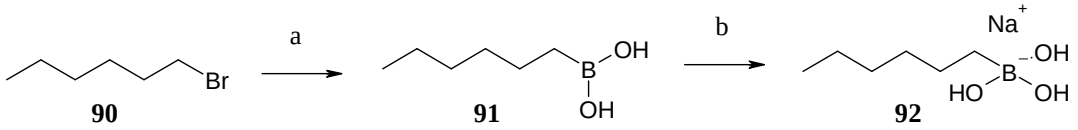
86 **85**

a) *n*-$H_{13}C_6B(OH)_2$ / PdL_2 / Base

*Scheme 2.3 - Synthesis of prototype dopant **85** under Suzuki-Miyaura conditions*

The required 1-hexylboronic acid **91** was available from a commercial source, however the high cost led us to synthesise it in house from cheaply available 1-bromohexane **90**. Quenching of the Grignard reagent, formed from **90**, with

trimethylborate and subsequent hydrolysis afforded the crude boronic acid (*Scheme 2.4*).

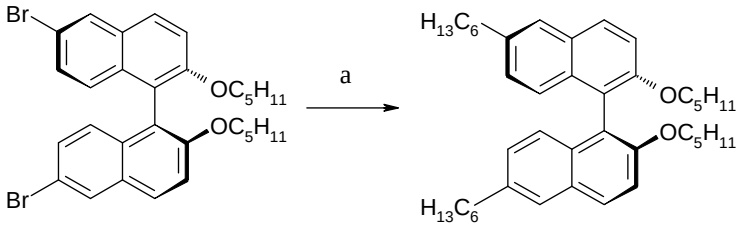


90 **91** **92**

a) i) Mg / Et_2O / reflux; ii) $B(OCH_3)_3$ / Et_2O / -78°C; iii) 1M HCl / rt;
b) Toluene / Δ / sat. NaOH

*Scheme 2.4 - Synthesis of 1-hexylboronic acid **91** and boronate salt **92***

Purification of the boronic acid proved difficult due to its waxy nature. It was decided to purify the boronic acid by conversion to the boronate salt **92**, and incorporate the boronate salt directly into the Suzuki-Miyaura coupling reaction, in accordance with the protocol recently developed by our group (*Scheme 2.5*).[122] Standard Suzuki-Miyaura conditions afforded prototype dopant **85** in 71% yield.

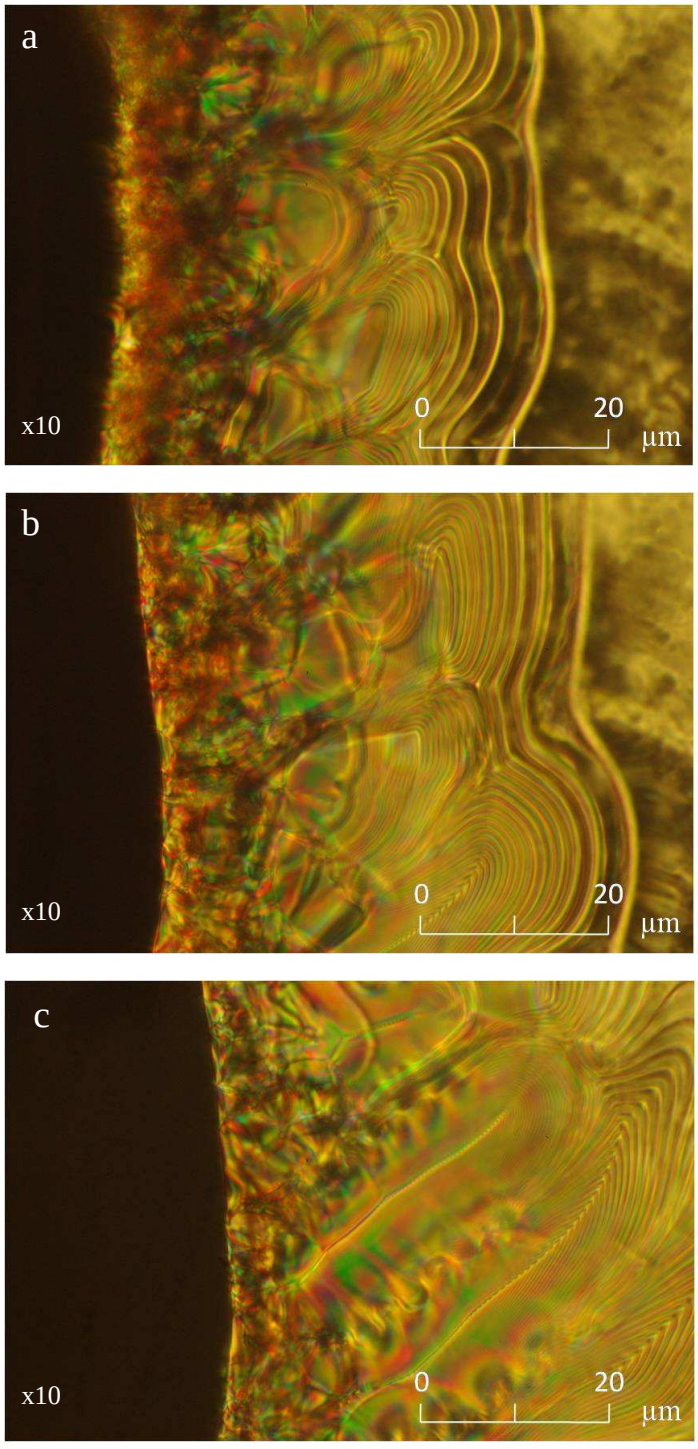


86 **85**

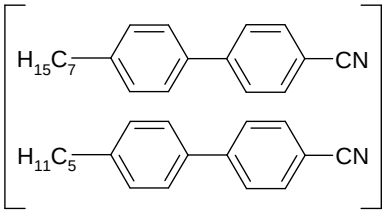
a) *n*-$H_{13}C_6B^-(OH)_3Na^+$ / $PdCl_2$(dppf) / Toluene / reflux (71%)

*Scheme 2.5 – Synthesis of dopant **85** employing the boronate salt protocol*

With the availability of dopant **85** our attention turned to the analysis of the dopant properties; most prominently the method by which helical twisting power would be determined. Nematic liquid crystal mixture E7 was selected as the host solvent, based on the general observation that biaryl dopants reveal the highest twisting powers in biaryl nematic solvents.[39] Whilst it was expected that the solubility of **85** would be adequate in E7, a simple contact experiment was first conducted to ascertain any solubility or phase separation problems. The suitability of E7 as the nematic host was confirmed, with no visible evidence of phase separation (*Figure 2.7*).



a) Time + 10 min; b) Time + 15 min; c) Time + 20 min



Nematic Liquid Crystal Mixture E7 – **93**

*Figure 2.7 - Contact experiment of dopant **85** in nematic host E7*

A number of spectroscopic and non-spectroscopic techniques have been devised to determine the helical twisting power (β_M) of a given chiral material. The studies involve the initial determination of the helical pitch length (p) at a known concentration (c), from which the helical twisting power can be calculated as:

$$\beta_M = (p.c)^{-1}$$

The earliest spectroscopic techniques were developed by Fergason,[128] using the helical model of chiral nematic liquid crystals proposed by Oseen[129] and de Vries.[130] It was determined that the pitch length (p) could be experimentally found by measurement of the wavelength of reflected light (λ_o), where $\bar{n}$ is the mean refractive index:

$$\lambda_o = \bar{n}.p$$

It was later discovered by Baessler that the wavelength of transmitted light could also be used to determine the pitch length.[131] Other spectroscopic techniques were also devised, including optical rotator dispersion (ORD)[26, 28, 29] and induced circular dichroism (ICD).[132, 133] To ascertain the pitch length via spectroscopic method, the helical axis of the liquid crystal first requires alignment parallel to the propagated light beam, as well as precise control of the temperature.

Non-spectroscopic techniques generally involve studying the liquid crystal phase under a polarising microscope and directly measuring the pitch length. The most commonly utilised method is the Granjean-Cano method, whereby a thin layer of chiral nematic liquid crystal is orientated with the helical axis parallel to the propagating light beam in a cell of variable thickness.[134, 135] Dark lines known as Grandjean-Cano steps are observed under a polarising microscope, with the distance between two lines being equal to half the pitch length (*Figure 2.8*).

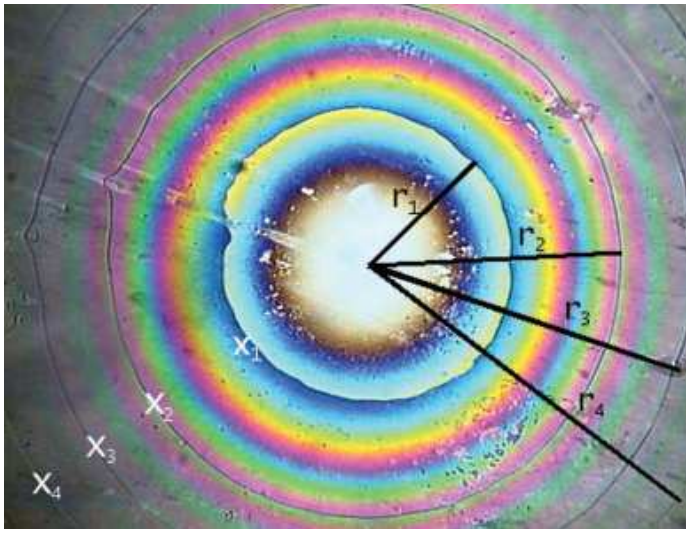


Figure 2.8 - Grandjean-Cano technique for helical twisting power determination[40]

The simplest approach to helical twisting power measurement is the droplet method.[136] In this method, an emulsion of doped nematic liquid crystal is suspended in a transparent and viscous medium such as glycerol. The individually formed droplets exhibit radial disclination lines, with the distance between two lines again equal to half the pitch length (*Figure 2.9*). The advantage of this method stems mainly from its simplicity, as no liquid crystal alignment techniques are necessary and only small quantities of material are required. These factors led us to select the droplet method for our helical twisting power measurements.

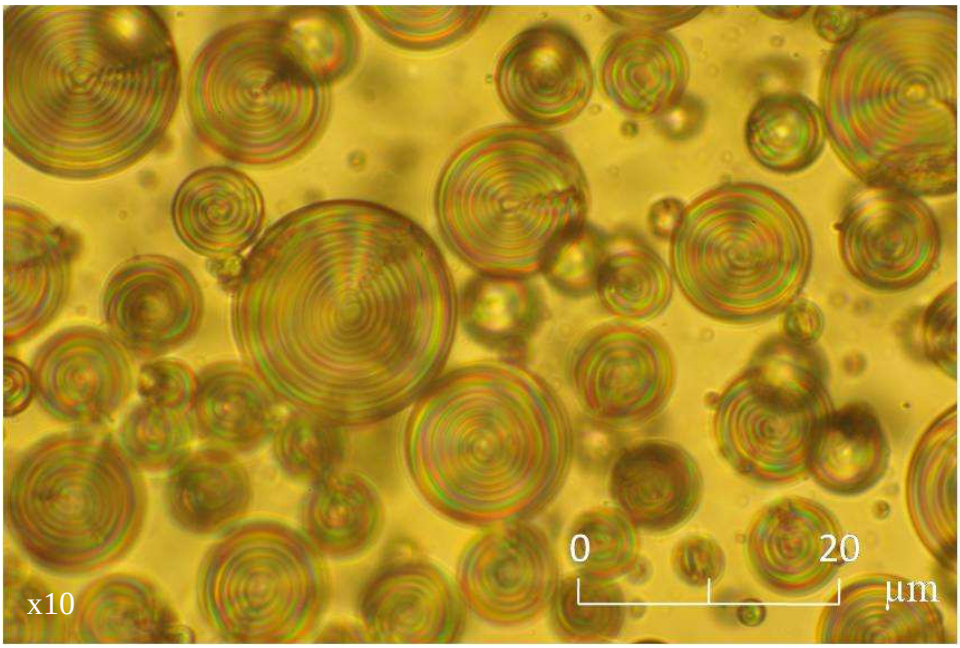
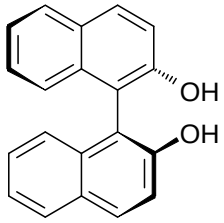


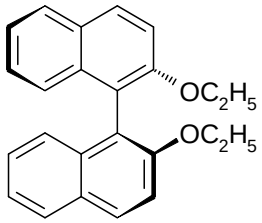
Figure 2.9 - Droplet method of helical twisting power determination

To ensure the accuracy of our measurements, it was first decided to calibrate our method through the determination of the helical twisting powers of some literature compounds, and their comparison to the literature values. Binaphthalene derivatives **89**[113] and **94**[119] were selected due to their availability and structural analogy to our compounds (*Figure 2.10*). To further enhance accuracy, measurements were taken over a minimum of ten separate readings and at two different dopant concentrations (e.g 0.5% & 1%). Comparison of the experimentally determined values with those in the literature provided us with the confidence to continue using the droplet method as our technique for helical twisting power measurement.



89

Derived $\beta_M = 31 \mu m^{-1}$ (K15)
Literature $\beta_M = 32\ \mu m^{-1}$ (K15)



94

Derived $\beta_M = 11\ \mu m^{-1}$ (E7)
Literature $\beta_M = 10.81\ \mu m^{-1}$ (LC 1277)

Figure 2.10 – Calibration of droplet method by comparison to literature values

The helical twisting power of dopant **85** was found to be 84 μm^{-1} and superior to the majority of conformationally flexible binaphthalene dopants in the literature. The success of the prototype dopant provided a platform for a continued study into the effects of structural elongation of the binaphthalene skeleton. In addition, it was decided to catalogue the effects of the substituent nature on helical twisting power.

2.1.3 – Design, Synthesis & Analysis of the First Series of Dopants

The performance of chiral nematic dopants has been reported to be dramatically improved through the incorporation of rigid aromatic substitutents.[57-59] This is most evident for the inclusion of bulky aromatic or naphthalene substituents onto 4,5'-diaryl-1,3-dioxolane and TADDOL derivatives. Whilst it is generally observed that centrally chiral materials possess lower helical twisting powers than their axially chiral counterparts, the inclusion of bulky aromatic groups has generated dopants based on the TADDOL or dioxolane structure with highly elevated helical twisting powers of up to 534 μm^{-1}.[31, 32, 137] The influence of the aromatic groups is believed to

induce chirality via a similar mechanism (chiral conformations) to the axially chiral binaphthalenes, although this has not been determined experimentally (*Figure 2.11*). The aromatic π-stacking interactions between dopant and host nematic are also considered vital to improve dopant host interactions.

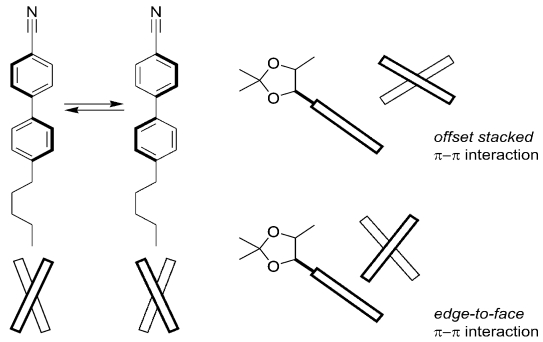
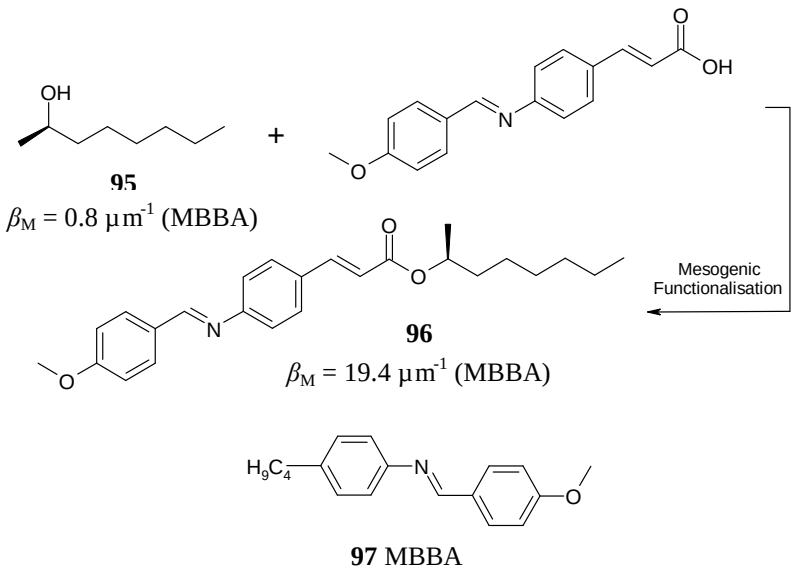


Figure 2.11 – Proposed transfer of chirality for 4,5-diaryl-2,3-dioxolane derivatives

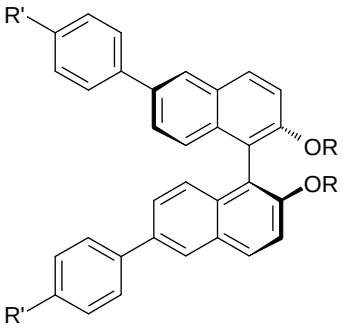
One proven approach to enhancing helical twisting power is through functionalisation with groups analogous to liquid crystal mesogens (mesogenic functionalisation).[138] It is predicted that the increases in helical twisting power are a result of increased dopant solubility and enhanced dopant-host interactions. This is evident in the example of (*R*)-2-octanol **95**, with a helical twisting power value of 0.8 μm^{-1} in nematic liquid crystal host MBBA **97** (4-methoxybenzylidene-4'-butylaniline). The lack of structural analogy with the nematic host induces an extremely low helical twisting power value. Functionalisation with a group of similar structure to the host nematic improves the helical twisting power considerably to 19.4 μm^{-1} for **96** (*Scheme 2.6*). To date mesogenic functionalisation has proved limited in its effects on materials possessing an asymmetric chiral carbon centre, with few examples producing exceptionally high helical twisting powers. Mesogenic functionalisation of axially chiral materials has proved far more successful.[139, 140]

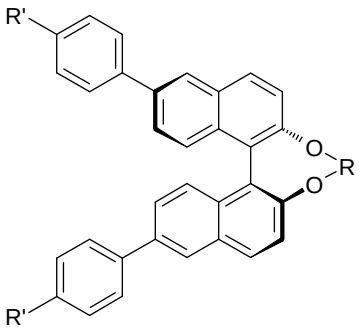


Scheme 2.6 - Mesogenic functionalisation of a chiral dopant

With these features in consideration, it was decided to base the first series dopant designs on three factors, in an attempt to improve helical twisting power. The primary interest was the extension of the binaphthalene molecular core in the 2,2'- and 6,6'-positions, which proved effective for the prototype dopant. The second design strategy was to attempt to increase dopant-host interactions through the introduction of aromatic substituents, enhancing π-stacking interactions. Finally, a degree of mesogenic functionalisation was to also be incorporated, to improve dopant solubility and to further improve dopant-host interactions. Although it was considered important to improve the dopant structural features, it was also noted that a compromise was required between enhancing the dopant structure and maintaining a relatively low molecular weight. This would prevent possible phase separation and minimise the effects of the foreign materials on the nematic host properties.[141, 142]

The designs for the first series of dopants are shown in *Figure 2.12*. It was decided to maintain the simple linear alkyl chains in the 2,2'-positions from the prototype, and to introduce aromatic functionalities into the 6,6'-positions. The inclusion of linearly, *para*-substituted phenyl rings was expected to sufficiently induce the desired effects, whilst maintaining a reasonable molecular mass. Mesogenic functionalisation was limited to the introduction of the linear *para*-alkyl/alkoxy chains, to induce structural similarities with the biphenyl host.



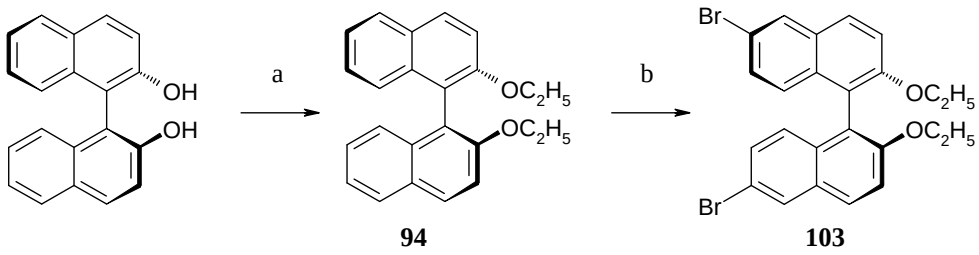


98	$R = C_5H_{11}$	$R' = OC_6H_{13}$	**102**	$R = (CH_2)_2$	$R' = OC_6H_{13}$
99	$R = C_5H_{11}$	$R' = C_7H_{15}$			
100	$R = C_2H_5$	$R' = OC_6H_{13}$			
101	$R = C_2H_5$	$R' = C_7H_{15}$			

Figure 2.12 - First series dopant designs

In addition to the development of dopants with high helical twisting powers, it was decided to investigate the effects of subtle substituent changes on dopant performance. This involved the nature of both the 2,2'-substituents and *para*-phenyl substituents. It has been previously mentioned that small, unlinked 2,2'-substituents generally possess low helical twisting powers due to dihedral angles close to 90°. Dopants **98** and **99** were designed to maintain the six-member chains (inclusive of the oxygen atom) from the prototype dopant, whilst dopants **100** and **101** included shortened three-member chains. It is also known that covalent bridging of the 2,2'-positions produces superior helical twisting powers in comparison to the unlinked derivatives. As the prototype dopant **85** possessed a similar helical twisting power to the bridged derivatives in the literature, we were eager to ascertain whether structural elongation would increase helical twisting power of the bridged derivatives on the same order of magnitude. To maintain a simplistic approach the investigation of the 6,6'-substituents was limited to that of *para*-hexyloxyphenyl and *para*-heptylphenyl groups.

Each of the syntheses was expected to be achieved via Suzuki-Miyaura cross-coupling with the appropriate 6,6'-dibromide intermediate. Synthesis of dibromide **103** was achieved in the same fashion as the previously utilised dibromide **86**, in 77% over the two-steps (*Scheme 2.7*).

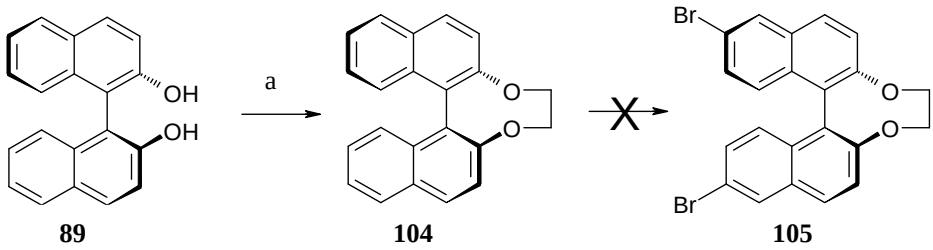


94 **103**

a) H_5C_2I / K_2CO_3 / Acetone (87%); b) Br_2 / DCM / -10°C / streaming N_2 (88%)

*Scheme 2.7 - Synthesis of dibromide intermediate **103***

It was also expected that the bridged dibromide intermediate would be readily accessible via the same synthetic route. Bridging of the 2,2'-hydroxyl groups was achieved using the non-racemising conditions, employing a bis-tolylsuphonate ester in preference to a 1,2-dihaloalkane due to the latter's volatility and toxicity. Bromination of the bridged compound was also attempted under the previously described conditions; however the reaction failed to yield any bromination products (*Scheme 2.8*). Compound **104** was subjected to various bromination conditions with no detection of the desired product (*Table 2.1*).



89 **104** **105**

a) $TsOCH_2CH_2OTs$ / K_2CO_3 / Acetone (42%)

*Scheme 2.8 - Synthesis of bridged dibromide **105***

Entry	Reagent	Solvent	Temperature	Product
i	Br_2	DCM	-10°C	No reaction
ii	Br_2	DCM	rt	No reaction
iii	Br_2	AcOH	rt	No reaction

*Table 2.1 - Bromination conditions applied to substrate **104***

Though this was initially unexpected, it can be rationalised through orbital distortion of the bridging ether groups. The prevention of electron donation into the aromatic ring system through orbital distortion would limit the ability of the ether oxygen atoms to stabilise the substitution intermediates. Meijer and co-workers revealed

similar observations during their studies of the 6,6'-nitration of bridged binaphthalene derivatives. Their studies revealed decreasing reactivity towards ring nitration with a decrease in bridging chain length (increased distortion).[143] Analysis of the UV/vis spectra for compounds **94** and **104** (*Figure 2.13*) confirmed a shift in the long wavelength absorption band from 338 nm to 325 nm for **94** and **104** respectively. This indicated decreased conjugation for the bridged compound **104**, consistent with the observations of Meijer.

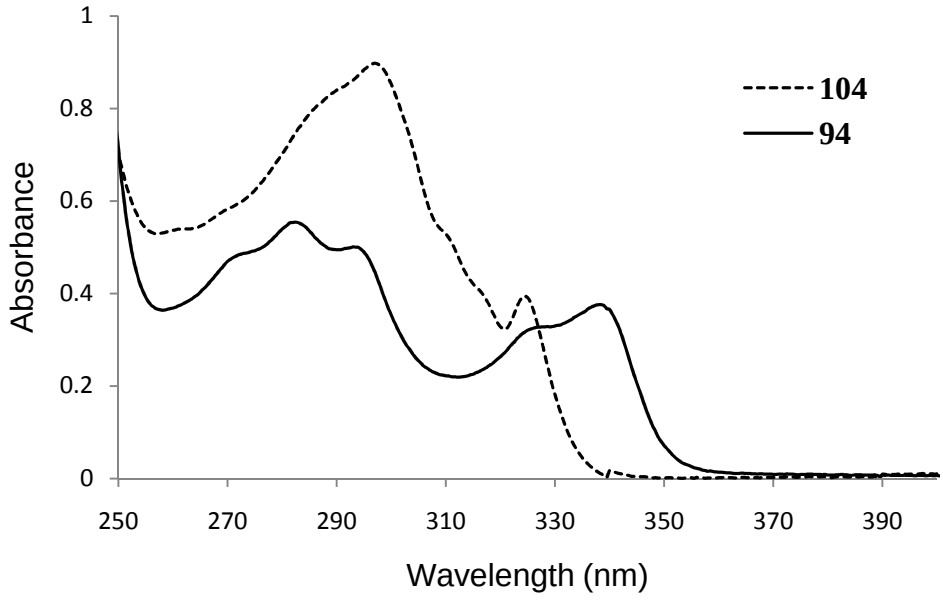
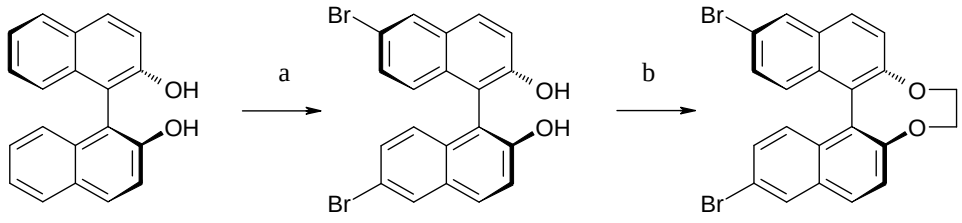


*Figure 2.13 – UV/Vis Spectra of compounds **94** and **104***

Due to the effects of increasing the dihedral angle on helical twisting power, increasing the length of the bridging chain was not considered feasible. Therefore dibromide **105** was produced via the initial bromination of 1,1'-bi(2-naphthol) **89**, according to the procedure of Cram.[144] Bridging of **106** with the bis-tolylsulphonyl ester afforded dibromide **105** in 57% overall yield (*Scheme 2.9*).



89 **106** **105**

a) Br_2 / DCM / -78°C (95%); b) $TsOCH_2CH_2OTs$ / K_2CO_3 / Acetone (60%)

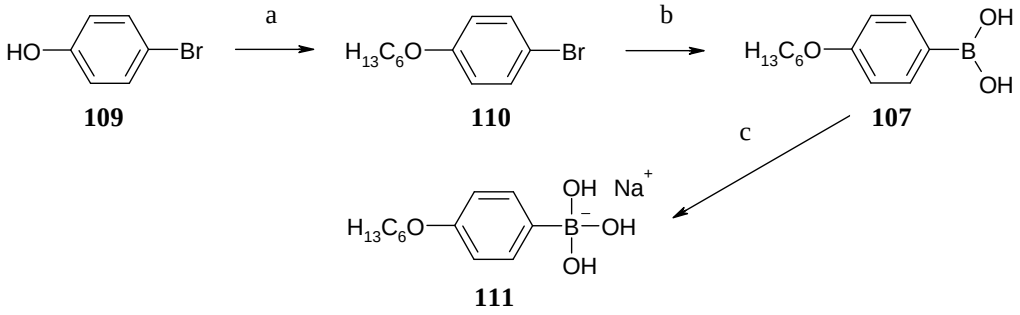
*Scheme 2.9 - Alternate synthesis of dibromide **105***

With the availability of the required dibromide intermediates, our attention turned to the synthesis of the organoboron coupling partners for application in the Suzuki-Miyaura cross-coupling. The required boronic acids are shown in *Figure 2.14*.

107 **108**

Figure 2.14 - Organoboron coupling partners

The synthesis of **107** produced few difficulties via alkylation of commercially available 4-bromophenol **109**, followed by conversion to the boronic acid via the Grignard reagent of **110**, to afford the product in 76% crude yield (*Scheme 2.10*).

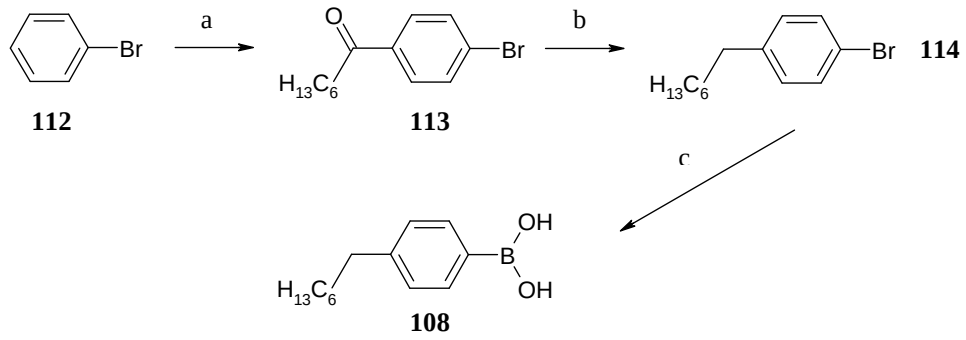


109 **110** **107** **111**

a) *n*-$H_{13}C_6Br$ / K_2CO_3 / Acetone (99%); b) i) Mg / Et_2O / reflux; ii) $B(OCH_3)_3$ / THF / -78°C; iii) 1M HCl, rt; c) Toluene / Δ / sat. NaOH

*Scheme 2.10 - Synthesis of 4-hexyloxybenzene boronic acid **107***

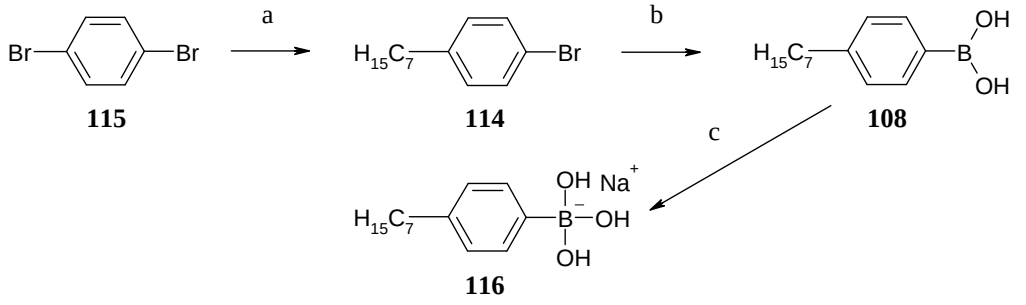
The synthesis of boronic acid **108** was expected to provide more of a challenge. A search of the literature revealed a procedure by Gray[145] for the synthesis of bromide **114**, involving a regioselective Friedel-Crafts acylation of **112**, followed by a modified Wolff-Kishner reduction of ketone **113**. The acylation reaction proceeded cleanly and smoothly with complete regioselectivity in a yield of 87%. The Wolff-Kishner reduction produced bromide **114** in respectable yield; however, the time consuming procedure, coupled with the harsh reaction conditions and hazardous reagents, led us to investigate an alternate means of preparation (*Scheme 2.11*).



i) *n*-$H_{13}C_6COCl$ / $AlCl_3$ / 0°C (87%); b) $H_2N_2.H_2O$ / KOH / DEG (73%); c) i) Mg / THF / reflux; ii) $B(OCH_3)_3$ / THF /-78°C; iii) 1M HCl / rt

*Scheme 2.11 – Synthesis of boronic acid **108** via modified Wolff-Kisnher reduction*

A further review of the literature uncovered a procedure by Yu,[146] involving a Kumada coupling of an alkylmagnesium bromide species with 1,4-dibromobenzene. Bromide **114** was produced in 59% yield, encountering only minor problems due to the presence of excess 1,4-dibromobenzene **115** in the crude mixture, which prevented simple purification. Conversion to boronic acid **108** afforded the crude product in 72% yield (*Scheme 2.12*).

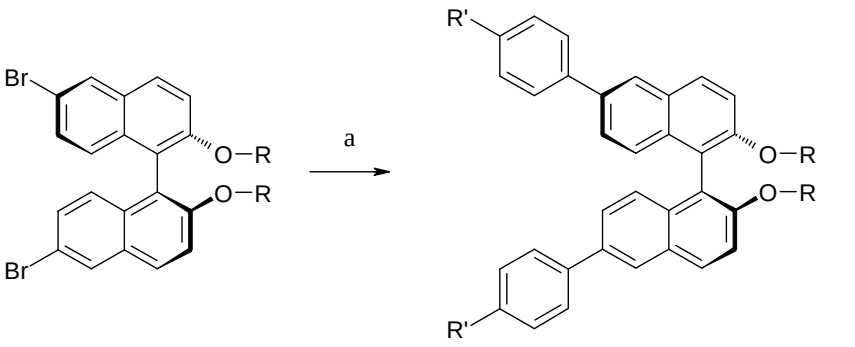


a) *n*-$H_{15}C_7MgBr$ / Et_2O / $PdCl_2(dppf)$ (59%); b) i) Mg / Et_2O / reflux; ii) $B(OCH_3)_3$ / Et_2O / -78°C; iii) 1M HCl / rt (72%); c) Toluene / Δ / sat. NaOH

*Scheme 2.12 - Synthesis of boronic acid **108** via Kumada coupling*

Again the waxy nature of the boronic acids prevented complete purification by standard techniques. It was decided, due to the success of the previous dopant synthesis and our confidence in the protocol, that the boronic acids would be converted to their boronate salts and employed directly. The purified boronate salts were subsequently utilised in the Suzuki-Miyaura coupling reaction with each of the dibromide intermediates (*Scheme 2.13*). The yields of the dopants proved respectable; however, the presence of minor quantities of unreacted dibromide and

mono-substituted product resulted in difficult and lengthy chromatographic separation times (*Table 2.2*).



98	R = C_5H_{11}	R' = OC_6H_{13}
99	R = C_5H_{11}	R' = C_7H_{15}
100	R = C_2H_5	R' = OC_6H_{13}
101	R = C_2H_5	R' = C_7H_{15}
102	R = -CH_2CH_2-	R' = OC_6H_{13}

a) $PdCl_2$(dppf) / Toluene / Boronate salt

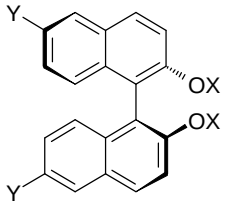
Scheme 2.13 – Dopant syntheses via Suzuki-Miyaura coupling

Entry	Dibromide	Boronate Salt	Time (hrs)	Yield[a]
i	**86**	**111**	48	70% (**98**)
ii	**86**	**116**	72	71% (**99**)
iii	**103**	**111**	72	82% (**100**)
iv	**103**	**116**	72	76% (**101**)
v	**105**	**111**	72	69% (**102**) + 11% (**117**)

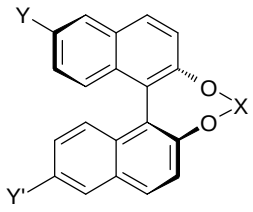
a) Isolated yields of column chromatographed material

Table 2.2 – Dopant syntheses via boronate salt Suzuki-Miyaura reaction protocol

The helical twisting power for each dopant was measured using the droplet method. As the effects of substituent on helical twisting power was also a high priority, it was decided to measure the twisting power of the parent binaphthalenes and the brominated compounds. The measureable quantity of mono-substituted bridged compound **117** recovered from the purification of **102** was also examined, to determine its performance (*Table 2.3*).



86	X = C_5H_{11}	Y = Br
98	X = C_5H_{11}	Y = *p*-$H_{15}C_7(C_6H_4)$
99	X = C_5H_{11}	Y = *p*-$H_{13}C_6O(C_6H_4)$
100	X = C_2H_5	Y = *p*-$H_{15}C_7(C_6H_4)$
101	X = C_2H_5	Y = *p*-$H_{13}C_6O(C_6H_4)$
103	X = C_2H_5	Y = Br



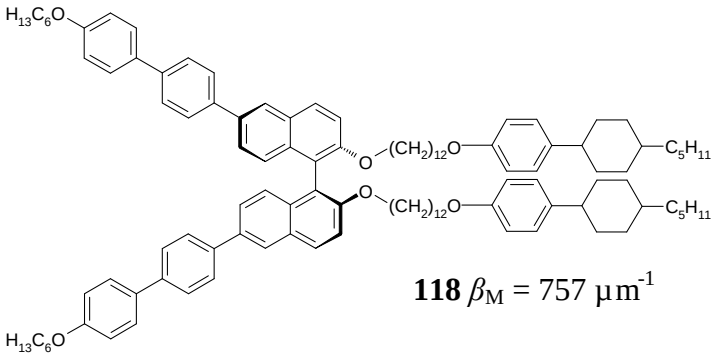
102	X = -CH_2CH_2-	Y = *p*-$H_{13}C_6O(C_6H_4)$
		Y' = *p*-$H_{13}C_6O(C_6H_4)$
105	X = -CH_2CH_2-	Y = Br Y' = Br
117	X = -CH_2CH_2-	Y = *p*-$H_{13}C_6O(C_6H_4)$
		Y' = H

Entry	Parent Compound	β_M (μm^{-1})[a]	Dopant	β_M (μm^{-1})[a]
i	**87**	26	**86**	45
ii			**98**	239
iii			**99**	145
iv	**94**	11	**103**	22
v			**100**	120
vi			**101**	69
vii	**104**	80	**105**	86
viii			**102**	96
ix			**117**	95

a) Helical twisting powers recorded as an average over 10 seperate measurements and at two concentrations in nematic liquid crystal host E7 (**93**)

Table 2.3 – Dopant and parent compound helical twisting powers

In addition to the high magnitude of helical twisting powers observed over the series of dopants, a number of noteworthy factors were also revealed. Dopants **98**, **99** and **100** (*entries ii, iii & v*), in particular, display significant helical twisting power values exceeding most literature examples for binaphthalene based compounds. These observations are all the more remarkable due to their nature as conformationally flexible dopants, which rarely exhibit values superior to the bridged derivatives. At the time of synthesis, dopant **98** (*entry ii*) displayed one of the highest known helical twisting powers for an axially chiral dopant of any class. This has recently been surpassed by the work of Akagi, with impressive values of up to 757 μm^{-1} reported for derivative **118** (*Figure 2.15*).[147]



118 β_M = 757 µm^{-1}

Figure 2.15 – Conformationally flexible dopant with highest reported helical twisting power

A more subtle trend over the entire series of dopants was the effect of the 2,2'-substituents. Previous observations have determined that small, unlinked substituents produce dopants with poor twisting ability. Our derivatives revealed an interesting property relating to chain length: Although it may be expected that an increase in 2,2'-position chain length may induce higher helical twisting powers based solely on the substituent size, it was revealed that the magnitude of twisting power was directly related to the length of the chain. In each of the parent compounds, dibromides and dopants, a doubling of chain length was accompanied by an approximate doubling of helical twisting power. It was assumed that this effect would be finite for increasing chain lengths. We therefore decided to synthesise binaphthalene compound **119** and determine the effects on twisting power (*Figure 2.16*). A slight decrease in twisting power was observed on increasing chain length further, suggesting a potential optimum chain length.

94 β_M = 26 µm^{-1} (E7) **119** β_M = 22 µm^{-1} (E7)

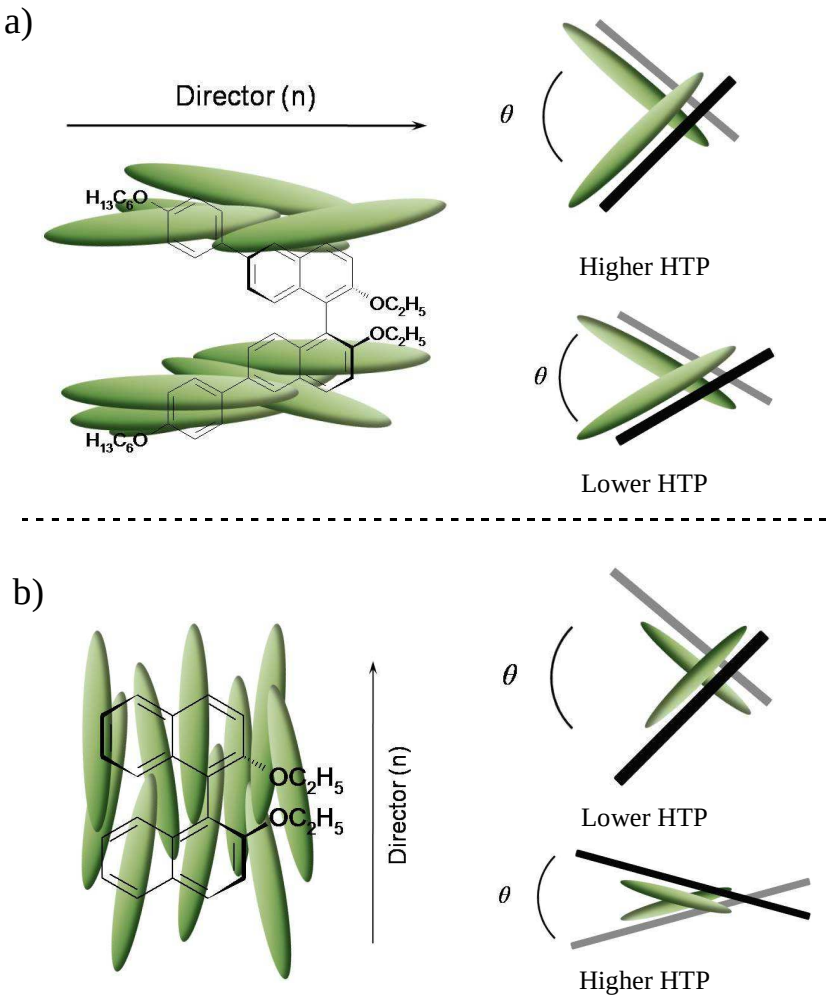
Figure 2.16 - Effect of 2,2'-position chain length on helical twisting power

Also of note was the large disparity in helical twisting power observed between dopants possessing the *para*-hexyloxyphenyl (*entries iii & vi*) and the *para*-heptylphenyl (*entries ii & v*) 6,6'-substituents. The origin of the difference is not

entirely clear, especially with regards to the magnitude. One possible explanation is that increased electron density, due to the presence of the chain oxygen atom, may disrupt the favoured liquid crystal alignment, as previously observed in certain liquid crystal systems.[148, 149]

Less impressive in terms of helical twisting power, although more intriguing, was the application of our structural extension design features to that of the bridged derivatives. Each of the conformationally flexible dopants revealed a minimum two-fold increase over the parent compound upon extension. It was expected that a similar improvement would be associated with the bridged derivatives upon their structural elongation, producing helical twisting power values circa 160 μm^{-1}. The assumption proved unfounded, with the helical twisting power of the bridged derivative **102** similar to that of parent compound **104** (*entry viii*). The results of the mono-substituted derivative **117** (*entry ix*) indicated that the presence of a singly extended naphthyl plane induced similar effects to the di-substituted derivatives. This assumption will be discussed in greater detail later in the chapter.

Whilst the results from the bridged compound results initially proved unexpected, it provided us with potential evidence for the theorised, alternate mechanism of chirality transfer. In the Gottarelli-Spada model, the helical twisting power is closely related to the dihedral angle between naphthyl planes; as previously stated, it has been calculated that the optimum angles for maximum helical twisting power are 45° and 135°. As the alignment of the nematic mesogens parallel to the two-fold symmetry axis prevents the transfer of chirality via chiral conformations, twisting of the director is thought to be possible through direct interaction of the two naphthyl ‘arms’, resulting in a twisted macrostructure. In such an orientation, an inverse relationship to that of the Gottarelli-Spada model between the helical twisting power and dihedral angle would be expected (*Figure 2.17*). Small dihedral angles, such as those observed for the bridged derivatives would induce a smaller twist angle to the nematic director, resulting in longer pitch lengths. This is seen as a plausible origin to the superior performance of the conformationally flexible dopants over the bridged derivatives.



Relationship between helical twisting power (HTP) and dihedral angle for the proposed mechanism of chiral induction (a) and the Gottarelli-Spada mechanism (b)

Figure 2.17 – Mechanism of chiral induction and the relationship to the dihedral angle

Whilst a detailed insight into the substituent effects was gained through the first series of dopants, a second series was planned for further examination. The negligible effects of structural elongation of the bridged derivatives led us to abandon their further development, concentrating instead on the successful implementation of our structural modification to the conformationally flexible derivatives. We were interested in determining the importance of the extended aromatic core, and the effects of non-linear aromatic substitution.

2.1.4 – Design, Synthesis & Analysis of the Second Series of Dopants

The designs of the second series dopants are shown in *Figure 2.18*. The 2,2'-substituents would again be maintained as for the previous dopants, with both chain

lengths examined. To induce rigid, linear extension of a non-aromatic nature it was decided to introduce long chain alkynyl derivatives into the 6,6'-positions. This would maintain a degree of π-stacking interactions, whilst limiting the extended aromatic core. As for the previous linearly extended aromatic dopants, non-linear extension was to utilise the alkyl/alkoxy chain in the 3-position of the phenyl ring.

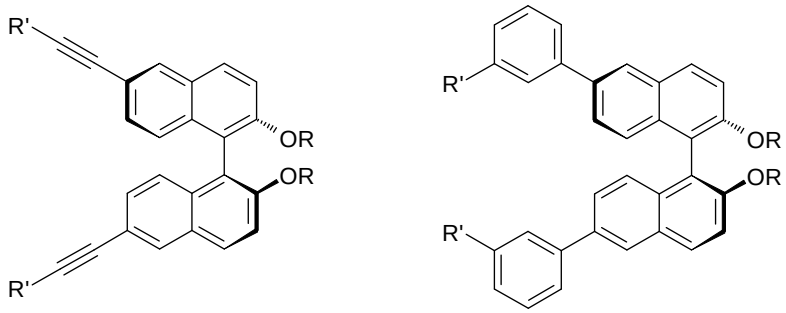
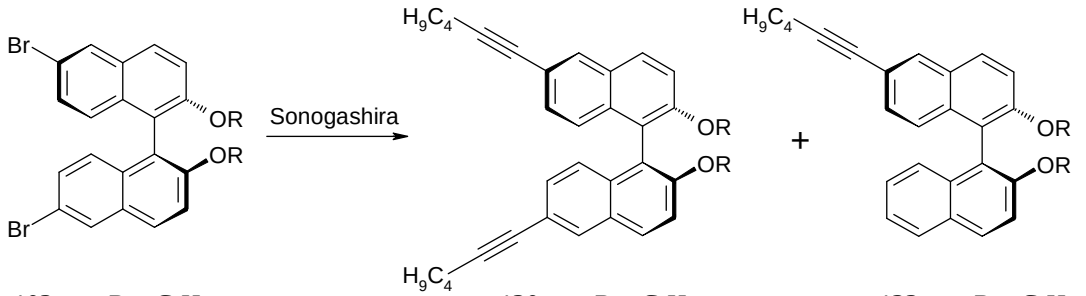


Figure 2.18 - Second series dopant designs

Again the synthesis was expected to be possible from the dibromide intermediates **86** and **103** used in the previous syntheses. Formation of the alkynyl derivatives were attempted via palladium catalysed Sonogashira cross-coupling, with commercially available 1-hexyne, under standard literature conditions (*Scheme 2.14*).[150]



103 R = C_2H_5
86 R = C_5H_{11}

120 R = C_2H_5
121 R = C_5H_{11}

122 R = C_2H_5
123 R = C_5H_{11}

Scheme 2.14 – Dopant synthesis via Sonogashira coupling reaction

Initial attempts (*Table 2.4*) proved ineffective, with only mono-substituted products **122** and **123** recovered in poor yield (*entries i & ii*). Increasing the number of equivalents of 1-hexyne and reaction time (*entry iii*) increased the yield of mono-substituted **122**; however, product **120** was not observed. Modification of the conditions was attempted, through the replacement of THF as the solvent with triethylamine as co-base and solvent.[150] This resulted in the recovery of target

compounds **120** and **121**, albeit in poor yield (*entries iv & v*). Further increases in the number of 1-hexyne equivalents were accompanied with increased yield of target compound; however, the mono-substituted derivatives continued to be obtained as the majority product. The increased yields with increasing numbers of 1-hexyne equivalents suggested problems maintaining the volatile reagent in solution. Sealed tube reactions (*entries vii & viii*) further increased product yields, but the target compounds remained as minority products, even with the high reagent equivalents.

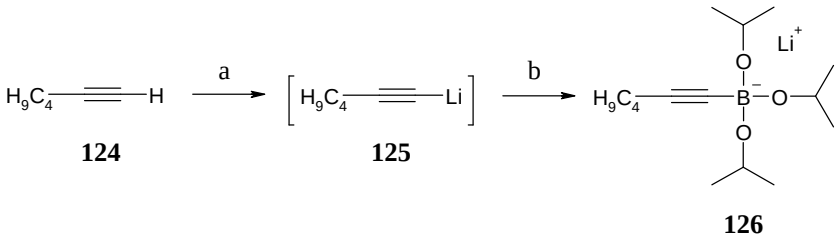
Entry[a]	Halide	Solvent	Base	eq. 1-hexyne	Time (hrs)	Product[b]
i	**103**	THF	Et_3N	4	48	12% (**122**)
ii	**86**	THF	Et_3N	4	48	9% (**123**)
iii	**103**	THF	Et_3N	10	72	27% (**122**)
iv	**86**	Et_3N	Et_3N	10	48	48% (**123**), 9% (**121**)
v	**103**	Et_3N	Et_3N	12	48	49% (**122**), 20% (**120**)
vi	**86**	Et_3N	Et_3N	12	48	53% (**123**), 16% (**121**)
vii[c]	**103**	Et_3N	Et_3N	15	72	48% (**122**), 32% (**120**)
viii[c]	**86**	Et_3N	Et_3N	15	72	42% (**123**), 39% (**121**)

a) $PdCl_2(PPh_3)$ catalyst system employed for each entry; b) Isolated yields of column chromatographed material; c) Sealed tube reactions.

Table 2.4 – Sonogashira coupling results

A search of the literature revealed a procedure by Oh[151] in which alkynylborate salts were employed successfully in the Sonogashira cross-coupling reaction. If the nature of the problem was maintaining the volatile alkyne in solution then the use of a solid reagent was expected to produce increased yields of target compound.

Preparation of the alkynylborate salt was achieved using the conditions of Chong,[152] involving lithiation of **124** to form intermediate **125**, which upon quenching with triisopropylborate gave borate salt **126** in good yield (*Scheme 2.15*). The borate salt was reported to be stable at refrigerated temperatures for up to one month.

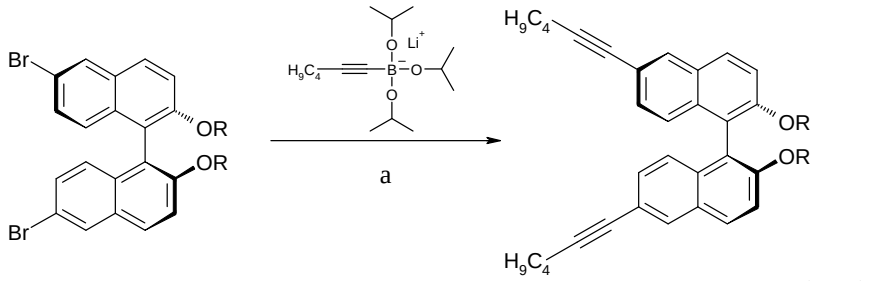


124 **125** **126**

a) *n*-BuLi / THF; b) (^{i}PrO)$_3$B / THF (66%)

Scheme 2.15 - Synthesis of lithium 1-hexynyl(triisopropoxy)borate salt

Subsequent Sonogashira coupling of borate salt **126** with dibromides **86** and **103**, using the conditions of Oh,[151] afforded the desired 6,6'-dialkynyl compounds **120** and **121** cleanly and smoothly in 69% and 82% yields respectively (*Scheme 2.16*).



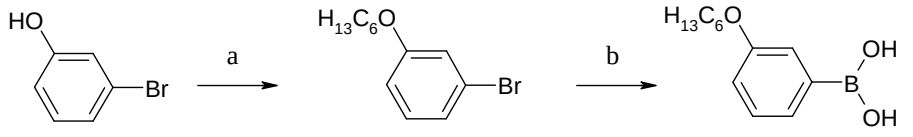
103 R = C_2H_5
86 R = C_5H_{11}

120 R = C_2H_5 (69%)
121 R = C_5H_{11} (82%)

a) $Pd(PPh_3)_4$ / CuI / DMF

*Scheme 2.16 - Sonogashira coupling employing borate salt **126***

Our attention then turned to the synthesis of the non-linear dopants. Synthesis of the organoboron coupling partner was first required. It was decided to avoid the more problematic synthesis of the alkylphenyl derivative, despite its superior performance to the alkoxyphenyl derivative. The *m*-hexyloxybenzeneboronic acid **128** was produced from 3-bromophenol via bromide **127** (*Scheme 2.17*).

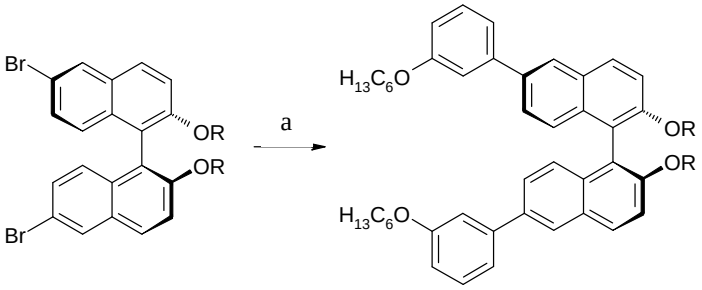


127 **128**

a) *n*-$H_{13}C_6Br$ / K_2CO_3 / Acetone; b) i) Mg / Et_2O / reflux; ii) $B(OCH_3)_3$ / Et_2O / -78°C; iii) 1M HCl / rt (69%)

*Scheme 2.17 - Synthesis of boronic acid **128***

Boronic acid **128** proved more crystalline than the previous derivatives, allowing purification to an acceptable standard. The boronic acid was therefore directly employed into the Suzuki-Miyaura coupling with dibromides **86** and **103** to afford the target dopants **129** and **130** in 77% and 68% yield respectively (*Scheme 2.18*).

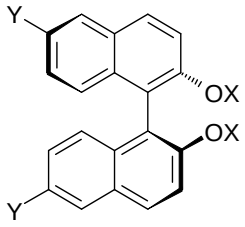


103	R = C_2H_5	**129**	R = C_2H_5 (77%)
86	R = C_5H_{11}	**130**	R = C_5H_{11} (68%)

a) *m*-$H_{13}C_6O(C_4H_6)B(OH)_2$ / $PdCl_2$(dppf) / CsF / Toluene

*Scheme 2.18 – Suzuki-Miyaura synthesis of non-linear dopants **129** & **130***

The helical twisting powers of the second series of dopants are shown in *Table 2.5*. Despite the unremarkable performance of the dopants in terms of the magnitude of helical twisting power, vital structural information was acquired. As with the previous series, the trend of increasing 2,2'-positions chain length is maintained in the second series of dopants, proving the non-coincidental nature of this effect. It was also observed that the introduction of non-aromatic linear substituents into the 6,6'-positions produces only limited increases in helical twisting power. Dopant **121** (*entry ii*) was shown to produce a similar twisting power value to that of the prototype dopant **85**, revealing the significance of aromatic extension of the binaphthalene core unit, as shown for dopants **98**-**101**.



120	X = C_2H_5	Y = $H_9C_4C{\equiv}C$-
121	X = C_5H_{11}	Y = $H_9C_4C{\equiv}C$-
129	X = C_2H_5	Y = *m*-$H_{13}C_6O(C_6H_4)$
130	X = C_5H_{11}	Y = *m*-$H_{13}C_6O(C_6H_4)$

Entry	Parent Compound	β_M (μm^{-1})[a]	Dopant	β_M (μm^{-1})[a]
i	**87**	11	**120**	40
ii	**94**	26	**121**	76
iii	**87**	11	**129**	13
iv	**94**	26	**130**	25

a) Helical twisting power values recorded as an average over 10 runs and at two different concentrations in nematic liquid crystal host E7

Table 2.5 - Second series dopant helical twisting powers

The results from dopants **129** and **130** (*entries iii & iv*) provide further evidence for the proposed, alternate mechanism of chiral induction. Each of the non-linear dopants displayed poor helical twisting powers, comparable to that of the parent binaphthalenes **87** and **94**. It was initially deduced that the non-linear substituents failed to effect the liquid crystal environment in any capacity; this was later deemed to be inaccurate.

It was reasoned that free rotation about the naphthyl-phenyl C(6)-C(1) bond would allow the alkoxy chains to orientate perpendicular to the two-fold symmetry axis, and away from the molecular core. This was later confirmed by X-ray crystallography, as shown in *Figure 2.19*. In such an orientation, the 6,6'-substitutents are expected to increase the tendency for the nematic director to align parallel with the naphthyl-naphthyl C(1)-C(1') bond, as per the Gottarelli-Spada model of chiral induction. This orientation is likely to result in inefficient chiral induction for the conformationally flexible dopants.

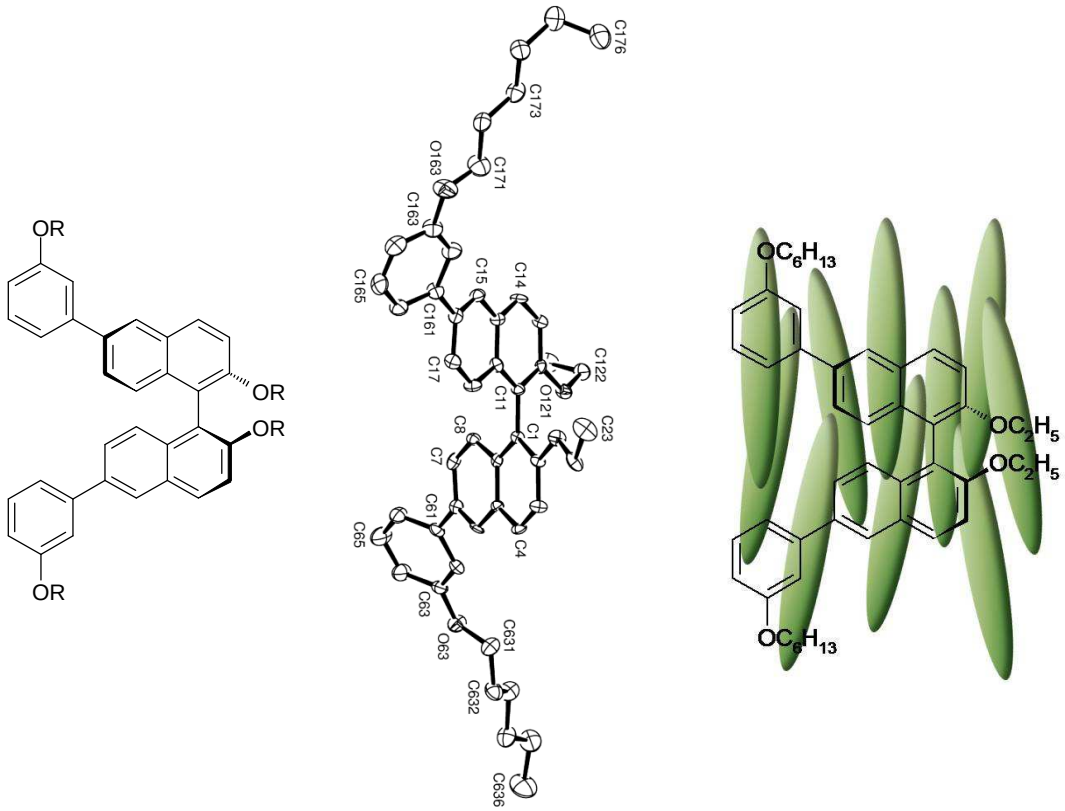


Figure 2.19 – Non-linear dopant structural orientation and proposed liquid crystal alignment

2.1.5 – Summary

A range of high twist chiral nematic dopants, based on the chiral binaphthalene skeleton, have been synthesised and their helical twisting powers recorded. The linearly extended dopants **98**, **100** and **101** all displayed helical twisting powers far in excess of the majority of conformationally flexible binaphthalene dopants in the literature

In addition to the successful design and synthesis of the dopant range, a number of structural effects on the helical twisting power were catalogued. This provided an in depth analysis of certain structural features that induce high helical twisting powers. Most notably, these features included the subtle effects of increasing 2,2'-position chain length, in which a doubling of chain length resulted in an approximate doubling of helical twisting power. This effect was found to be finite with a possible optimum chain length. The importance of aromatic extension was also noted, which improved dopant-host interactions and dopant solubility and led to enhanced chiral induction.

Most significantly, evidence for an alternate mechanism of chiral induction was proposed, differing from that of the Gottarelli-Spada model. Linear extension of the binaphthalene core, resulting in a disc-like to rod-like molecular shape transition, was predicted to cause alignment of the nematic director with the long binaphthalene axis. Due to the prevention of chiral induction via chiral conformations, it was proposed that direct twisting of the director was achieved by the individual binaphthalene 'arms'. The proposed model accounted for the apparent inverse relationship between dihedral angle and helical twisting power seen for the Gottarelli-Spada model. The development of the non-linearly extended dopants provided further evidence for our proposed model, as the poor helical twisting powers were indicative of chiral induction via the Gottarelli-Spada model.

It is clear that further evidence is required to confirm or disprove the alternate mechanism of chiral induction, with a spectroscopic analysis of the liquid crystal alignment being a possibility. This research has provided a basis for such work and for further insight into the structural effects on helical twisting power.

2.2 – Type 3 Bistable Dopants

The development of 'molecular machinery' and nanotechnology has received particular attention in recent times.[45] The molecular switch forms an essential element of such technologies, resulting in the development of a number of systems that display switching at the molecular level. The key concept is the ability of a molecule to exist in two or more stable states (bistability). Access to the individual states is achieved through the application of external stimuli such as heat, pressure, pH, light, and magnetic and electric fields.[46, 153-155] One main avenue of research into chiral nematic dopants is the development of bistable dopants capable of switching at the molecular level. Incorporation of bistability into chiral dopants presents the possibility of controlling the supramolecular chemistry of such liquid crystal systems, with the potential for display and optical memory application.

Switchable dopants can be classified into three distinct groups.[45, 64] Type 1 dopants display switching based on an enantiomeric relationship between molecular states. Irradiation with unpolarised light results in racemisation of the dopant, from which an enantiomeric excess can be regenerated by application of circularly polarised light (CPL). Type 2 switches are based on the similar concept of switching between diastereomers (pseudo-enatiomeric switching), where the chiral properties of the switch are inversed. Selective inter-conversion between the diastereomeric states is achieved by the application of unpolarised light. Type 3 switches comprise distinct chiral and switchable molecular fragments; whilst the chiral unit of the molecule is unaffected by switching, changes in the molecular conformation affect the chiral structure and therefore the chiral properties of the molecule as a whole (*Figure 2.20*). The remainder of this sub-chapter will be concerned with Type 3 molecular switches.

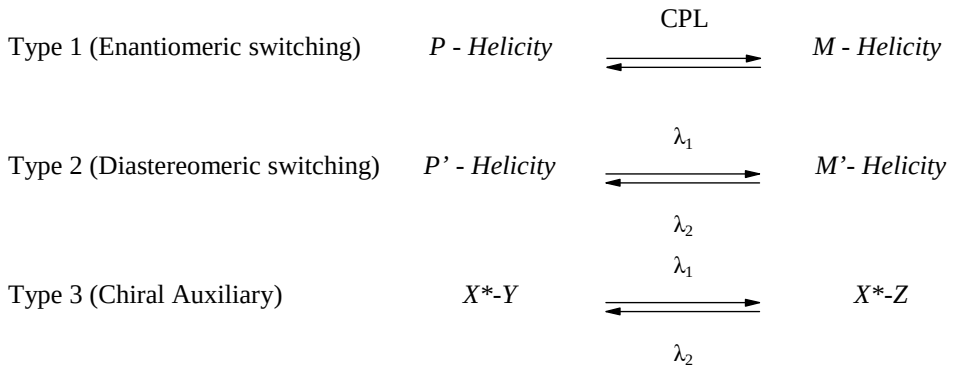
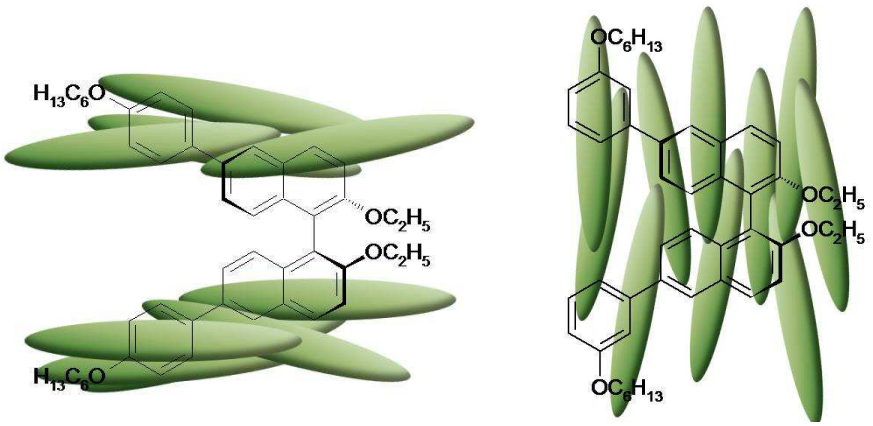


Figure 2.20 – Types of chiral molecular switches[45]

2.2.1 – Proposed Bistable Dopant Switching System

The studies into the effects of substituents on helical twisting power, as detailed in the previous chapter, revealed that the introduction of non-linear substituents into the 6,6'-positions produced dopants with poor helical twisting powers. This was in contrast to the linearly substituent dopants, which displayed remarkably high helical twisting powers (*Figure 2.21*). It was reasoned that the disparity was due to different mechanisms of chiral induction and that the large disparity could be exploited to induce successful switching of a liquid crystal system.



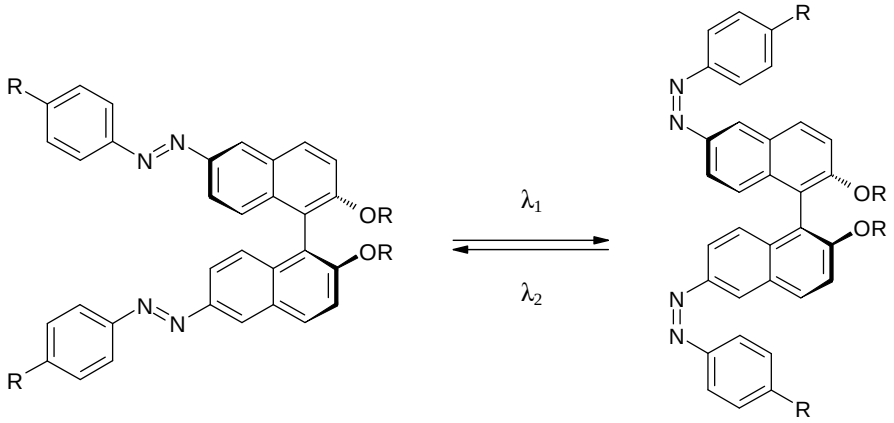
100 β_M = 145 µm^{-1} (E7) **129** β_M = 13 µm^{-1} (E7)

Figure 2.21 – Linear & non-linear dopant twisting powers

To achieve this, a suitably structured binaphthalene dopant, incorporating photochromic substituents into the 6,6'-positions capable of *cis-trans* (*E-Z*) isomerism, would produce a successful switching system. The proven compatibility of azobenzenes with liquid crystal systems, the linear and non-linear shape of the

trans and *cis* isomers, and the ability to selectively induce *cis-trans* isomerism, led us to attempt the synthesis of a 6,6'-azobenzene dopant.[30, 46, 156-158]

The design of the dopant was to be based on the structural features that proved so successful in the previous studies, so as to effectively induce chirality and to maximise the potential of the switching effects (*Figure 2.22*). Similarly designed dopants have previously been reported in the literature by the groups of Gottarelli[62, 63] and Li,[61] with the focus on introduction of the switchable moieties into the 2,2'-positions.

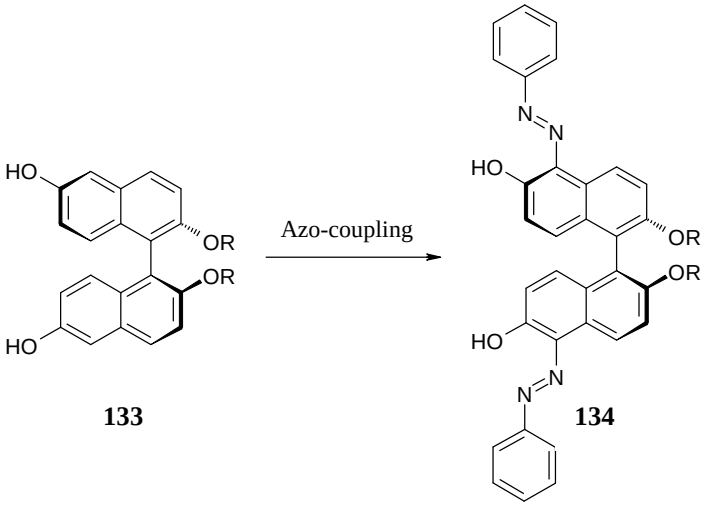


(*E,E)*-**131** (*Z,Z)*-**132**

Figure 2.22 – Chiroptical switchable dopant design

2.2.2 – Synthesis of an Azobenzene Dopant

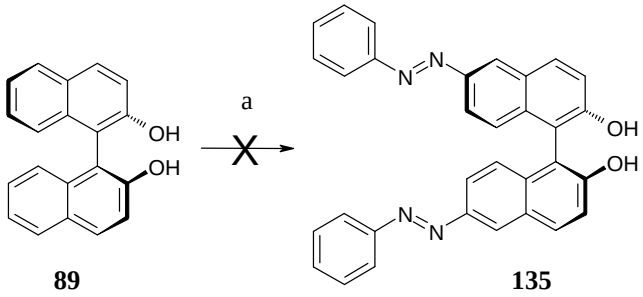
The introduction of an azobenzene functionality onto the binaphthalene skeleton has been successfully demonstrated by Feringa and Rosini, albeit in limited yield, via direct azo-coupling with benzenediazonium tetrafluoroborate (*Scheme 2.19*).[64] However, further substitution of the naphthyl rings was first required to direct the coupling reaction, which risked inducing negative effects on the dopant performance.



133 **134**

Scheme 2.19 – Azo-coupling reaction successfully applied by Feringa and Rosini

Our initial efforts attempted an ambitious azo-coupling of 1,1'-bi(2-naphthol) **6** with benzenediazonium tetrafluoroborate, using the conditions described by Feringa and Rosini (*Scheme 2.20*). Unsurprisingly azobenzene **135** was not identified from the reaction with traces of the *ortho*-substituted product recovered.

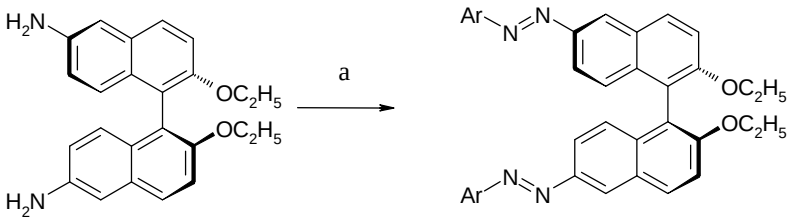


89 **135**

a) Pyridine / K_2CO_3 / THF / $H_5C_6N_2^+$ BF_4^- / -10°C

*Scheme 2.20 – Attempted synthesis of azo-derivative **135***

The syntheses of the 2,2'-azobenzene derivatives reported by Gottarelli[63] and Li[61] utilised optically pure 2,2'-diamino-1,1'-binaphthalene (BINAM). The successful introduction of amine functionalities into the 6,6'-positions was expected to allow a subsequent azo-coupling to form the desired structure (*Scheme 2.21*).

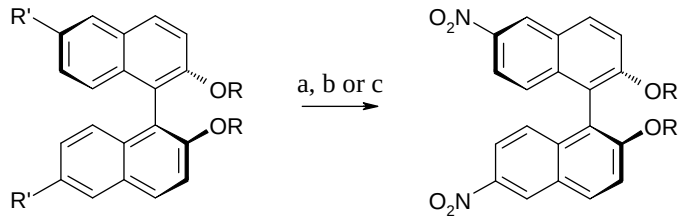


136

a) i) HCl / H_2O / $NaNO_2$ / 0°C, ii) ArOH / NaOH / H_2O

*Scheme 2.21 – Azo-coupling of 6,6'-diamino binaphthalene **136***

It was revealed that literature examples of 6,6'-diaminobinaphthalenes are few, with nitration of the 6,6'-positions and subsequent reduction employed in the vast majority of synthetic procedures. Chen[159] reported the synthesis of 6,6'-dinitro binaphthalene **137** from optically pure 1,1'-bi(2-naphthol) **89** in good yield, followed by reduction to the amine with no loss of optical purity. Nitration has also been reported by Meijer[143] on a number of 2,2'-protected binaphthalene derivatives in moderate yields. It was also deemed possible to synthesise a 6,6'-dinitro derivative via Zincke nitration of dibromide **106**; however, regiocontrol is reported difficult to achieve (*Scheme 2.22*).



89	R' = H	R = H	**137**	R = H
94	R' = H	R = C_2H_5	**138**	R = C_2H_5
106	R' = Br	R = H		

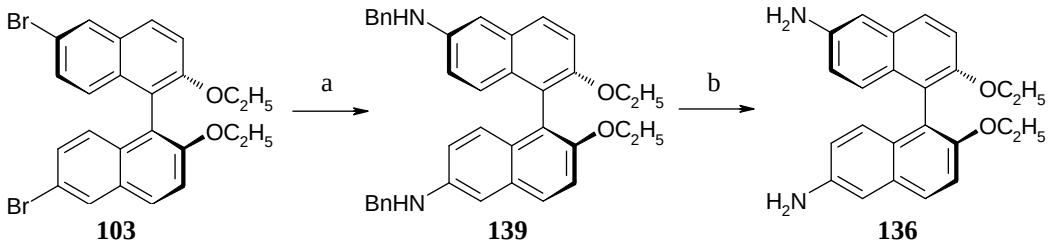
a) **89** / AcOH:DCM (1:1) / 100% HNO_3 / rt; b) **94** / AcOH / 100% HNO_3 / rt; c) **106** / $NaNO_2$ / HNO_3

Scheme – 2.22 – Synthesis of 6,6'-dinitro binaphthalene derivatives

The nitration of **89** and **94** was attempted using the conditions of Chen[159] and Meijer,[143] with each set of conditions producing poor regiocontrol and a number of nitrated products. Separation of the expected 3,3'-, 6,6'-, 8,8'-, 3,6'-, 3,8'-, and 6,8'-isomers, also observed by Meijer,[143] proved unsuccessful.

An alternate route was devised employing a Buchwald-Hartwig amination of dibromide **103** with a protected amine derivative. A search of the literature revealed a procedure by Lee,[160] in which diamine **136** was produced via Buchwald-Hartwig

amination using benzylamine, followed by subsequent deprotection of the secondary amine under palladium catalysed hydrogenation conditions (*Scheme 2.23*).

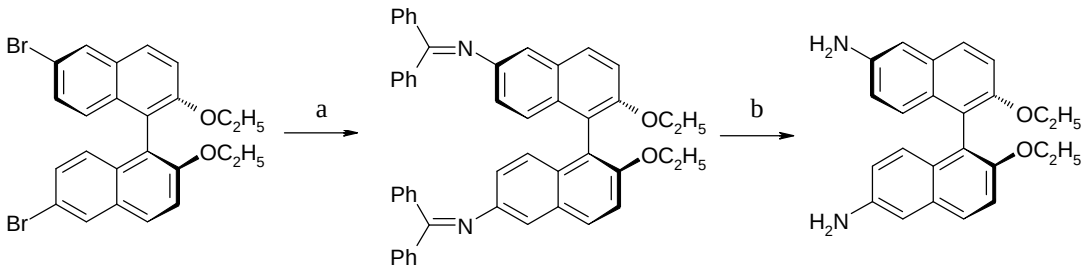


103 **139** **136**

a) $BnNH_2$ / ^tBuONa / PdL_2 / Toluene / 100°C; b) Pd/C / H_2 / MeOH

Scheme 2.23 – Synthesis of a 6,6'-diamino binaphthalene via Buchwald-Hartwig amination

Despite the feasibility of the reaction sequence, the increasing number of potentially troublesome steps was hoped to be avoided. A further literature search revealed a procedure by Buchwald[161] in which benzophenone imine was used as a masked ammonia equivalent to introduce the free amine, potentially omitting the need for a catalytic hydrogenation to remove the protecting group. Dibromide **103** was subjected to conditions modified from those detailed by Buchwald, using a $Pd(OAc)_2$/dppf catalyst system to afford 6,6'-bis-imine **140** in good yield. Previous demonstration of a binaphthyl imine deprotection by acidic hydrolysis, reported by Buchwald and Singer,[162] led to our attempt to deprotect **140** using this method. Diamine **136** was produced in almost quantitative yield, using simple ambient temperature hydrolysis with dilute hydrochloric acid, and in 68% over the two steps (*Scheme 2.24*). Diamine **136** was observed to oxidise fairly rapidly under standard atmospheric conditions.

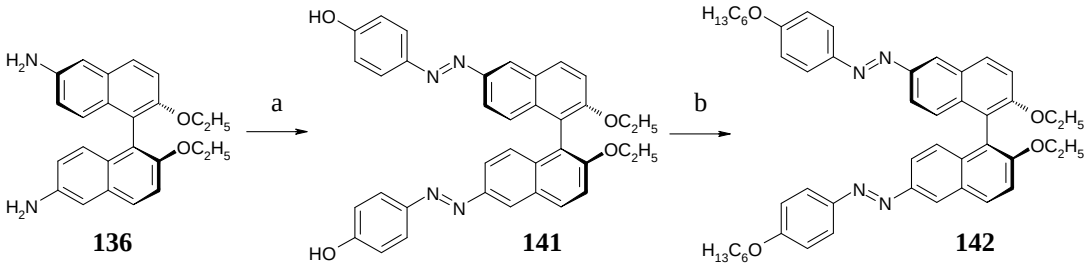


103 **140** **136**

a) $Pd(OAc)_2$ / dppf / ^tBuONa / $(Ph)_2C{=}NH$ / Toluene / 80°C (72%); b) THF / 2M HCl / rt (94%)

*Scheme 2.24 – Synthesis of diamine **136** via Buchwald-Hartwig amination*

With the availability of 6,6'-diamine **136** our attention turned to the azo-coupling with phenol. Gottarelli and Spada described the formation of a 2,2'-azobenzene derivative via *in situ* formation of the 2,2'-diazonium species, and the subsequent coupling with phenol.[62] Diamine **136** was subjected to the conditions of Gottarelli and Spada to afford 6,6'-bis-azophenol **141** in 59% yield. Protection of the phenolic hydroxyl groups was achieved under standard Williamson ether synthesis conditions with bromohexane, affording the azobenzene dopant **142** in 46% isolated yield (*Scheme 2.25*).



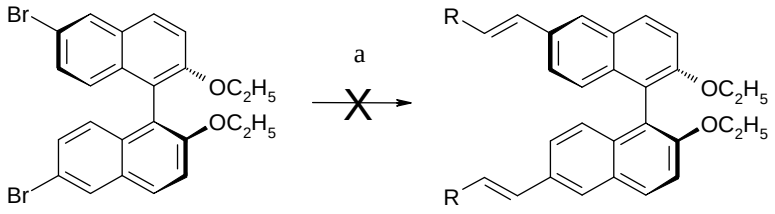
a) i) H_2O / conc. HCl / $NaNO_2$ / 2°C, ii) H_5C_6OH / NaOH / 2°C (59%);
b) *n*-$H_{13}C_6Br$ / K_2CO_3 / Acetone / reflux (46%)

*Scheme 2.25 – Synthesis of bis(azobenzene) derivative **142***

Unfortunately it was observed that binaphthalenes **141** and **142** were prone to decomposition, making their purification problematic. Despite the initial desirability of the azobenzene dopant class due to their proven reversible switching properties, the instability and highly coloured nature of the derivatives made them unsuitable as chiroptical molecular switches. This led to us attempting the synthesis of the conceptually similar, and more stable, stilbene derivatives to assess the feasibility of our switching system.

2.2.3 – Synthesis and Analysis of Stilbene Derivatives

Due to our previous success with transition metal catalysed cross-coupling reactions, it was decided to attempt the synthesis of the 6,6'-vinyl derivatives via Heck reaction of dibromide **103**, with a suitable acrylate or styrene derivative (*Scheme 2.26*). The propensity for *trans*-selectivity was also favourable, allowing for determination of the helical twisting power of the more effective linear isomer.



103

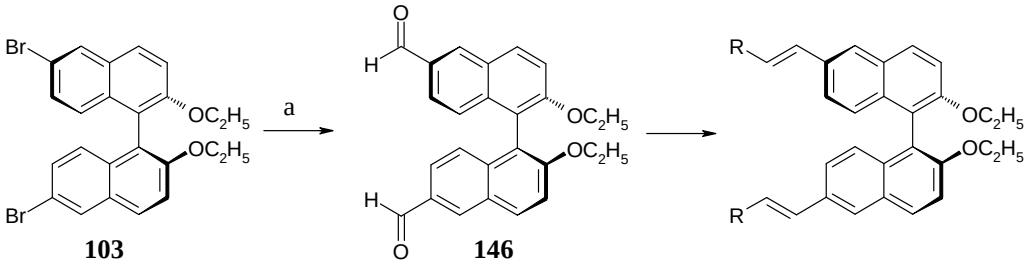
144 R = PhOOC
145 R = Ph

a) $Pd(OAc)_2$ / PPh_3 / Et_3N / MeCN / Styrene or Acrylate

*Scheme 2.26 – Synthesis of alkene derivative **144** and **145** via Heck reaction*

Synthesis of the 6,6'-vinyl derivatives **144** and **145** were attempted under standard literature Heck conditions,[163-165] but no coupled products were observed by ^{1}H NMR or mass spectrometry. The failure to detect any Heck coupling products led us to abandon further attempts of the synthesis via this particular method, and to seek an alternative synthetic route.

Similarly structured 6,6'-divinyl derivatives have previously been reported by Persoons *et al.*, under Knoevenagle condensation and Horner-Wadworth-Emmons conditions, from dialdehyde **146**.[125] Despite the inclusion of an extra synthetic step over the Heck procedure, the reportedly high attainable yields made this somewhat redundant. The Horner-Wadsworth-Emmons reaction was expected to provide the predominant *trans*-selectivity desired, and to allow increased scope for the tailoring of the required phosphonate substrates, maximising liquid crystal compatibility.



103 **146**

a) i) *n*-BuLi / THF / -78°C; ii) DMF / -78°C; iii) conc. HCl/Ice (83%);

Scheme 2.27 – Synthesis of 6,6'-vinyl binaphthalene derivatives via Horner-Wadsworth-Emmons reaction

Dialdehyde **146** was synthesised according to the procedure of Persoons. Lithiation of dibromide **103** was followed by subsequent quenching with anhydrous DMF to

form the hemiaminal, which upon acid hydrolysis afforded the target compound in 83% yield (*Scheme 2.27*). With the availability of **146** in respectable yield, our attention turned to the design and synthesis of the phosphonates.

The design of the phosphonates took three factors into consideration. Our initial concern was producing a target compound with the potential for *cis-trans* isomerism. To maximise the switching potential, a pseudo-stilbene derivative was considered essential. It was also considered necessary to incorporate linear substituents capable of the appropriate interactions with the nematic liquid crystal host. Finally, electron withdrawing functionalities were required to facilitate the final elimination step of the reaction.[166] The final phosphonate designs are shown in *Figure 2.23*.

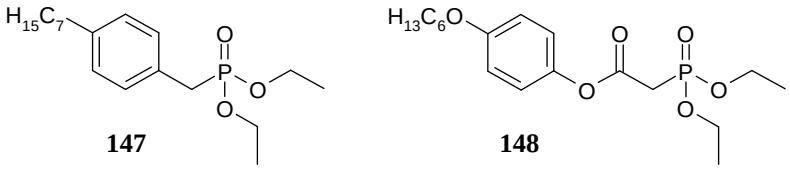
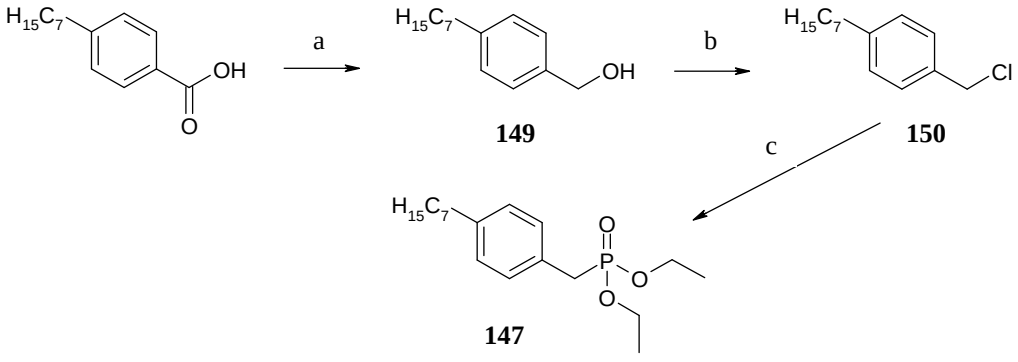


Figure 2.23 – Phosphonate design for Horner-Wadsworth-Emmons reaction

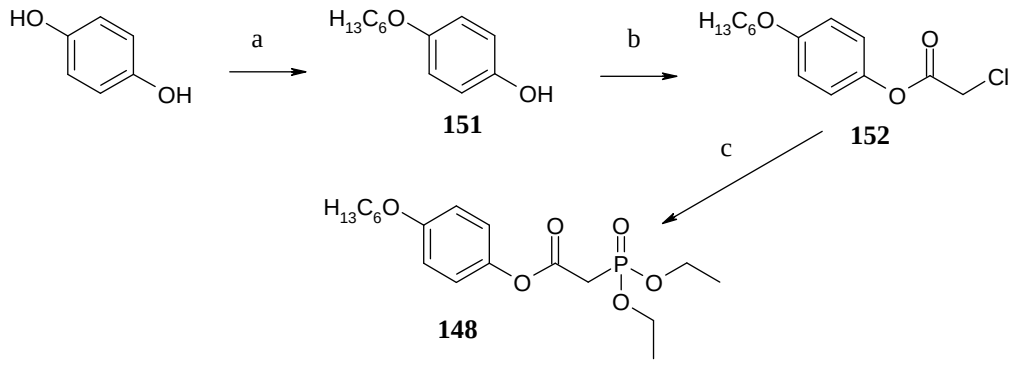
The synthesis of phosphonate **147** was achieved via reduction of commercially available 4-heptylbenzoic acid to benzyl alcohol **149**, and subsequent conversion to benzyl chloride **150** upon treatment with thionyl chloride. Formation of the phosphonate was achieved under Michaelis-Arbuzov conditions in 84% yield over the three steps (*Scheme 2.28*).



a) $LiAlH_4$ / THF:Et_2O (3:1) (99%); b) $SOCl_2$ / DCM / rt (86%);
c) KI / $P(OEt)_3$ / Acetone:MeCN (5:3) (99%)

*Scheme 2.28 – Synthesis of phosphonate **147***

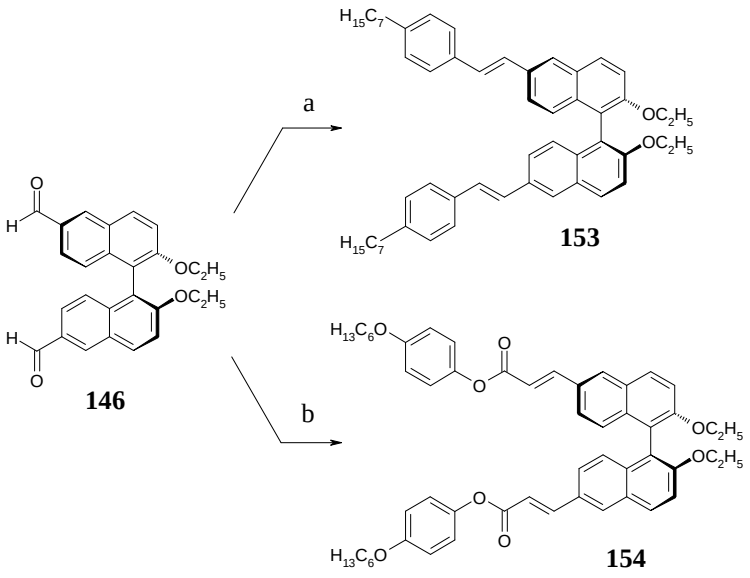
It was expected that the synthesis of phosphonate **148** was achievable from commercially available phenol **151**; however, the high cost led us to synthesise it in house from cheaply available hydroquinone. Reaction of phenol **151** with chloroacetyl chloride afforded chloroester **152**, which afforded phosphonate **148** under Michaelis-Arbuzov conditions in 42% overall yield. The majority loss of yield was a direct result of the phenol protection step (*Scheme 2.29*).



a) *n*-$H_{13}C_6Br$ / K_2CO_3 / Acetone / reflux (46%); b) Chloroacetyl chloride / Et_3N / Et_2O / 0°C (96%); c) KI / $P(OEt)_3$ / Acetone:MeCN (5:3) (95%)

*Scheme 2.29 – Synthesis of phosphonate **148***

Phosphonates **147** and **148** were subsequently employed with dialdehyde **146** in the Horner-Wadsworth-Emmons reaction, affording 6,6'-vinyl derivatives **153** and **154** in above average yields with complete *trans*-selectivity (*Scheme 2.30*).



a) NaH / **147** / THF / 50°C (57%); b) NaH / **148** / THF / 0°C (64%)

*Scheme 2.30 – Horner-Wadswoth-Emmons synthesis of compounds **153** & **154***

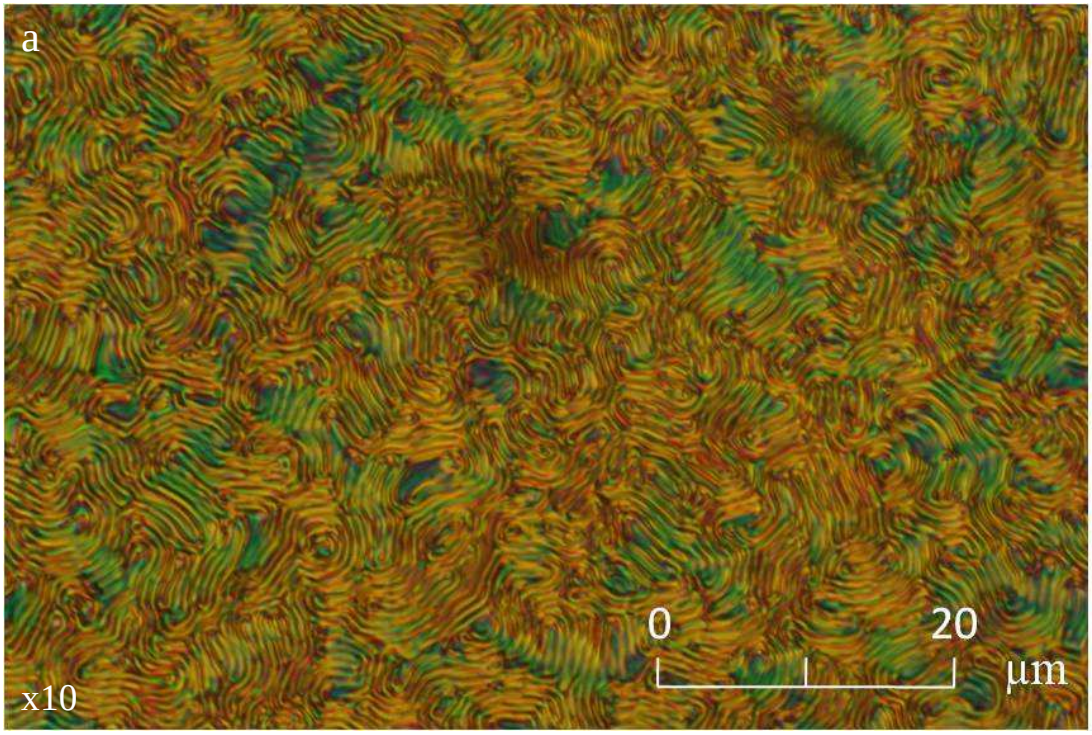
The 6,6'-vinyl compounds **153** and **154** were evaluated to determine their helical twisting power before the assessment of switching was attempted. The helical twisting powers were again recorded using the droplet method, with the results shown in *Table 2.6*. The positive effects of linear extension of the binaphthalene core were once again confirmed by dopants **153** and **154**. The high helical twisting power values also presented the potential for a significant effect on the helical macrostructure in the event of successful isomerisation.

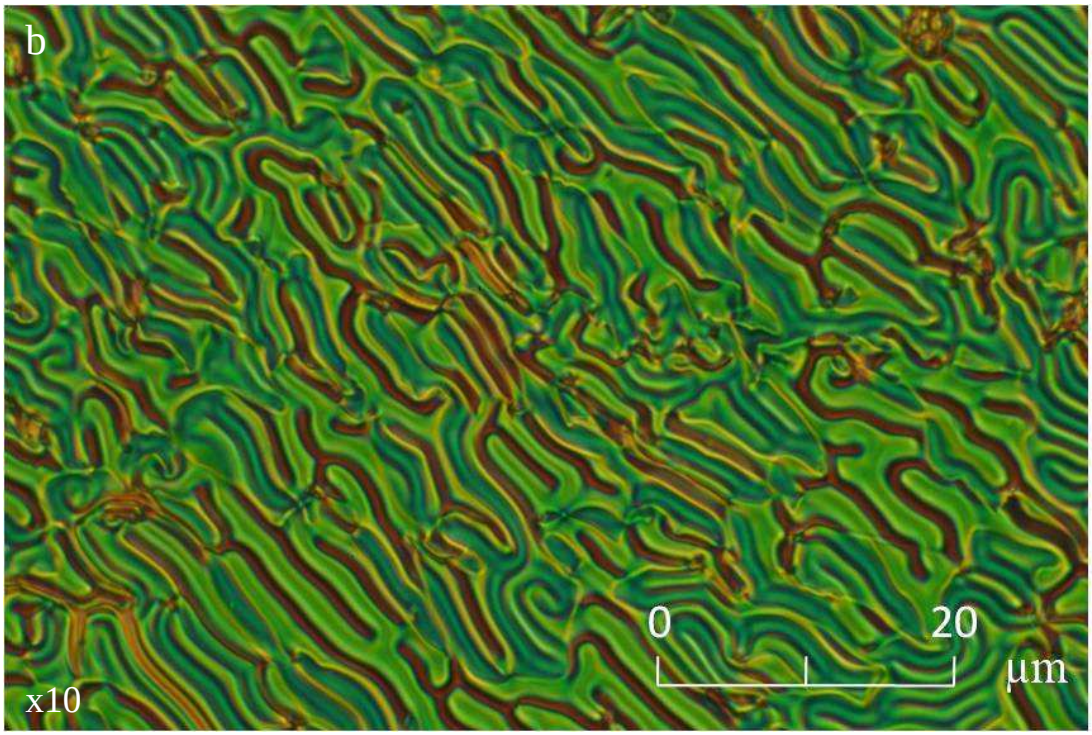
Entry	Dopant	β_M (μm^{-1})[a]
i	**153**	176
ii	**154**	172

a) Helical twisting powers recorded as an average over 10 runs and at two concentrations in nematic liquid crystal host E7 (**93**)

Table 2.6 – Helical twisting powers of 6,6'-divinyl binaphthalene derivatives

To determine the effects of switching, the helical twisting power of a film of nematic host E7 doped with binaphthalene **153** was recorded, before being subjected to a ultra-violet light source. The effects on the helical macrostructure were visibly apparent upon viewing under a polarising microscope (*Figure 2.24*). Prior to irradiation the pitch length was measured to be 3.2 μm^{-1}, which increased to 12.3 μm^{-1} upon irradiation/isomerisation.



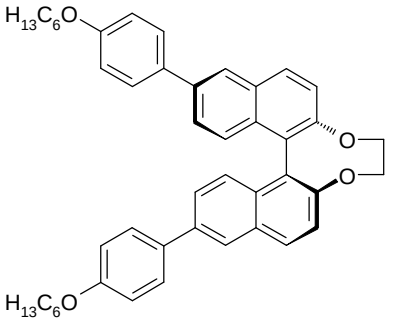


a) Pre-irradiation (β_M = 3.2 µm^{-1} in E7); b) Post-irradiation (β_M = 12.3 µm^{-1} in E7)

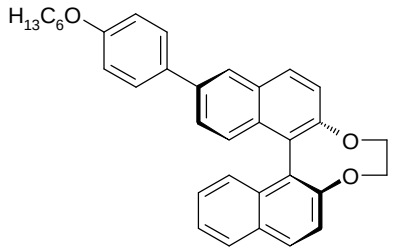
Figure 2.24 – Effects of switching on helical macrostructure with Ultra-Violet irradiation

The substantial change in pitch length confirmed the effectiveness of our switching system on modifying the chiral nematic helical macrostructure. Dopant **154** was subjected to the same irradiation conditions; however, decomposition was observed after relatively short exposure times, possibly as the result of a Norrish-type mechanism.

We were aware that the presence of the two switchable 6,6'-functionalities would likely result in a mixture of *E,E, E,Z* and *Z,Z* isomers upon irradiation. The unknown concentration of each isomer, and unknown effects of the *E,Z* isomer on the liquid crystal environment, would potentially affect the magnitude of switching potential.[167] Our previous studies into the substituent effects on helical twisting power for the bridged derivatives **102** and **117**, suggested the difference in performance between the mono and di-substituted derivatives was negligible (*Figure 2.25*). It was expected that the synthesis of a mono-substituted vinyl derivative would induce chirality as efficiently as the di-substituted derivative, whilst eliminating the presence of the *E,Z* isomer.



102 β_M = 96 µm^{-1} (E7)

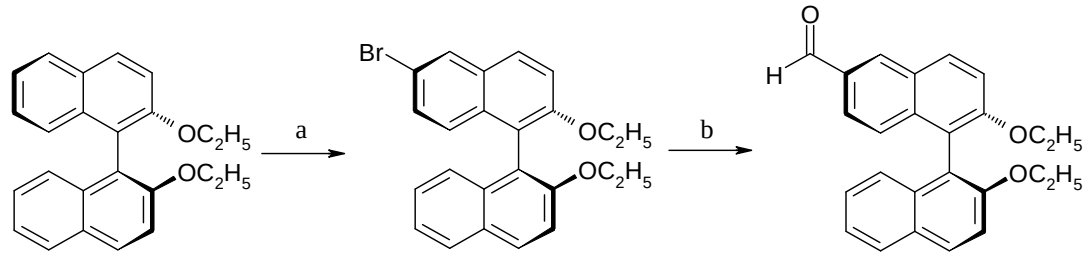


117 β_M = 95 µm^{-1} (E7)

Figure 2.25 – Similarity in helical twisting power for mono and di-substituted binaphthalene dopants

2.2.4 – Synthesis & Analysis of Mono-substituted Dopants

The synthesis of the mono-vinyl binaphthalene compounds first required the synthesis of the mono-aldehyde. De Vains reported the synthesis of mono-aldehyde **156** from mono-bromide **155**, using conditions similar to our previous aldehyde syntheses (*Scheme 2.31*).[168] The poor overall yield of 21% led us to attempt the synthesis via an alternate method.



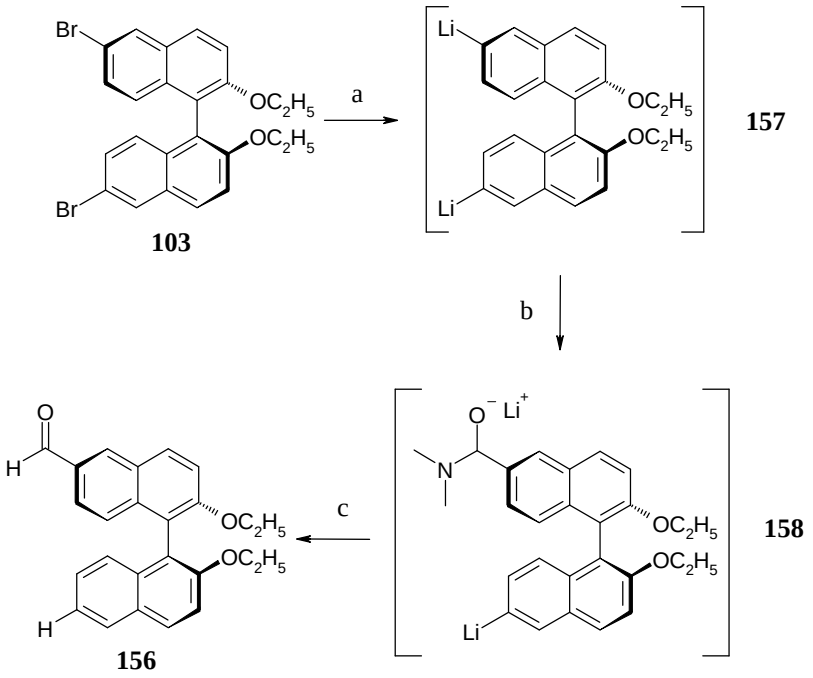
94 **155** **156**

a) 1eq. Br_2 / DCM / -10°C / streaming N_2;
b) i) *n*-BuLi / THF / -78 °C; ii) DMF / -78°C; iii) conc. HCl / Ice

*Scheme 2.31 – Synthesis of monoaldehyde **156***

Our initial attempt at the synthesis of **156** was from dibromide **103**, modifying the conditions of the previous aldehyde syntheses. It was expected that lithiation of **103** with two equivalents of *n*-BuLi, followed by quenching with one equivalent of DMF, would form hemiaminal intermediate **158**, which upon acidic work-up would afford mono-aldehyde **156** in moderate yields (*Scheme 2.32*). Unfortunately

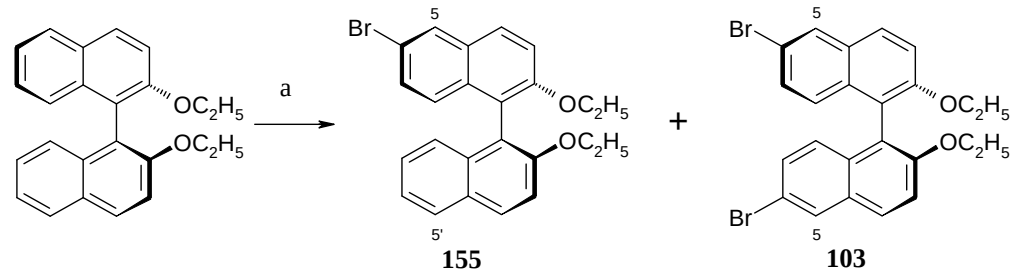
aldehyde **156** was only recovered in trace quantities, with dialdehyde **146** and debrominated **103** recovered as majority products.



a) 2 eq. *n*-BuLi / THF / -78°C; b) 1 eq. DMF / -78°C; c) conc. HCl / Ice

*Scheme 2.32 – Synthesis of **156** from dibromide **103***

Failure to produce **156** from dibromide **103** required us to attempt the synthesis from mono-bromide **155**. The procedure reported by De Vains[168] employed one equivalent of elemental bromine, and led to the recovery of unreacted starting material, mono-bromide **155** and dibromide **103** as reaction products. Due to our concerns with poor yield, we decided to increase the efficiency of the procedure by ensuring the complete consumption of starting material, whilst in tandem minimising the conversion of **155** to dibromide **103**. It was expected that this would allow for simpler chromatographic purification of the products, whilst forming the synthetically useful dibromide **103** as a reaction side product (*Scheme 2.33*). Bromides **155** and **103** were produced in an approximately 50:50 ratio mixture, upon complete consumption of starting material, as determined by ^{1}H NMR (*Figure 2.26*).



a) Br_2 / DCM / -10°C / streaming N_2

*Scheme 2.33 – Improved synthesis of mono-bromide **155***

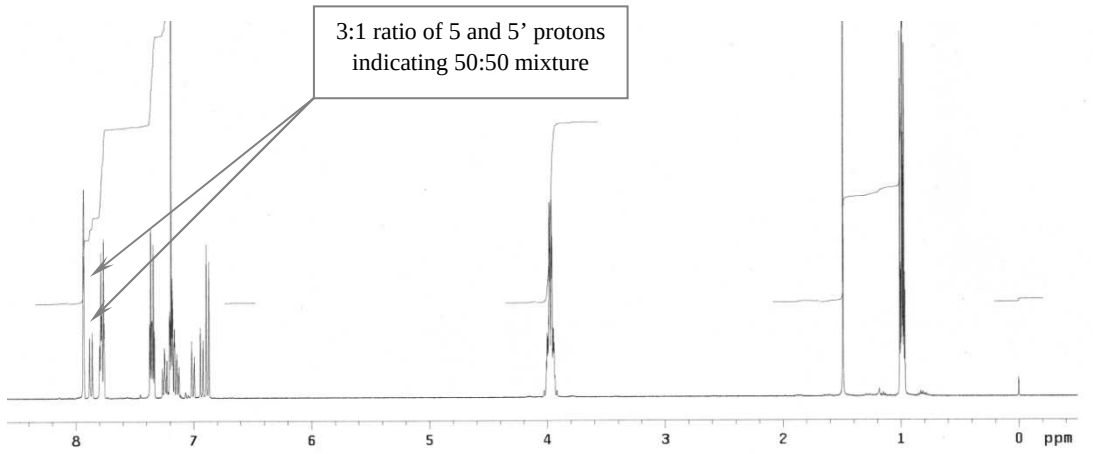
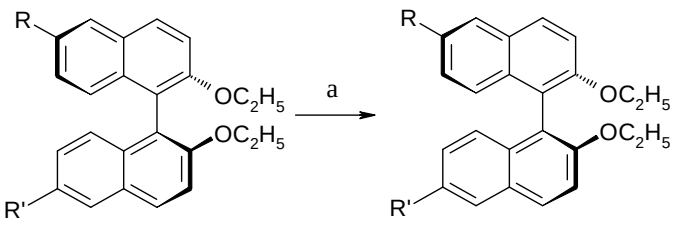


*Figure 2.26 – ^{1}H NMR indicating 50:50 ratio mixture of bromides **155** and **103***

Chromatographic separation of **155** and **103**, whilst possible, proved difficult and time consuming due to the similar R_f values of the two compounds. It was decided to convert the 50:50 bromide mixture directly to a mixture of aldehydes, with expected simpler separation. The aldehyde mixture was found to be easily separable via column chromatography and afforded mono-aldehyde **156** in 41% overall yield, with the synthetically useful dialdehyde **146** also recovered in 40% yield (*Scheme 2.34*). This represented a substantial increase in yield over the method reported by De Vains.[168]



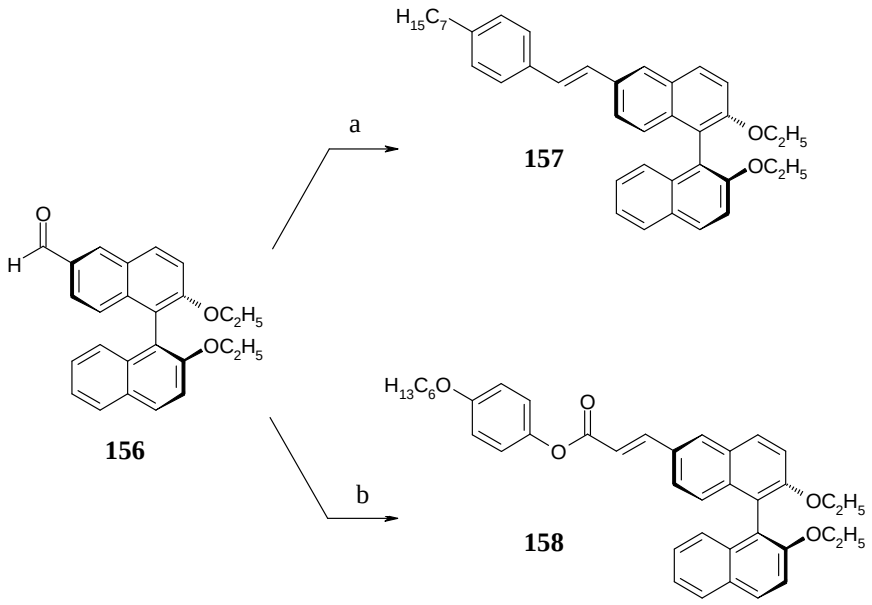
155 R = Br R' = H
103 R = Br R' = Br

156 R = HCO R' = H
146 R = HCO R' = HCO

a) i) *n*-BuLi / THF / -78°C, ii) DMF / -78°C iii) conc. HCl/Ice (41% **156**) (40% **146**)

*Scheme 2.34 – Synthesis of aldehydes **146** and **156***

Aldehyde **156** was employed in the Horner-Wadsworth-Emmons reaction with phosphonates **147** and **148** using the previously employed conditions, affording vinyl binaphthalenes **157** and **158** in 63% and 66% yield respectively (*Scheme 2.35*).



a) NaH / **147** / THF / 50°C, (63%); b) NaH / **148** / THF / 0°C, (66%)

*Scheme 2.35 – Synthesis of vinyl derivatives **157** and **158***

Prior to evaluation of the switching properties, the helical twisting powers of the mono-vinyl derivatives **157** and **158** were recorded, as shown in *Table 2.7*. Contrary to our earlier assumptions, it was discovered that the helical twisting powers of the mono-substituted derivatives were poor and comparable to that of the parent

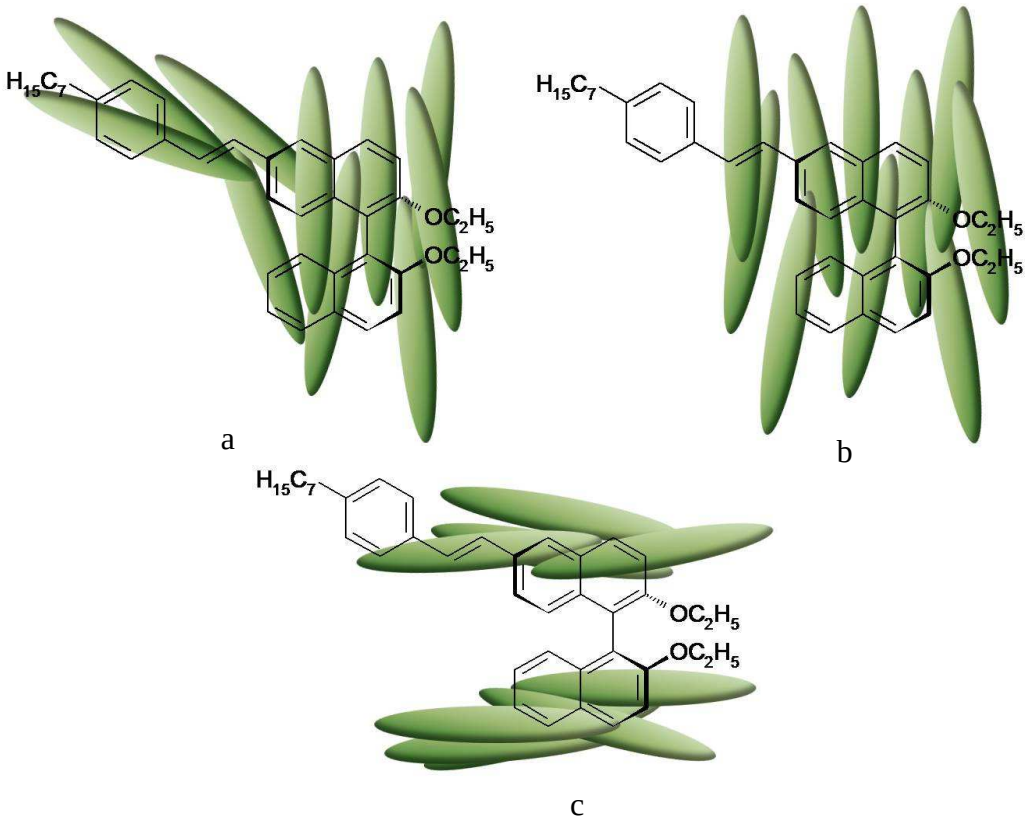
compounds. Whilst this proved unexpected, the results further enforced our theory of an alternate mechanism of chiral induction.

Entry	Compound	β_M (μm^{-1})[a]
i	**157**	15
ii	**158**	12

a) Helical twisting powers recorded as an average over 10 runs and at two different concentrations in nematic liquid crystal host E7 (**93**)

*Table 2.7 – Helical twisting powers of compounds **157** and **158***

As previously detailed, extension of both naphthyl planes is expected to promote alignment of the nematic director with the long molecular axes of the dopants. Due to the similarity in helical twisting power between the mono and di-substituted derivatives **102** and **117**, it was assumed that extension of a single naphthyl plane induced a similar alignment. The previous study was, however, concerned with bridged binaphthalene derivatives, whilst the mono-substituted vinyl compounds are conformationally flexible. The transfer of chirality is therefore likely to be affected either by disruption of the nematic phase through competing alignment of the director parallel to the naphthyl-naphthyl C(1)-C(1') bond, as for the Gottarelli-Spada model, or the ineffective twisting of the nematic director by an individual naphthalene 'arm' (*Figure 2.27*). Coincidentally, these effects were masked by the similar helical twisting powers between the bridged derivatives and came to light on the study of the mono-vinyl compounds.



a) Disruption of nematic phase through competing alignments; b) Nematic alignment as for the Gottarelli-Spada model; c) Inefficient induction of the helical twist by one naphthyl 'arm'

Figure 2.27 – Potential effects of unsymmetrical binaphthalenes on liquid crystal system

2.2.5 – Summary

A novel series of chiroptical dopants have been designed and synthesised, with their switching based on the linear/non-linear dopant phenomenon discovered in the initial study into high twist nematic dopants. Early attempts to produce an azobenzene derivative were successful, but the materials were highly coloured and prone to decomposition, making them unsuitable for application as nematic dopants and chiroptical switches. Successful synthesis of the conceptually similar stilbene derivatives induced significant changes to the helical macrostructure upon irradiation.

Efforts to reduce the number of potential isomers upon irradiations led to the synthesis of the mono-vinyl binaphthalenes. The helical twisting powers of the conformationally flexible mono-substituted derivatives were poor, and comparable

to the parent compounds. Inadvertently, this provided further evidence for our proposed, alternate mechanism of chiral induction.

Further evidence for the alternate mechanism of chiral induction was also acquired through the synthesis of the mono-substituted unsymmetrical binaphthalene derivatives, which displayed helical twisting powers comparable to that of the parent compounds. This furthered our belief that chirality is transferred from the extended binaphthalene dopants through the direct twisting of the nematic director by the extended naphthyl ‘arms’. Extension of one naphthyl plane was found to be inefficient at transferring chirality, either through disruption of the nematic phase through competing alignment, or through the inability to effectively twist the director.

2.3 –Enantiomeric Chiroptical Switch Feasibility Study

2.3.1 – Enantiomeric Switching

The control of chirality has long been a significant objective in chemistry, particularly in the case of asymmetric synthesis. More recently the manipulation of chirality in liquid crystal systems has been investigated, with the potential for application in display technologies and optical memory devices.

Numerous examples of molecular switching systems have been developed to date, some of which exhibit chirality and are theoretically applicable as chiral nematic dopants. The greatest successes in chiroptical dopants, in terms of design and function, have been for the Type 3 switches previously detailed. However, practical applications are limited and the systems are permanently chiral. The development of Type 1 (enantiomeric) and Type 2 (diastereomeric) switches are considered substantially more desirable.

Type 1 molecular switches concerns the switching between bistable states which share an enantiomeric relationship. Switching is achieved via irradiation with circularly polarised light (CPL), inducing preferential excitation of one enantiomer over the other generating an enantiomeric excess. Irradiation of a racemic sample with CPL of a certain handedness generates one enantiomer preferentially until a photostationary state is reached, inducing a nematic to chiral nematic phase transition. Switching between enantiomers is possible using CPL of the opposite handedness, whilst irradiation with linear polarised light (LPL) regenerates the racemate. This represents a three-way switching system (*Figure 2.28*).[46]

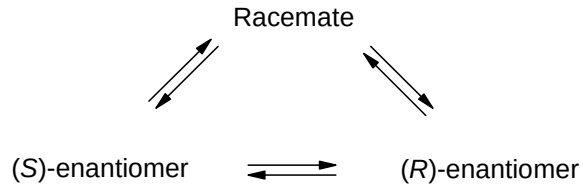


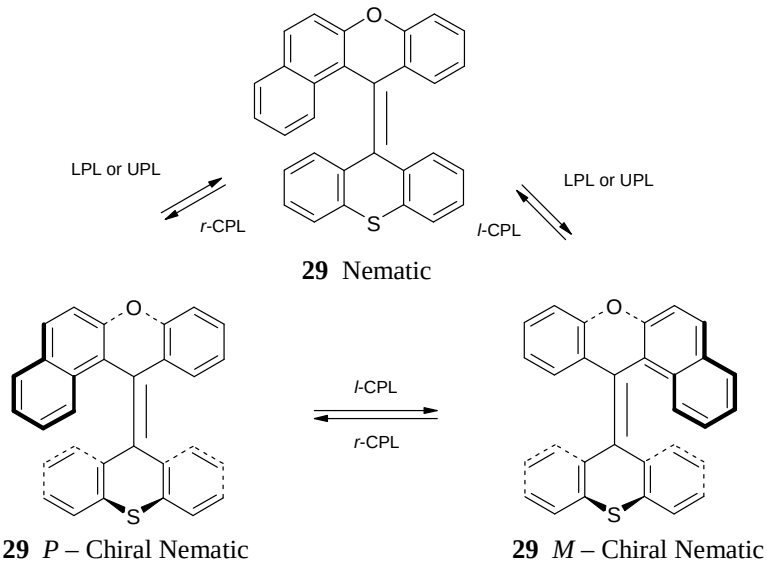
Figure 2.28 – Three-way enantiomeric switching cycle of Type 1 switches

The enantiomeric excess achieved at the photostationary state (ee_{PSS}) is ultimately defined by the Kuhn anisotropy factor g_λ, where $\Delta\varepsilon$ is the ratio of circular dichroism and ε the extinction coefficient.[46, 169] The enantiomeric excesses generated rarely

exceed 0.5% due to the Kuhn anisotropy factors rarely exceeding 1%, except in certain cases.[170]

$$ee_{\mathrm{PSS}} = \frac{g_\lambda}{2} = \frac{\Delta\varepsilon}{2\varepsilon}$$

The switching system was experimentally proven by Feringa and co-workers for the sterically overcrowded alkene class of compound. Successful demonstration of the switching potential was achieved, however the system suffered from low Kuhn anisotropy values, producing enantiomeric excesses of only 0.07% for derivative **158** (*Figure 2.29*). It was found that application to a liquid crystal environment was successful in producing nematic to chiral nematic phase transitions, however the poor helical twisting powers limited the scope of control on the pitch length.[47, 49]



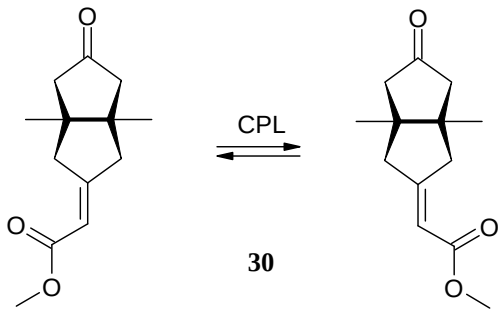
29 Nematic

29 *P* – Chiral Nematic

29 *M* – Chiral Nematic

Figure 2.29 – Overcrowded alkene class of Type 1 molecular switches

Schuster designed the cycloalkenone class of chiroptical molecular switch for the intended purpose of liquid crystal application.[50-53] In certain cases, impressive Kuhn anisotropy values were achieved producing enantiomeric excesses of up to 0.4%. Again liquid crystal compatibility proved exceptionally poor, with low helical twisting powers limiting their application as a successful switchable dopant system (*Figure 2.30*).

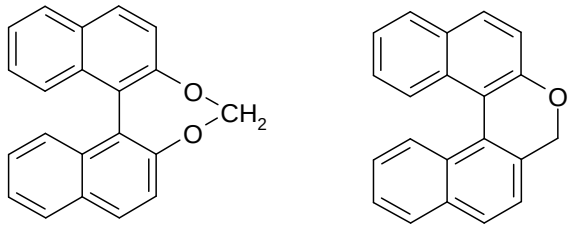


30

Figure 2.30 – Axially chiral cycloalkenone Type 1 switching system

In addition to the complex design features required for a successful chiroptical molecular switch (Kuhn anisotropy factor, thermal stability, fatigue resistance, etc.), it is clear that application to a liquid crystal environment requires additional challenging factors to be addressed, such as liquid crystal compatibility and helical twisting power.

Efforts to develop switching systems based upon structures known to be liquid crystal compatible, have led to attempts to develop switchable dopants based on the bridged chiral binaphthalene structure (*Figure 2.31*).[171] Racemisation of the binaphthalenes occurs as for other 1,1'-binaphthalene derivatives, in the triplet state, which is dependent on the activation energy barrier for the two naphthyl rings to adopt a planar configuration in the excited state. Photoresolution of derivatives such as **159** and **160** were not observed, as a possible consequence of low Kuhn anisotropy values or inefficient photoracemisation. The development of a molecular switch based upon a structure with proven liquid crystal compatibility remains highly desirable and yet elusive.



159 **160**

Figure 2.31 – Type 1 switches base on the 1,1'-binaphthalene structure

The binaphthalene structure is known to adopt an axially chiral configuration, corresponding to the energy minima, in which there is a small but significant degree of π-overlap between the naphthyl planes. It was reasoned that strategic placement of

a donor and acceptor substituent on each of the naphthalene rings, would potentially induce a low energy transition through conjugation between substituents (*Figure 2.32*). More significantly, the conjugation pathway describes a helix of opposite handedness for each enantiomer. Such a transition was expected to induce high Kuhn anisotropy values due to the low value of the extinction coefficient ε and high Δε value from the CD spectrum. The main objective of the study was the generation of optically pure materials, and the examination of the absorption spectra (CD and UV), to determine the feasibility of the switching system.

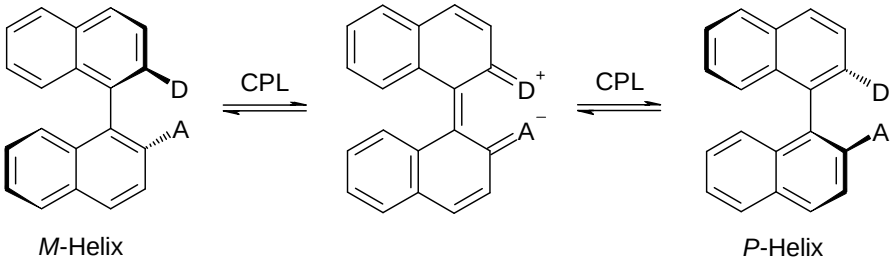


Figure 2.32 – Photoracemisation and optical enrichment by CPL

2.3.2 – Dopant Design, Synthesis & Analysis

Dopant design was intended to be based on the chiral binaphthalene skeleton with strategic placement of the donor/acceptor groups. It is apparent that many combinations of donor/acceptor group placements are possible, which maintain conjugation (*Figure 2.33*). It was decided that due to the requirement for optically pure materials, the use of an optically pure starting material such as 1,1'-bi(2-naphthol) limited the substituents to the 2,2'-positions. This also prevented substantial lowering of the barrier to racemisation through removal of the steric interactions between the 2,2'-substituents. Alkoxy groups were selected as donor groups and nitriles for acceptor groups, due to their proven application in liquid crystal systems.

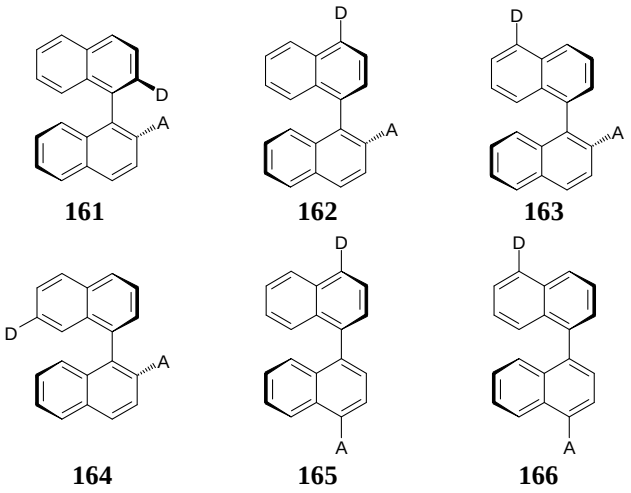
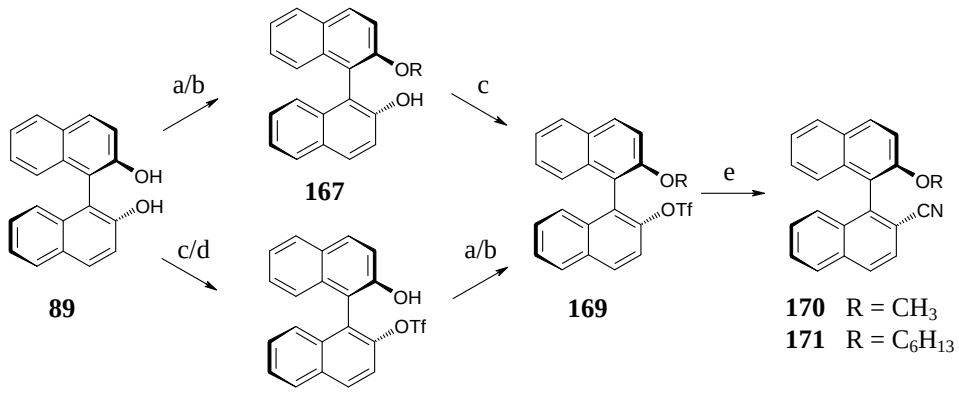


Figure 2.33 – Possible donor/acceptor conjugation pathways

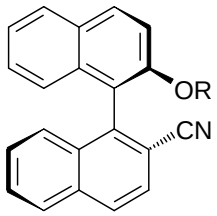
The synthesis of the donor/acceptor dopants was expected to be achieved from optically pure 1,1'-bi(2-naphthol), via the routes shown in *Scheme 2.36*. Although it was possible to introduce the nitrile functionality earlier in the synthesis, we were concerned with its sensitivity towards subsequent reaction conditions. The initial step required mono-substitution of one hydroxyl group, either as the alkoxyl or triflate. Synthesis of mono-triflate **168** has previously been reported using triflic anhydride.[172] Mono-substitution proved successful for the synthesis of the triflate **168** or methyl ether **167**, however the procedures were inefficient, with yields of 37% and 47% respectively. A literature search revealed a procedure by Hayosa,[173] which utilised the milder triflating agent *N*-phenylbis(trifluoromethanesulphonyl imide). Employing the conditions of Hayosa, mono-triflate **168** was afforded in 76% yield, with alkylation of the remaining hydroxyl group achieved in 96%.



a) H_3CI / K_2CO_3 / Acetone; b) $H_{13}C_6Br$ / K_2CO_3 / Acetone; c) Tf_2O / Pyridine / DCM / 0°C; d) Tf_2NPh / 2,4,6-Collidine / DMAP / DCM / reflux; e) $Pd_2(dba)_3$ / dppf / $ZnCN_2$ / DMF

*Scheme 2.36 – Synthesis of switchable dopants **170** & **171***

With the availability of mono-triflate **169** in decent yield, our attention turned to installation of the nitrile functionality. The transition metal catalysed conversion of aryl triflates to aryl nitriles is prevalent in the literature.[172, 174-178] Zinc cyanide has been reported to offer substantial advantages over other cyanide ion sources, such as hexacyanoferrate, due to its low solubility preventing formation of a tetracyanopalladium species, which is incapable of participation in the catalytic cycle.[178, 179] Cyanation of **169** was attempted using the conditions of Hanack[174] affording nitriles **170** and **171** in 31% and 27% yield respectively (*Scheme 2.36*). Despite the poor yields, the availability of the optically pure dopants allowed for determination of their helical twisting powers (*Table 2.8*) and analysis of their absorption spectra.



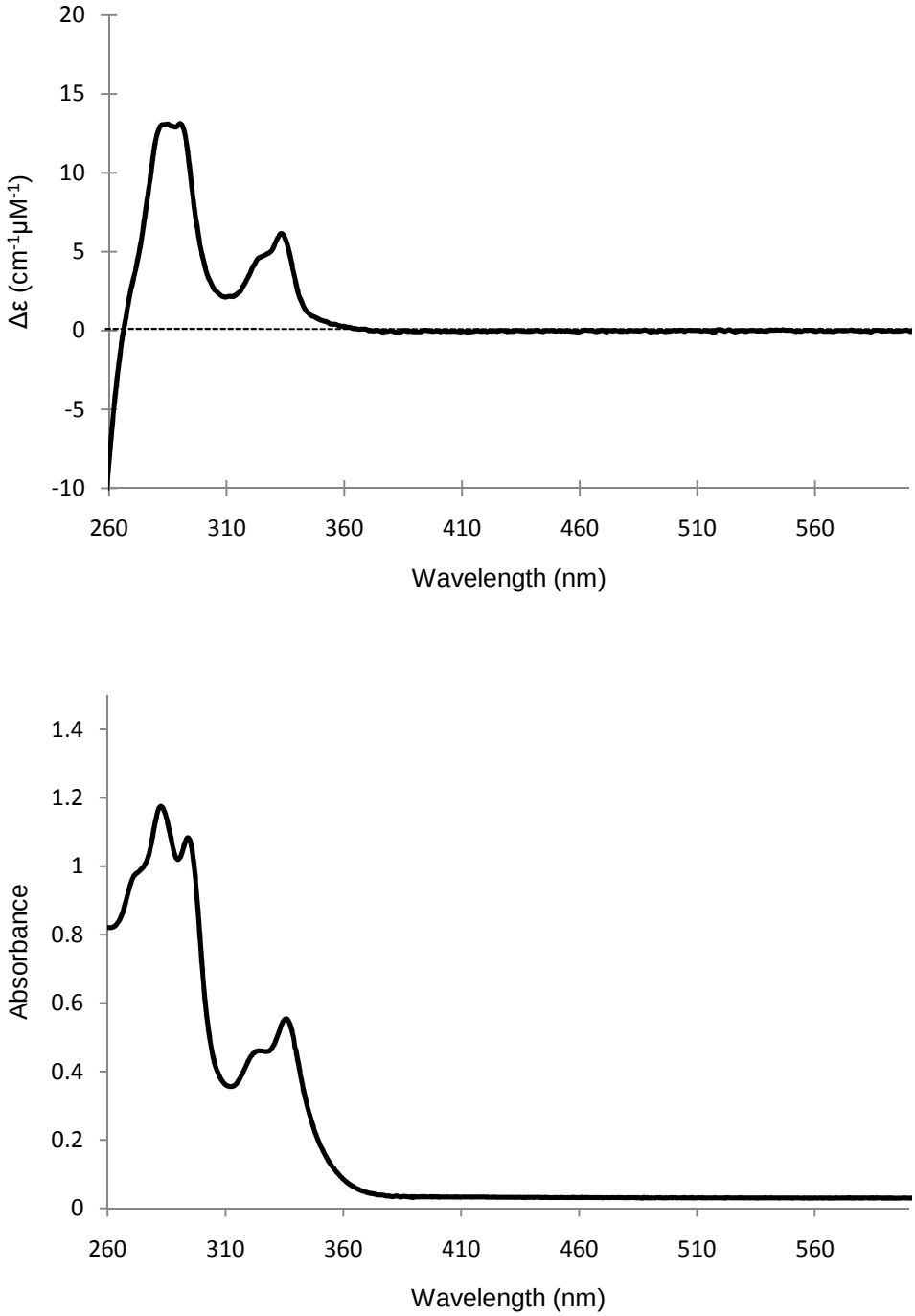
170 R = CH_3
171 R = C_6H_{13}

Entry	Dopant	β_M (μm^{-1})[a]
i	**170**	20.7
ii	**171**	27.4

a) Helical twisting powers measured as an average over 10 separate runs and at two concentrations in nematic liquid crystal host E7 (**93**)

*Table 2.8 – Helical twisting powers of dopants **170** and **171***

As expected, the helical twisting powers were higher than any previously reported Type 1 molecular switches and similar to the majority of 2,2'-substituted binaphthalenes in the literature. It was expected that similar circular dichroism and UV spectra would be obtained for each of compounds **170** and **171**, therefore analysis of the methyl derivative **170** was used to assess the feasibility of the switching system.



Circular Dichroism (Top) / UV-Vis (Bottom) of a 0.89×10^{-3} M solution of **170** in DCM

*Figure 2.34 – Absorption spectra for compound **170***

The absorption spectra of compound **170** are shown in *Figure 2.34*. Unfortunately, the anticipated long wavelength helical conjugation pathway is not evident from the UV-Vis spectra, with the CD spectrum following the absorption profile. Calculation of the Kuhn anisotropy factor values ($g_\lambda = \Delta\varepsilon/2\varepsilon$), as a function of wavelength, were

plotted (*Figure 2.35*),[48,180] and suggested photoresolution to a maximum enantiomeric excess (ee_{max}) of 0.029% ee at a wavelength of 290 nm. It was clear that dopants based on the parent structure of **170** were unlikely to yield materials which could be switched effectively.

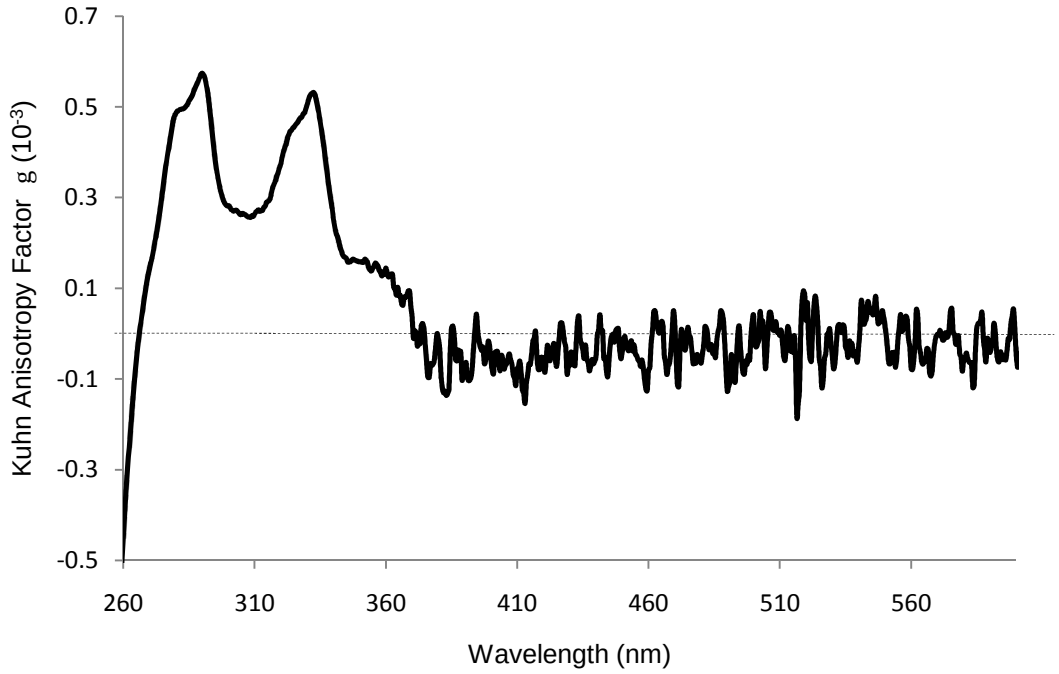
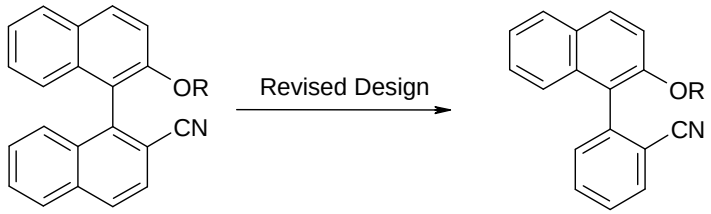


*Figure 2.35 – Plot of Kuhn anisotropy factor (g) values as a function of wavelength for compound **170***

2.3.3 – Revised Dopant Design

The results from dopant **170** suggested an alternate structure may prove more effective at photoresolution. It was reasoned that removal of the steric bulk from one naphthyl plane may enhance π-overlap between the aromatic rings, inducing the helical conjugation pathway. The design of the dopant was therefore based on the parent structure **172**, maintaining the nitrile and alkoxy groups from the previous design (*Figure 2.36*).

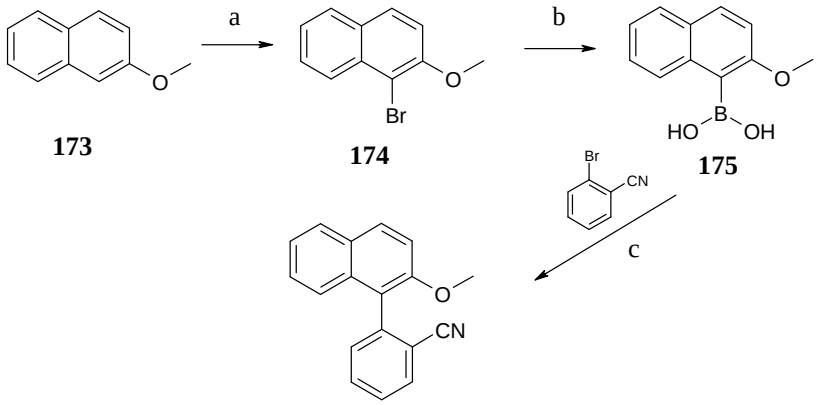


172

Figure 2.36 – Revised design of the enantiomeric chiroptical switch

Due to the lack of an available chiral source of the 1-phenylnaphthalene structure, a racemic coupling and subsequent optical resolution, or asymmetric coupling, was required to produce the optically pure materials. It was decided to attempt the synthesis of **172** via a racemic cross-coupling, and utilise the deprotected hydroxyl group to introduce a chiral auxiliary for optical resolution.

Synthesis of the required boronic acid was achieved from commercially available 2-methoxynaphthalene. Bromination of the protected naphthol was achieved using the conditions reported by Majetich,[181] followed by conversion to the boronic acid under standard conditions. Racemic **176** was obtained in poor-average yield via cross-coupling with 2-bromobenzonitrile (*Scheme 2.37*). A highly coloured side-product was also recovered which will be discussed in greater detail later in the chapter.



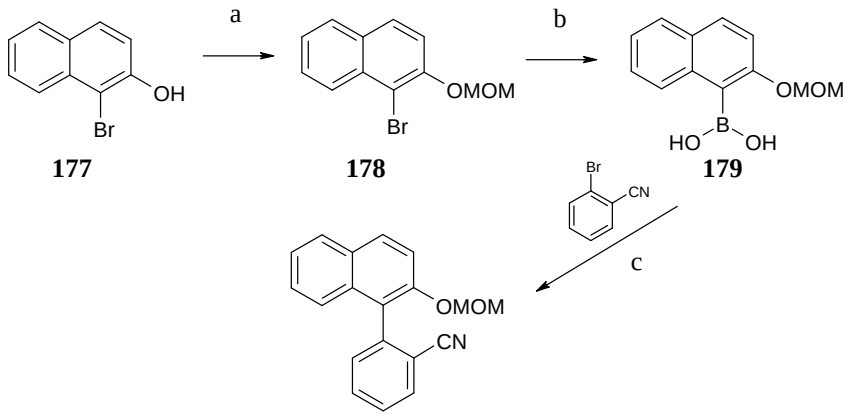
173 **174** **175** **176**

a) HBr / DMSO / AcOH (94%); b) i) Mg / Et_2O / reflux; ii) $B(OCH_3)_3$ / Et_2O / -78°C; iii) 1M HCl / rt (83%); c) $PdCl_2(dppf)$ / K_3PO_4 / DME (34%)

*Scheme 2.37 – Racemic synthesis of **176** via Suzuki-Miyaura cross-coupling*

Unfortunately, deprotection of the methyl ether was unsuccessful using BBr_3[182] and the thiolate ion deprotection reported by Chakraborti.[183] The coupling was attempted utilising an alternately protected boronic acid. A MOM ether protecting group was selected due to its expected resistance towards the coupling conditions and limited

size. Synthesis of boronic acid **179** was achieved from commercially available 1-bromo-2-naphthol **177**. The *in situ* generation of a MOM chloride toluene solution produced protected bromide **178**, which was converted to the boronic acid under standard conditions. Coupling with 2-bromobenzonitrile afforded racemic **180** in average-good yield (*Scheme 2.38*).



177 **178** **179** **180**

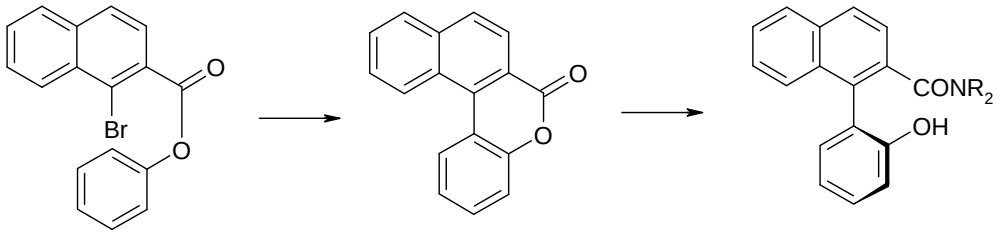
a) ~2M MOMCl in Toluene / DIPEA (94%); b) i) *n*-BuLi / Et_2O / -78°C;
ii) $B(OCH_3)_3$ / Et_2O / -78°C; iii) sat. NH_4Cl / rt (63%); c) $PdCl_2$(dppf) / CsF / DME / reflux (48%)

Scheme 2.38 – MOM protected dopant synthesis

Deprotection of the ether protecting group was expected to be difficult due to the sensitivity of the nitrile to various conditions. Simple acid hydrolysis was attempted at ambient temperatures with dilute hydrochloric acid, which failed to yield the deprotected biaryl. Nitrile hydrolysis was observed upon raising the temperature.

2.3.4 – Future Studies

The failure to successfully deprotect and resolve compounds **176** or **180**, limited the study of the adapted dopant design. Future studies are likely to be based around the design of alternate synthetic strategies towards the target compounds, or the investigation into binaphthalene based dopants utilising alternate substitution patterns. In particular, the bridging lactone synthetic strategy may offer the possibility to form the desired 1-phenyl-naphthalene structures in good yield and stereoselectivity (*Scheme 2.39*).

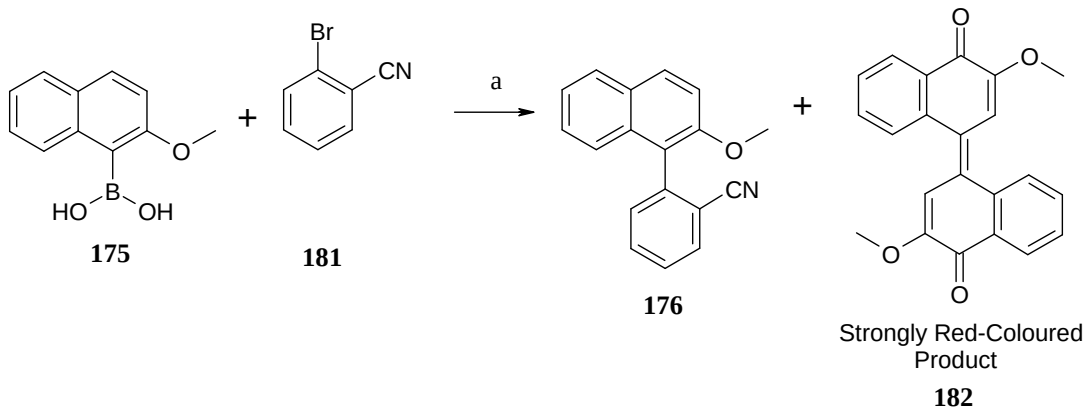


Scheme 2.39 – Potential synthesis of donor/acceptor parent structure via bridging lactone method

2.3.5 – An Unexpected Side-Product

2.3.5.1 – Initial Observations

The synthesis of the Type 1 switchable dopants produced an unidentified, strongly red-coloured side-product upon the routine Suzuki-Miyaura cross-coupling between boronic acid **175** and bromide **181**, along with the desired product **175** in 34% yield (*Scheme 2.40*). Initial attempts to isolate the red compound failed due to its apparent instability. Eventual isolation led to the structure being determined as that of compound **181**.

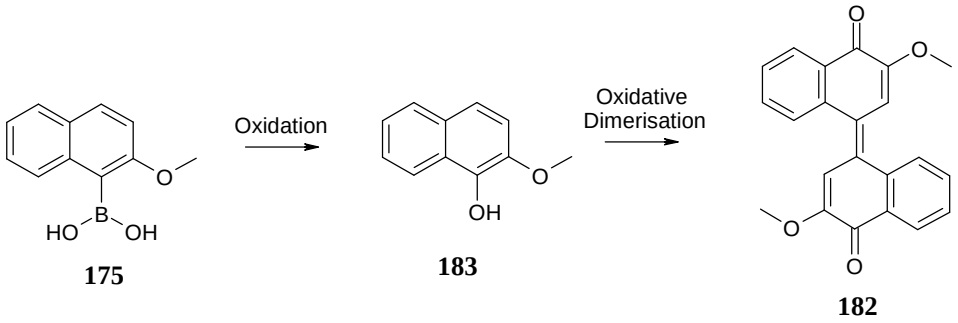


a) $PdCl_2(dppf)$ / K_3PO_4 / Toluene / reflux

Scheme 2.40 – Routine Suzuki-Miyaura cross-coupling producing an unexpected side-product

Similarly structured compounds are relatively common in the literature, being formed via oxidative coupling and oxidative dimerisation of hydroxyarenes, employing metal salts,[184-188] Lewis acids,[153, 189-191] aerobic oxidation[192, 193] and semi-conductor catalysts.[194-196] Although limited, examples of the formation of phenolic species during palladium catalysed couplings, employing boronic acids, have been

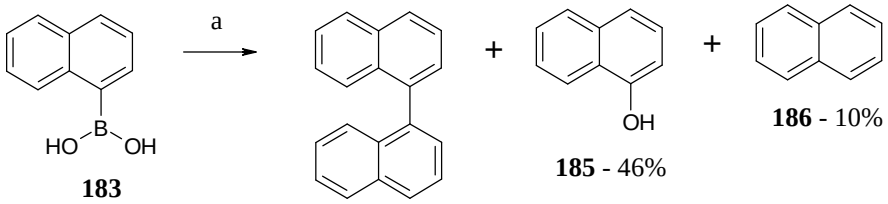
reported in the literature.[197-199] The observed side-product appeared to be consistent with literature reports of a palladium catalysed boronic acid to hydroxyarene conversion, and its subsequent dimerisation (*Scheme 2.41*).



175 **183** **182**

*Scheme 2.41 – Potential synthetic route to derivative **182***

Jackson *et al.* reported the recovery of phenolic side-products from palladium catalysed homo-coupling of boronic acids, under a range of different conditions. In the synthesis of **184**, naphthol **185** was recovered as the majority product, in addition to deboronated **186**. Optimum conditions, for phenol formation reported by Jackson, employed barium hydroxide as the base in an aqueous ethanol solution, open to the atmosphere (*Scheme 2.42*).



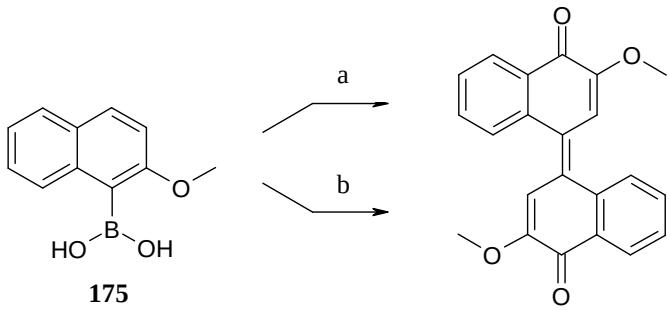
183 **184** - 29% **185** - 46% **186** - 10%

a) $Ba(OH)_2$ / $Pd(OAc)_2$ / H_2O:EtOH (1:19)

Scheme 2.42 – Homo-coupling of naphthyl boronic acid reported by Jackson[199]

Whilst our original observation of the dimerised product occurred in the presence of the arylbromide coupling partner, it was expected that it was not essential for the formation of the hydroxyarene, and its subsequent dimerisation. It was decided to attempt the purposeful synthesis of the dimerised product, employing the optimal conditions of Jackson *et al.*, in the absence of the arylbromide coupling partner. A control experiment was also conducted in the absence of a catalytic species. The palladium catalysed conditions afforded dimer **182** in quantitative yield, however more significantly, compound **182** was recovered in quantitative yield, in the catalyst

free control experiment (*Scheme 2.43*). To our knowledge, this was the first instance of such a transformation, and led to us investigating the process further.



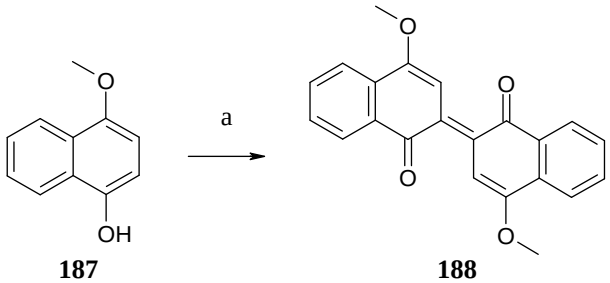
175 **182**

a) $Pd(OAc)_2$ / $Ba(OH)_2$ / Toluene:H_2O:Ethanol (3:1:3) / O_2 / rt (99%); b) $Ba(OH)_2$ / Toluene:H_2O:Ethanol (3:1:3) / O_2 / rt (99%)

*Scheme 2.43 – Synthesis of dimer **182***

Relatively few boronic acid to phenol conversions are described in the literature, with oxidation upon treatment with aqueous hydrogen peroxide perhaps the most commonly employed method.[200-203] Effective oxidation has also been reported employing milder reagents such as Oxone,[204] sodium perborate[205] and hydroxylamine.[202] Oxidation of boronic acids in atmospheric oxygen has also been reported, but is typically slow, with increased boronic acid stability in the presence of water.[206]

Whilst it was speculated that a boronic acid to naphthol conversion, and subsequent dimerisation, was the origin of the dimer species, we attempted to ascertain whether our conditions would induce dimerisation on a starting naphthol species. Commercially available naphthol **187** was subjected to our boronic acid conversion conditions to afford the strongly blue-coloured dimer **188** in quantitative yield (*Scheme 2.44*).



187 **188**

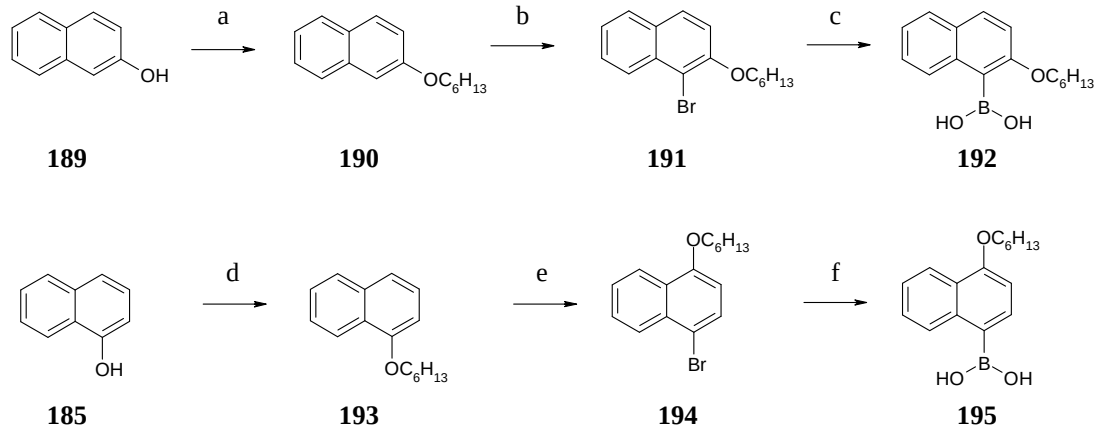
a) $Ba(OH)_2$ / Toluene:Water:Ethanol (3:1:3) / O_2 / rt (99%)

*Scheme 2.44 – Oxidative dimerisation of naphthol **187***

The rapid and quantitative conversion of the naphthalene boronic acids to the corresponding naphthols, and their subsequent dimerisation, under catalyst free conditions is essentially unprecedented. It is evident that this would have clear implications for reaction protocols employing boronic acids. A concise and systematic study was therefore conducted to ascertain the effects of the nature of the boronic acid, and reaction conditions which influence the process.

2.3.5.2 – A Novel Boronic Acid Conversion

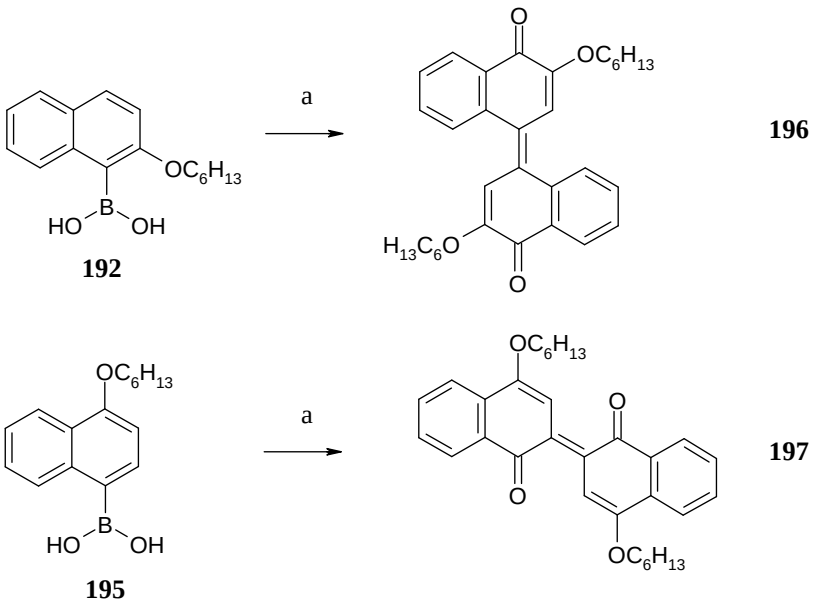
Boronic acids **192** and **195** were selected for the preliminary investigation and synthesised, in house, from the commercially available naphthols **189** and **185**, in 62% and 51% overall yield, respectively (*Scheme 2.45*).



a) *n*-$H_{13}C_6Br$ / K_2CO_3 / Acetone / reflux (90%); b) 48% HBr / AcOH / DMSO (90%); c) i) *n*-BuLi / Et_2O / -78°C; ii) $B(OCH_3)_3$ / Et_2O / -78°C; iii) 1M HCl / rt (77%); d) *n*-$H_{13}C_6Br$ / K_2CO_3 / Acetone / reflux (88%); e) NBS / MeCN / rt (87%); f) i) Mg / Et_2O / reflux; ii) $B(OCH_3)_3$ / Et_2O / -78°C; iii) 1M HCl / rt (67%)

*Scheme 2.45 – Synthesis of boronic acids **192** and **195***

The initial investigation was primarily focused on the nature of the base. The rapid dimerisation of the naphthols prevented their direct isolation and quantification. Their detection was therefore based purely on the recovery of the dimerised compounds **196** and **197** (*Scheme 2.46*). The results of the preliminary investigations are shown in *Table 2.9*.



a) Base / Toluene:Water:Ethanol (3:1:3) / rt / O_2

Scheme 2.46 – Effects of base selection

Entry	Boronic Acid	Solvent System	Base[a]	Product
i	**192**	Toluene/H_2O/Ethanol (3:1:3)	$Ba(OH)_2$	**196**[b] (99%)
ii	**195**	Toluene/H_2O/Ethanol (3:1:3)	$Ba(OH)_2$	**197**[b] (99%)
iii	**192**	Toluene/H_2O/Ethanol (3:1:3)	NaOH	**196**[c]
iv	**195**	Toluene/H_2O/Ethanol (3:1:3)	NaOH	**197**[c]
v	**192**	Toluene/H_2O/Ethanol (3:1:3)	KOH	**196**[c]
vi	**195**	Toluene/H_2O/Ethanol (3:1:3)	KOH	**197**[c]
vii	**192**	Toluene/H_2O/Ethanol (3:1:3)	K_2CO_3	No Product[d]
viii	**192**	Toluene/H_2O/Ethanol (3:1:3)	K_3PO_4	**196**[b] (99%)
ix	**192**	DCM/H_2O/Ethanol (3:1:3)	$Ba(OH)_2$	**196**[b] (99%)

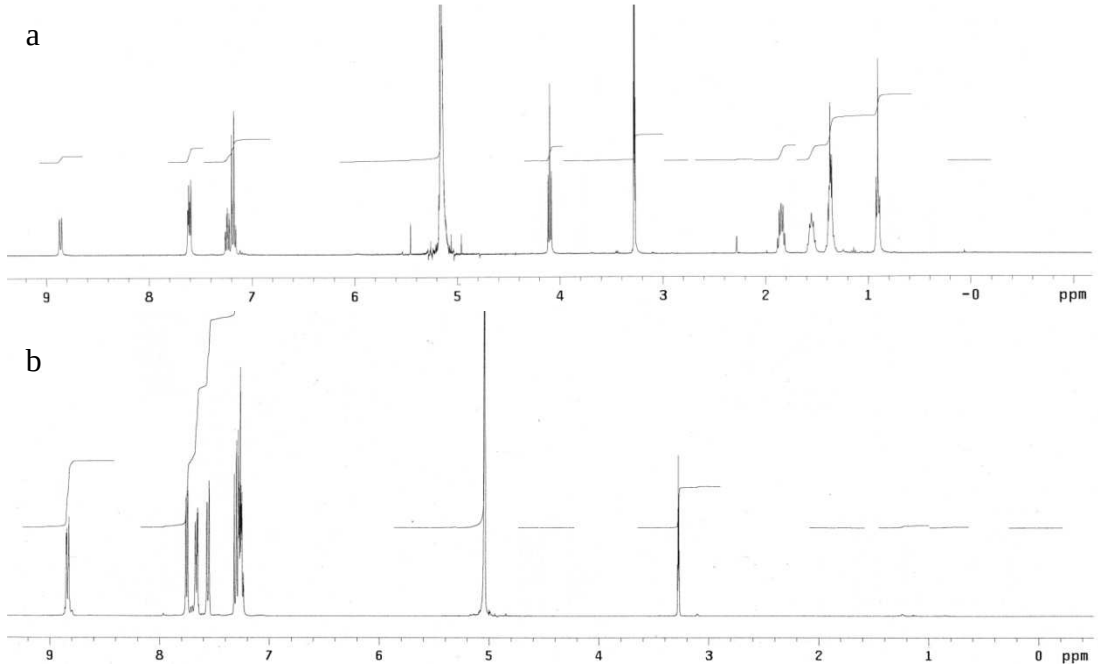
a) 2 Eq. base to boronic acid; b) Isolated products; c) Product visually identified before degredation; d) Starting material recovered

Table 2.9 – Results of base selection

It became apparent that conversion of the boronic acids to the dimer compounds was possible utilising each of the three hydroxide bases employed. Quantitative recovery of compounds **196** and **197** proved possible employing barium hydroxide (*entries i & ii*), however, upon application of potassium or sodium hydroxide, visual identification of the coloured products was followed by rapid decomposition, preventing their isolation (*entries iii-vi*). Successful recovery of the dimeric

compound was also observed using tripotassium phosphate, although the rate of conversion was markedly slower than for the hydroxide bases (*entry viii*).

Despite the relative success of the conversions, it was decided to attempt observation of the predicted intermediate naphthol species. The conversion reaction was attempted under anaerobic conditions, in degassed deuterated solvent, to permit monitoring by ^{1}H NMR, as shown in *Figure 2.37*. The nature of the species observed by ^{1}H NMR was initially unclear, although the distinct peak close to 9 ppm suggested the formation of the boronate salt or naphtholate salt. Due to the rapid formation of the dimerised compound in atmospheric oxygen, handling of the formed species was difficult. Instead, the purposeful formation of a naphthalene boronate salt was attempted from 1-naphthalene boronic acid, under the premise that dimerisation would not be induced on the unsubstituted naphthalene. Treatment of 1-naphthaleneboronic acid with barium hydroxide indicated the formation of the boronate salt by ^{1}H NMR, as shown for naphthalene boronic acid **192** under anaerobic conditions (*Figure 2.37*).

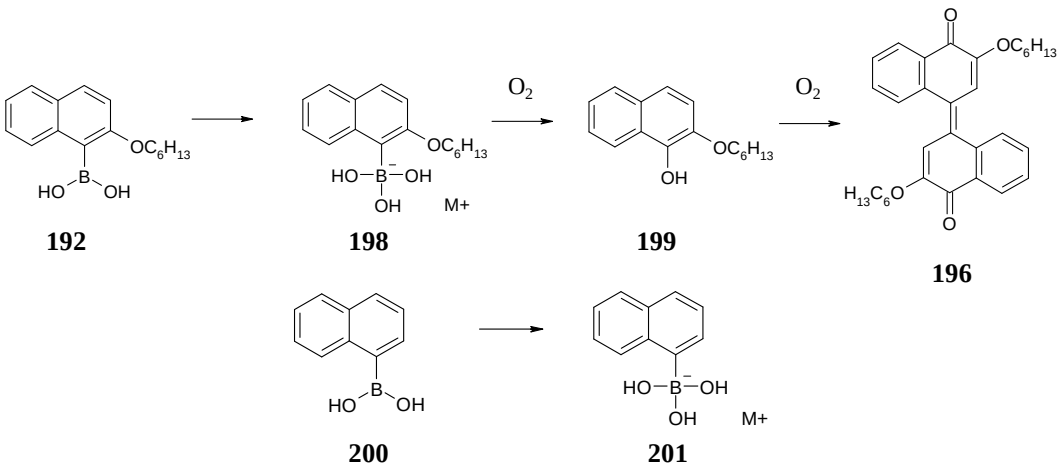


a) Treatment of boronic acid **192** with $Ba(OH)_2$ under anaerobic conditions (CD_3COD)
b) Treatment of boronic acid **200** with $Ba(OH)_2$ under aerobic conditions (CD_3COD)

Figure 2.37 – Naphthalene boronate salt species, determined by ^{1}H NMR

The initial step of the procedure was therefore identified as formation of the naphthalene boronate salt. Electron rich naphthalene boronate salts are shown to

rapidly oxidise under atmospheric conditions, to the dimerised compounds. It was expected that oxidation of the boronate salt formed the intermediate naphthol, however formal identification of the naphthol species was not achieved, with the evidence based purely on the purposeful naphthol dimerisation experiment previously discussed (*Scheme 2.47*).



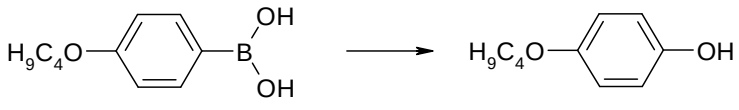
192 **198** **199** **196**

200 **201**

Scheme 2.47 – Naphthalene boronic acid conversion via boronate salt

2.3.5.3 – Further Investigation

With the successful implementation of our protocol to the naphthalene boronic acids, we were eager to assess whether structurally different boronic acids, in particular, the benzene boronic acids, also underwent conversion in the absence of a catalyst. Commercially available 4-butyloxybenzeneboronic acid was selected for the preliminary investigations and subjected to our previously customised conversion conditions (*Scheme 2.48*), with the results shown in *Table 2.10*.



202 **203**

a) Base / Toluene:H_2O:EtOH (3:1:3) / O_2

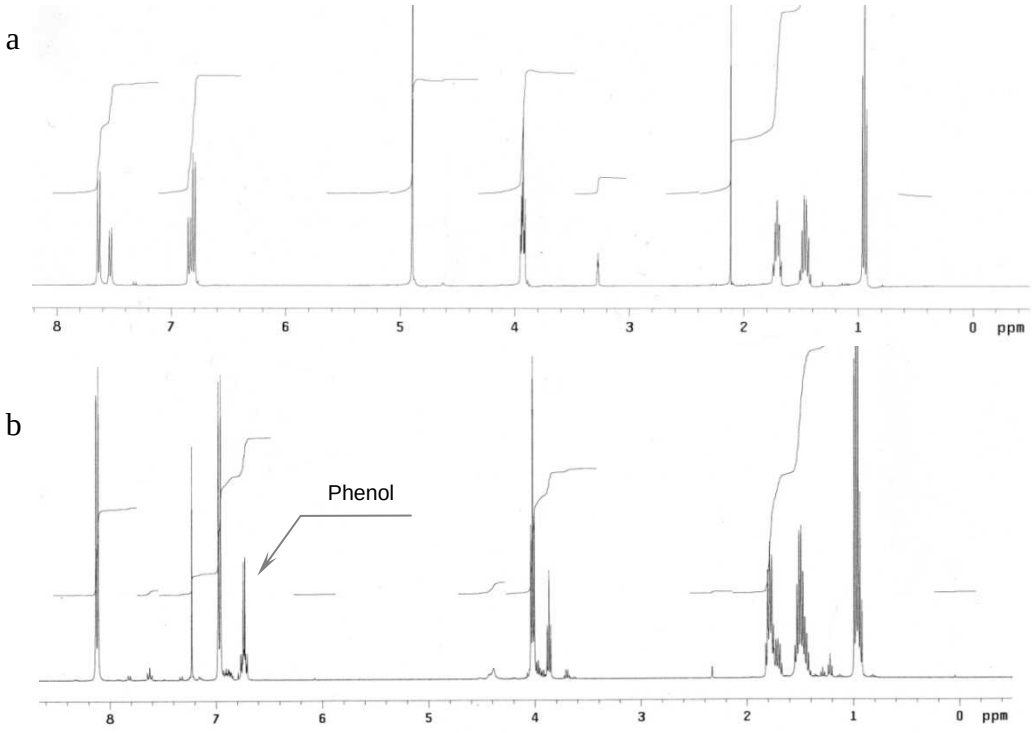
*Scheme 2.48 – Conversion of boronic acid **202***

Entry	Boronic Acid[a]	Base[b]	Temp	Time (hrs)	Product
i	**202**	$Ba(OH)_2$	rt	96	Recovery of **202** (100%)
ii	**202**	KOH	rt	96	Recovery of **202** (100%)
iii	**202**	$Ba(OH)_2$	60°C	120	Partial conversion to **203**[c]
iv	**202**	$Ba(OH)_2$	100°C	120	Partial conversion to **203**[c]
v	**202**	KOH	60°C	24	Partial conversion to **203**[c]

a) Mixture of free boronic acid and boronic anhydride identified by ^{1}H NMR; b) 2 eq. hydroxide base to 1 eq. boronic acid; c) Phenol identified by ^{1}H NMR

*Table 2.10 – Results of boronic acid **202** oxidation*

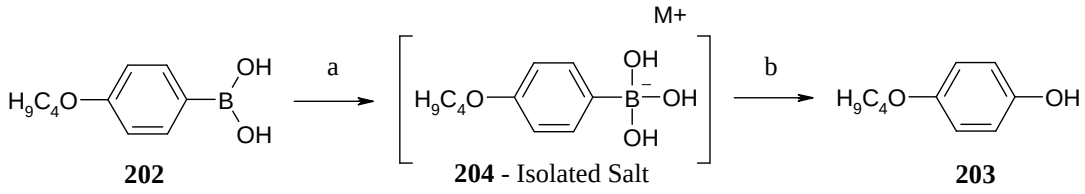
Initial assessment of the boronic acid by ^{1}H NMR revealed it to be a composition of both free boronic acid and boronic anhydride. Initial conversion attempts were conducted at ambient temperatures and failed to induce any conversion to the phenol (*entries i & ii*). At elevated temperatures, employing both barium and potassium hydroxide as the base, partial conversion of the boronic acid to the phenol was observed by ^{1}H NMR (*Figure 2.38*), however complete conversion was not observed even with prolonged reaction times (*entries iii-v*).



a) Boronic acid/boronic anhydride composition (D_3COD)
b) Observation of phenol by ^{1}H NMR ($CDCl_3$)

Figure 2.38 – Boronic acid conversion to phenol observed by ^{1}H NMR

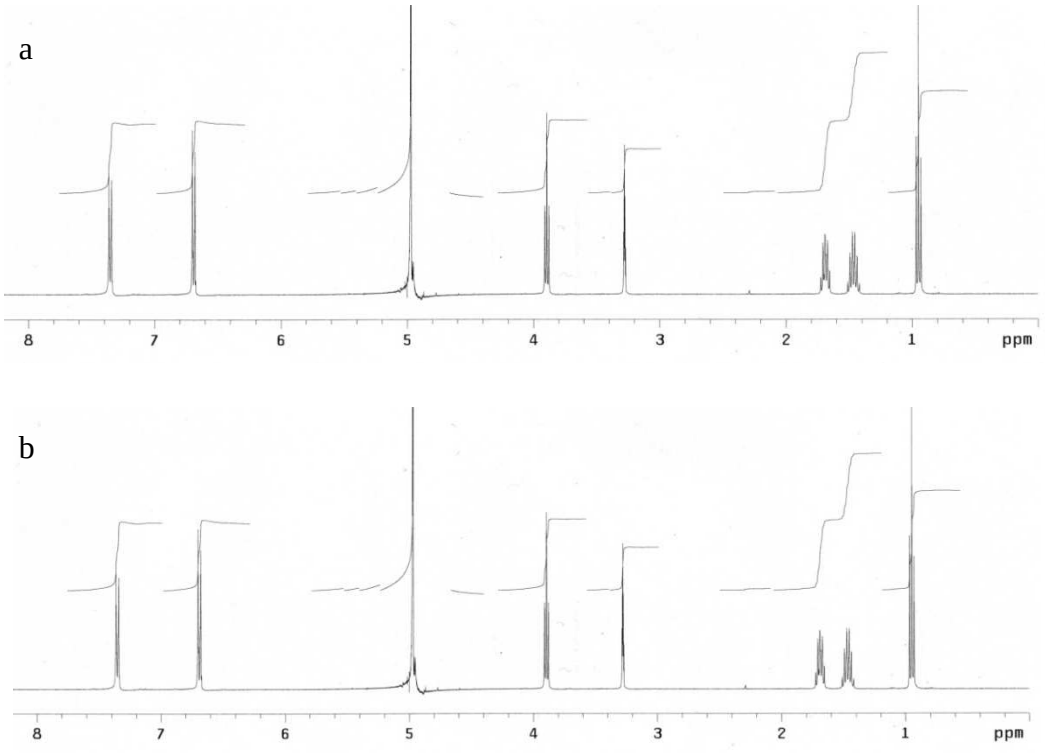
As our previous investigation had identified the formation of the boronate salt to be the initial step in the naphthalene boronic acid conversions, it was expected a prepared sample of benzene boronate salt would undergo conversion to the corresponding phenol (*Scheme 2.49*). The isolated boronate salt **204** was subjected to the conversion conditions, at elevated temperatures, with no conversion to the phenol or product degradation observed by ^{1}H NMR after 168 hours (*Figure 2.39*). Due to our previous observations, the stability of the benzene boronate salt towards conversion/oxidation was unexpected, however, reports in the literature have suggested that coordination of water or hydroxide ions to the Lewis acidic boron atom protects against atmospheric oxidation.[206]



202 **204** - Isolated Salt **203**

a) Toluene / MOH; b) $Ba(OH)_2$ / 60°C / 168 hrs / O_2

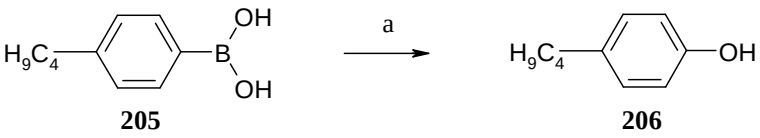
Scheme 2.49 – Attempted phenol conversion on trihydroxyborate salt



a) Isolated borate salt **204** (CD_3OD); b) Reaction time - 168 hours (CD_3OD)

*Figure 2.39 – Attempted conversion of borate salt **204***

Further assessment of the scope of the boronic acid conversion was attempted with the structurally similar, but less electron rich 4-butylbenzeneboronic acid **205** (*Scheme 2.50)*. Efforts to induce conversion to the phenol failed under each of the attempted conditions, with complete recovery of starting materials (*Table 2.11*).



205 **206**

a) Hydroxide base / Toluene:H_2O:EtOH (3:1:3)

Scheme 2.50 – Effects of substituent on boronic acid oxidation

Entry	Base	Temp	Time (hrs)	Product
i	$Ba(OH)_2$	rt	120	Recovery of **205** (100%)
ii	$Ba(OH)_2$	60°C	120	Recovery of **205** (100%)
iii	$Ba(OH)_2$	100°C	120	Recovery of **205** (100%)
iv	KOH	60°C	120	Recovery of **205** (100%)
v	KOH	100°C	120	Recovery of **205** (100%)

*Table 2.11 – Results of boronic acid **205** conversion*

2.3.6 – Summary

The feasibility study of the chiroptical enantiomeric switching system, based on the primary parent binaphthalene structure, revealed that photoresolution would not induce sufficient enantiomeric excess for successful application. The development of a secondary structural design was limited, due to the inability to obtain an optically active source. Further efforts are required to obtain the optically active secondary parent structure and examine the potential for enantiomeric switching.

Synthetic efforts to produce optically pure materials revealed an unidentified side-product in addition to the desired compound. The nature of the compound was identified to be that of an oxidative homocoupled dimer formed from a naphthol species. Investigation into the process discovered the conversion of boronic acids to the corresponding hydroxyarenes under catalyst free conditions. This has clear implications for reaction protocols employing boronic acids in alkaline reaction

media. Naphthalene boronic acids have been shown to be readily and rapidly converted to the dimerised compounds, via the naphthols, upon treatment with strong base in atmospheric oxygen.

Attempted conversion of benzene boronic acids was limited in its success, with partial conversion of electron rich benzene boronic acids to the phenolic compound under certain conditions. The less electron rich boronic acids resisted conversion even under harsh reaction conditions. From a mechanistic perspective, it was initially predicted that the primary step of the reaction would be the formation of the borate salt, although this was experimentally confirmed for the naphthalene boronic acids, the benzene boronate salt species resisted conversion even at high temperatures and for prolonged periods.

Chapter 3

Experimental

3.1 – General Experimental Methods

3.1.1 – Physical Methods

^{1}H NMR 300 & 400 MHz and ^{13}C NMR 101 MHz were recorded on a Varian Gemini 300 Spectrometer and a Varian 400 Lambda spectrometer respectively. All NMR spectra were carried out in solution using deuterated chloroform unless otherwise stated. Signals are quoted in ppm as δ downfield from tetramethylsilane (δ = 0.00) and coupling constants *J* are quoted in Hertz. Ultra-violet spectra were recorded on a Hitachi u-3000 recording spectrophotometer. Circular dichroism spectra were recorded on a Jasco J810 spectropolarimeter fitted with a 450W xenon arc lamp. Infra-red spectra were recorded on a Perkin-Elmer 1720X FT-IR spectrophotometer as thin films or Nujol mulls using NaCl plates or on a Perkin Elmer Spectrum BX ATR spectrometer. Optical rotations were recorded on a Bellingham and Stanley ADP440 polarimeter in the solvents stated, with concentrations quoted in grams per 100 mL. Low resolution EI, ES, CI and HRMS were obtained *via* the EPSRC National Mass Spectrometry Service Centre at Swansea University, Wales. TLC analysis was carried out on Merck aluminium backed silica gel 60 F_{254} coated plates and were visualised by one or a combination of the following methods: (a) viewing under UV light at 254 nm or 365 nm; (b) exposure to iodine vapour; (c) exposure to an aqueous potassium permanganate solution, containing 3 g of $KMnO_4$, 10 g K_2CO_3, 2.5 mL of aqueous 2M NaOH and 150 mL of H_2O; (d) exposure to a ferric chloride solution, containing 2 g of $FeCl_3$, 50 mL of methanol and 50 mL of H_2O; (e) exposure to a solution of ninhydrin, containing 0.75 g of ninhydrin, 50 mL of ethanol and 1.5 mL of glacial acetic acid; (f) exposure to a solution of 2,4-dinitrophenylhydrazine, containing 3 g 2,4-dinitrophenylhydrazine, 15 mL concentrated sulphuric acid, 50 mL ethanol and 20 mL H_2O. Column chromatography was performed at ambient temperature using Davisil® chromatographic silica media LC60Å 40-63µm, with solvent systems given as volume ratios. Melting points are uncorrected and were recorded using a Reichert Thermovar melting point apparatus with a Reichert Jung hot stage. Liquid crystal samples were observed on an Olympus BH-2 microscope.

3.1.2 – Reagents, Solvents and Reaction Conditions

Unless otherwise stated, all chemicals were obtained from commercial sources and used as received. *N*-bromosuccinimide was recrystallised from water at 100°C. Tetrahydrofuran, diethylether and dimethoxyethane were freshly distilled from sodium and benzophenone; dichloromethane, *N*,*N*-dimethylformamide, triethylamine and *n*-pentane were freshly distilled from calcium hydride and toluene was freshly distilled from sodium. Other solvents were SLR-grade and used without further purification. Water refers to deionised water and brine to a saturated aqueous solution of sodium chloride. The evaporation of solvents was carried out on a Buchi rotary evaporator at reduced pressure. Temperatures quoted in the reaction conditions refer to that of the cooling or heating bath, with all reactions conducted using flame dried glassware.

3.2 – Experimental Procedures

3.2.1 – Liquid Crystal Technique Procedures

Contact Experiment Procedure

A sample of dopant was centred on a glass cover slip and was heated to its melting point before recooling to ambient temperature. A second smaller glass cover slip was placed over the sample and a drop of nematic liquid crystal was added to the top slide edge. Capilliary action was allowed to produce a dopant-liquid crystal interface and solvation of the dopant was observed under a polarising microscope.

Droplet Method Procedure

A sample of dopant was solvated in nematic liquid crystal host E7 in a 1% or 0.5% weight/weight ratio. The mixture was heated above the liquid crystal host clearing point and mixed thoroughly on a rotamixer, with the process repeated three times. A small sample of the doped nematic was added to glycerol which was thoroughly mixed to produce an even droplet suspension. A sample of the suspension was added to a single glass cover slip (without covering) and observed under a polarising microscope at x10 or x20 magnitude. Individual droplet diameters were measured using a micrometer and the number of dark bands recorded. The droplet diameter was divided by half the number of dark bands to produce the chiral nematic pitch

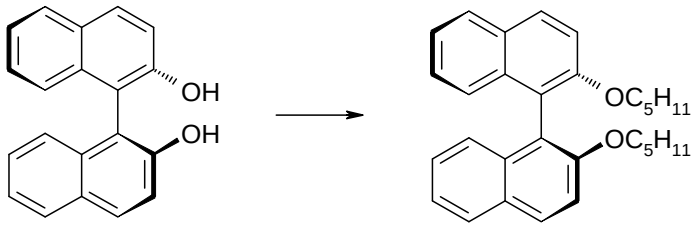
length which was used along with the concentration of the doped nematic to formulate the helical twisting power. A minimum of ten separate reading were collated in order to produce an accurate measurement.

Azobenzene/Stilbene Switching Procedure

A 1% solution of dopant in nematic liquid crystal host E7 was prepared and the helical twisting power of the system was recorded as a thin film on a glass cover slip. The doped nematic was irradiated with a 400W Ultra-Violet lamp, with the system regularly observed at 60 second intervals under a polarising microscope to determine the post-irradiation helical twisting power.

3.2.2 – Synthetic Experimental Procedures

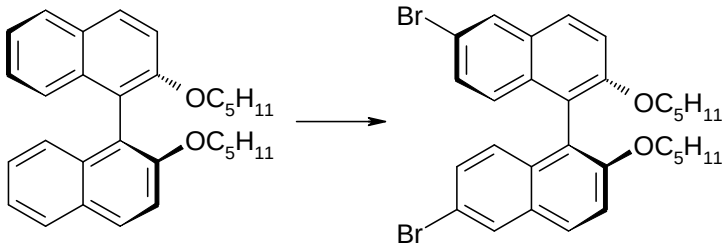
(S)-2,2'-Dipentoxy-1,1'-binaphthalene - 87:[127]



To a solution of optically pure (*S*)-1,1'-bi(2-naphthol) (5.171 g, 18.060 mmol) in acetone (50 mL) was added potassium carbonate (7.512 g, 57.691 mmol) and iodopentane (10.733 g, 54.193 mmol, 7.1 mL). The mixture was heated to reflux for 48 hours monitoring the reaction by TLC. The reaction mixture was filtered, washed with acetone (50 mL) and the solvent removed under reduced pressure. The crude product was dissolved in dichloromethane (100 mL) and washed with dilute hydrochloric acid (1M, 50 mL), water (50 mL) and brine (50 mL). The solution was dried (Na_2SO_4) and the solvent removed under reduced pressure. Purification by silica gel column chromatography (Hexane/DCM 2:1) afforded the *title compound* as a colourless oil (5.622 g, 73%), $[\alpha]_D^{25}$ -67.65 (*c* 0.34, chloroform). δ_H (400 MHz, $CDCl_3$) 7.95 (2H, d, *J* 8.99), 7.87 (2H, d, *J* 8.22), 7.44 (2H, d, *J* 8.99), 7.33 (2H, ddd, *J* 8.06, 5.73, 2.22), 7.22 (4H, m), 3.96 (4H, m), 1.44 (4H, m), 1.04 (4H, m), 0.93 (4H, m), 0.69 (6H, t, *J* 7.28); δ_C (101 MHz, $CDCl_3$) 154.48, 134.19, 129.20, 128.96, 127.71, 125.96, 125.46, 123.31, 120.65, 115.76, 69.66, 29.03, 27.79, 22.13, 13.87;

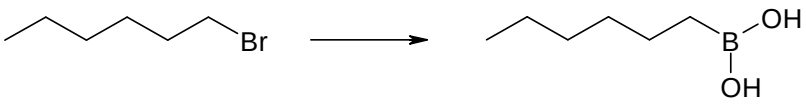
m/z (CI) 444.4 ($M+NH_4^+$, 100%), 427.4 (39); HRMS: Found 444.2892 $C_{30}H_{38}NO_2$ ($M+NH_4^+$) Requires 444.2897.

(S)-6,6'-Dibromo-2,2'-dipentoxy-1,1'-binaphthalene - 86:[125]



A solution of bromine (8.421 g, 52.691 mmol, 2.71 mL) in dichloromethane (25 mL) was added dropwise to a stirred solution of (*S*)-2,2'-dipentoxy-1,1'-binaphthalene (5.625 g, 13.187 mmol) in dichloromethane (80 mL) at -10°C with streaming N_2. The reaction was monitored to completion by TLC. Sodium metabisulphite solution (10%, 50 mL) was added and the layers separated. The organic layer was washed with water (50 mL), brine (50 mL), dried (Na_2SO_4) and the solvent removed under reduced pressure. Purification by silica gel column chromatography (Hexane/DCM 2:1) afforded the *title compound* as a colourless oil (7.07 g, 92%), $[\alpha]_D^{26}$ -64.1 (*c* 0.31, chloroform). δ_H (400 MHz, $CDCl_3$) 8.00 (2H, s), 7.83 (2H, d, *J* 9.06), 7.40 (2H, d, *J* 9.03), 7.26 (2H, d, *J* 9.06), 6.98 (2H, d, *J* 9.06), 3.92 (4H, m), 1.40 (4H, m), 1.02 (4H, m), 0.89 (4H, m), 0.67 (6H, t, *J* 7.27); δ_C (101 MHz, $CDCl_3$) 154.94, 132.78, 130.38, 129.95, 129.64, 128.58, 127.33, 120.20, 117.41, 116.55, 69.71, 29.17, 28.07, 22.36, 14.12; *m/z* (CI) 584.2 ($M+H^+$, 74%), 444.1 (100); HRMS: Found 582.0763 $C_{30}H_{33}Br_2O_2$ ($M+H^+$) Requires 582.0764.

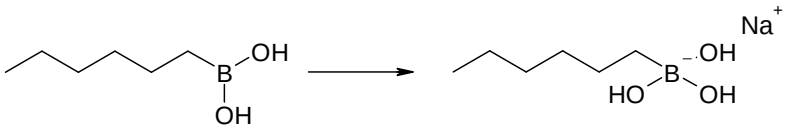
1-Hexylboronic acid - 91:[122]



1-Bromohexane (5.029 g, 30.464 mmol, 4.3mL) in anhydrous diethylether (20 mL) was added to magnesium turnings (0.815 g, 33.510 mmol) in anhydrous diethyl ether (30 mL) at a sufficient rate as to maintain reflux. After addition the reaction mixture was heated to reflux for 2 hours. The solution was cooled and added dropwise to a solution of trimethylborate (6.331 g, 60.928 mmol, 6.9 mL) in anhydrous diethyl

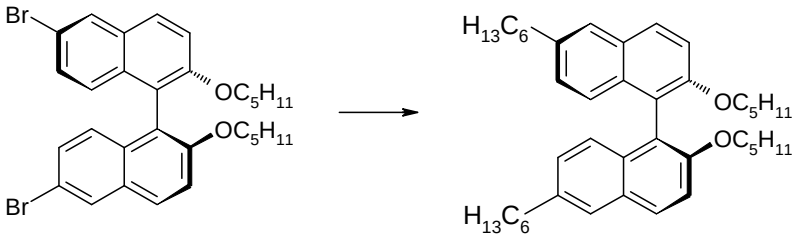
ether (20 mL) at -78°C. After addition the mixture was allowed to warm to ambient temperature over 12 hours before being quenched with dilute hydrochloric acid (1M, 50 mL) and stirred for 90 minutes. The crude product was extracted with dichloromethane (2x75 mL) and the organic layer washed with water (100 mL), dried (Na_2SO_4) and the solvent removed under reduced pressure to afford the title compound as a white solid (2.686 g, 68%), m.p. 89-95°C (lit. 85-90°C). δ_H (400 MHz, $CDCl_3$) 1.57-1.49 (2H, m), 1.32-1.16 (6H, m), 1.04 (2H, t, *J* 6.94), 0.86 (3H, t, *J* 6.98).

Sodium 1-hexyl(trihydroxy)borate - 92:[122]



1-Hexylboronic acid (2.513 g, 19.335 mmol) was dissolved in toluene (40 mL) with heating. The hot solution was filtered and saturated sodium hydroxide solution added dropwise until precipitation ceased. The precipitate was vacuum filtered through a sinter and dried in a desiccator over phosphorus pentoxide to afford the title compound as a white solid (3.028 g, 98%), m.p. >200°C. δ_H (400 MHz, D_3COD) 4.83 (3H, brs), 1.13-0.96 (10H, m), 0.69 (3H, t, *J* 6.89).

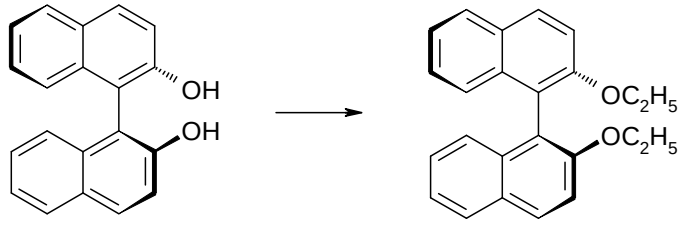
(S)-6,6'-Bis(1-hexyl)-2,2'-dipentoxy-1,1'-binaphthalene - 85:[122]



(*S*)-6,6'-Dibromo-2,2'-dipentoxy-1,1'-binaphthalene (1.01 g, 1.740 mmol), 1-hexyl(trihydroxy)boronate sodium salt (1.183 g, 6.962 mmol) and 2mol% $PdCl_2$(dppf) (0.0284 g, 0.0348 mmol) were dissolved in toluene (30 mL) and the reaction mixture heated to reflux for 72 hours. The crude material was diluted with dichloromethane, filtered through celite and the solvent removed under reduced pressure. Purification by silica gel column chromatography (Hexane/DCM 4:1) afforded the *title compound* as a colourless oil (0.737 g, 71%), $[\alpha]_D^{25}$ 39.48 (*c* 0.25,

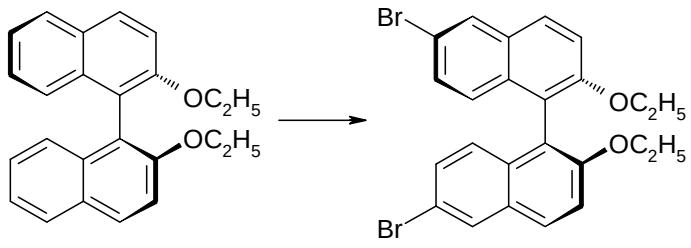
chloroform). δ_H (400 MHz, $CDCl_3$) 7.89 (2H, d, *J* 8.97), 7.67 (2H, s), 7.42 (2H, d, *J* 8.97), 7.17 (2H, d, *J* 8.68), 7.11 (2H, d, *J* 8.68), 3.96 (4H, m), 2.76 (4H, t, *J* 7.96), 1.72 (4H, m), 1.42 (16H, m), 1.06 (4H, m), 0.95 (10H, m), 0.71 (6H, t, *J* 7.21); δ_C (101 MHz, $CDCl_3$) 153.93, 137.71, 132.65, 129.43, 128.30, 127.58, 126.03, 125.46, 120.94, 116.01, 69.86, 35.86, 31.78, 31.32, 29.09, 27.80, 22.15, 14.10, 13.87; *m/z* (CI) 595.6 ($M+H^+$, 45%), 594.5 (100), 55.2 (53); HRMS: Found 594.4429 $C_{42}H_{58}O_2$ (M^+) Requires 594.4431.

(S)-2,2'-Diethoxy-1,1'-binaphthalene - 94:[127]



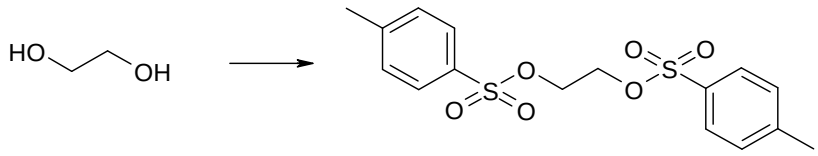
To a solution of optically pure (*S*)-1,1'-bi(2-naphthol) (5.322 g, 15.542 mmol) in acetone (100 mL) was added potassium carbonate (7.261 g, 55.764 mmol) and iodoethane (8.526 g, 54.664 mmol, 4.4 mL). The mixture was heated to reflux for 48 hours monitoring the reaction by TLC. The reaction mixture was filtered, washed with acetone (50 mL) and the solvent removed under reduced pressure. The crude product was dissolved in dichloromethane (100 mL) and washed with dilute hydrochloric acid (1M, 50 mL), water (50 mL) and brine (50 ml). The solution was dried (Na_2SO_4) and the solvent removed under reduced pressure. Recrystallisation from ethanol afforded the title compound as white crystals (5.551 g, 87%), m.p. 138-139°C (lit. 139°C). δ_H (400 MHz, $CDCl_3$) 7.92 (2H, d, *J* 8.97), 7.84 (2H, d, *J* 8.13), 7.40 (2H, d, *J* 8.97), 7.29 (2H, ddd, *J* 8.02, 6.61, 1.32), 7.18 (2H, ddd, *J* 8.02, 6.61, 1.32), 4.02 (4H, m), 1.03 (6H, t, *J* 6.98).

(S)-6,6'-Dibromo-2,2'-diethoxy-1,1'-binaphthalene - 103:[125]



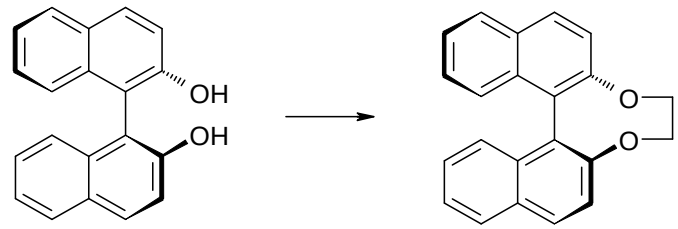
A solution of bromine (2.729 g, 17.075 mmol, 0.87 mL) in dichloromethane (20 mL) was added dropwise to a stirred solution of (*S*)-2,2'-diethoxy-1,1'-binaphthalene (2.651 g, 7.742 mmol) in dichloromethane (80 mL) at -10°C with streaming N_2. The reaction was monitored to completion by TLC. Sodium metabisulphite solution (10%, 50 mL) was added and the mixture stirred for a further 30 minutes. The layers were separated and the organic layer was washed with water (50 mL), brine (50 mL), dried (Na_2SO_4) and the solvent removed under reduced pressure. Recrystallisation from ethanol afforded the title compound as white crystals (3.422 g, 88%), m.p. 160-161°C (lit. 161-162°C) . δ_H (400 MHz, $CDCl_3$) 7.92 (2H, s), 7.75 (2H, d, *J* 9.05), 7.33 (2H, d, *J* 9.05), 7.17 (2H, d, *J* 9.05), 6.87 (2H, d, *J* 9.05), 3.95 (4H, m), 0.97 (6H, t, *J* 6.99).

1,2-Bis(toluenesulphonyloxy)ethane:[207]



1,2-Ethylene glycol (2.507 g, 40.404 mmol) was dissolved in pyridine (200 mL) and the solution cooled to 0°C. Tosyl chloride (30.879 g, 0.162 mol) was added in six equal portions over a 1 hour period whist stirring. The reaction mixture was kept at 0°C for 12 hours before adding to mixture of 50:50 ice/water (1 L) and concentrated hydrochloric acid (37%, 50 mL). The precipitate was filtered and recrystallised from ethanol to afford the title compound as white crystals (14.391 g, 97%), m.p. 124-125°C (lit. 126°C). δ_H (400 MHz, $CDCl_3$) 7.70 (4H, d, *J* 7.87), 7.32 (4H, d, *J* 7.87), 4.16 (4H, s) 2.44 (6H, s).

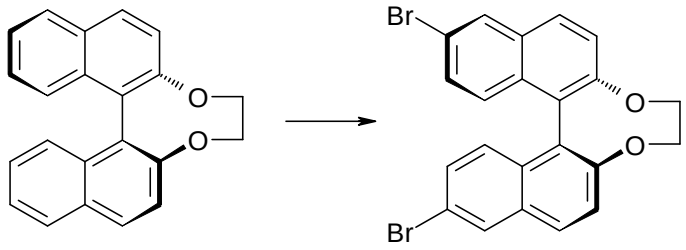
(S)-2,2'-(Ethylenedioxy)-1,1'-binaphthalene - 104:[127]



To a solution of optically pure (*S*)-1,1'-bi(2-naphthol) (2.811 g, 9.817 mmol) in acetone (50 mL) was added potassium carbonate (7.728 g, 59.350 mmol) and 1,2-

bis(toluenesulphonyloxy)ethane (4.073 g, 10.995 mmol). The mixture was heated to reflux for 48 hours monitoring the reaction by TLC. The reaction mixture was filtered, washed with acetone (50 mL) and the solvent removed under reduced pressure. The crude product was dissolved in dichloromethane (100 mL) and washed with dilute hydrochloric acid (1M, 50 mL), water (50 mL) and brine (50 ml). The solution was dried (Na_2SO_4) and the solvent removed under reduced pressure. Purification by silica gel column chromatography (Hexane/DCM 1:1) afforded the title compound as white crystals (1.271 g, 42%), m.p. 195-197°C (lit. 197.5-198.5°C). δ_H (400 MHz, $CDCl_3$) 7.98 (2H, d, *J* 8.79), 7.89 (2H, d, *J* 8.17), 7.44 (2H, d, *J* 8.79), 7.40 (2H, dd, *J* 8.17), 7.23 (4H, m), 4.29 (4H, m).

(S)-6,6'-Dibromo-2,2'-(ethylenedioxy)-1,1'-binaphthalene - 105:



i) In DCM at -10°C

A solution of bromine (0.499 g, 3.119 mmol, 0.16 mL) in dichloromethane (5 mL) was added dropwise to a stirred solution of (*S*)-2,2'-(ethylenedioxy)-1,1'-binaphthalene (0.253 g, 0.780 mmol) in dichloromethane (40 mL) at -10°C with streaming N_2. The reaction was monitored by TLC with no brominated products observed and recovery of starting material.

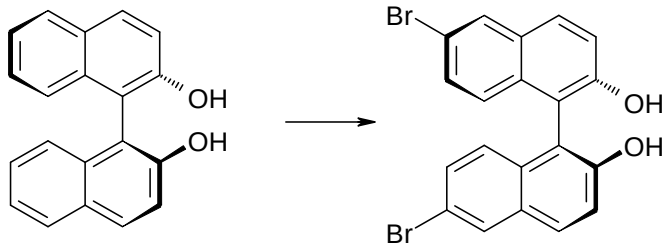
ii) In DCM at ambient temperature

A solution of bromine (0.617 g, 3.859 mmol, 0.198 mL) in dichloromethane (5 mL) was added dropwise to a stirred solution of (*S*)-2,2'-(ethylenedioxy)-1,1'-binaphthalene (0.313 g, 0.965 mmol) in dichloromethane (40 mL) at ambient temperature with streaming N_2. The reaction was monitored by TLC with no brominated products observed and recovery of starting material.

iii) In acetic acid at ambient temperature

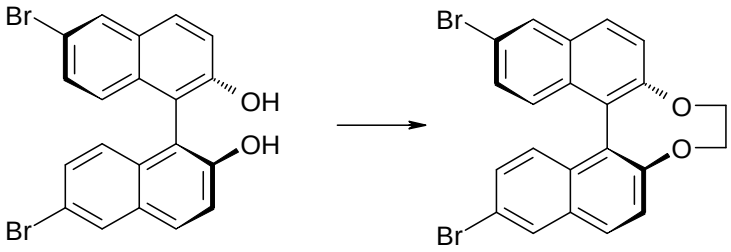
A solution of bromine (0.506 g, 3.169 mmol, 0.16 mL) in acetic acid (5 mL) was added dropwise to a stirred solution of (*S*)-2,2'-(ethylenedioxy)-1,1'-binaphthalene (0.257 g, 0.792 mmol) in acetic acid (40 mL) at ambient temperature with streaming N_2. The reaction was monitored by TLC with no brominated products observed and recovery of starting material.

(S)-6,6'-Dibromo-2,2'-dihydroxy-1,1'-binaphthalene - 106:[144]



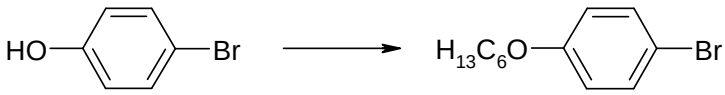
(*S*)-1,1'-bi(2-naphthol) (2.136 g, 7.459 mmol) was dissolved in dichloromethane (100 mL) and cooled to -78°C. Bromine (2.384 g, 14.918 mmol, 0.76 mL) was dissolved in dichloromethane (20 mL) and added dropwise to the solution over 30 minutes with vigorous stirring. The solution was allowed to warm to ambient temperature over 2.5 hours and stirred for a further 12 hours. Aqueous sodium metabisulphite solution (10%, 50 mL) was added and the mixture stirred for a further 30 minutes. The layers were separated and the organic layer washed with water (100 mL), brine (100 mL) and dried (Na_2SO_4). The solvent was removed under reduced pressure to give the title compound as a white solid (3.147 g, 95%), m.p. 197-199°C (lit. 197-198°C). δ_H (400 MHz, $CDCl_3$) 8.05 (2H, s), 7.89 (2H, d, *J* 9.01), 7.39 (2H, d, *J* 9.01), 7.36 (2H, d, *J* 9.01), 6.96 (2H, d, *J* 9.01), 5.05 (2H, s).

(S)-6,6'-Dibromo-2,2'-(ethylenedioxy)-1,1'-binaphthalene - 105:[127]



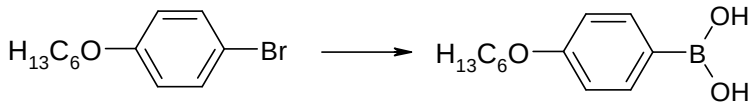
To a solution of (*S*)-6,6'-dibromo-2,2'-dihydroxy-1,1'-binaphthalene (1.055 g, 2.375 mmol) in acetone (50 mL) was added potassium carbonate (0.988 g, 7.588 mmol) and 1,2-bis(toluenesulphonyloxy)ethane (1.323 g, 3.571 mmol). The mixture was heated to reflux for 48 hours monitoring the reaction by TLC. The reaction mixture was filtered, washed with acetone (100 mL) and the solvent removed under reduced pressure. The crude product was dissolved in dichloromethane (100 mL) and washed with dilute hydrochloric acid (1M, 50 mL), water (50 mL) and brine (50 ml). The solution was dried (Na_2SO_4) and the solvent removed under reduced pressure. Purification by silica gel column chromatography (Hexane/DCM 4:1) afforded the *title compound* as a white solid (1.541 g, 60%), m.p. 167-168°C, $[\alpha]_D^{26}$ 320.83 (*c* 0.24, chloroform). δ_H (400 MHz, $CDCl_3$) 7.93 (2H, s), 7.75 (2H, d, *J* 8.88), 7.32 (2H, d, *J* 8.88), 7.18 (2H, d, *J* 9.07), 6.95 (2H, d, *J* 9.07), 4.14 (4H, m); δ_C (101 MHz, $CDCl_3$) 157.02, 132.30, 131.55, 130.31, 130.25, 129.96, 128.78, 124.17, 123.93, 119.15, 73.13; *m/z* (CI) 488.1 ($M+NH_4^+$, 18%), 330.3 (100); HRMS: Found 467.9361 $C_{22}H_{15}Br_2O_2$ ($M+H^+$) Requires 467.9355.

1-Bromo-4-hexyloxybenzene - 110:[208]



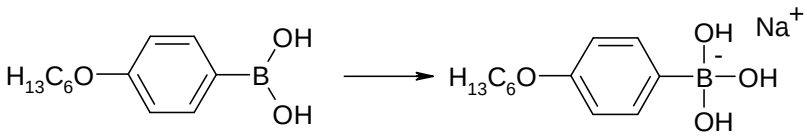
To a solution of 4-bromophenol (15.103 g, 87.304 mmol) in acetone (300 mL) was added potassium carbonate (24.187 g, 0.175 mol) and 1-bromohexane (28.889 g, 0.175 mol, 24.6 mL). The mixture was heated to reflux for 48 hours monitoring the reaction by TLC. The reaction mixture was filtered, washed with acetone and the solvent removed under reduced pressure. The crude product was dissolved in dichloromethane (100 mL) and the organic layer washed with water (50 mL), brine (50 mL), dried (Na_2SO) and the solvent removed under reduced pressure. Purification by distillation (114-116°C, 1 mmHg) afforded the title compound as a colourless oil (22.23 g, 99%). δ_H (400 MHz, $CDCl_3$) 7.34 (2H, d, *J* 8.79), 6.76 (2H, d, *J* 8.79), 3.90 (2H, t, *J* 6.58), 1.75 (2H, m), 1.44 (2H, m), 1.32 (4H, m), 0.90 (3H, t, *J* 6.91).

4-Hexyloxybenzeneboronic acid - 107:[208]



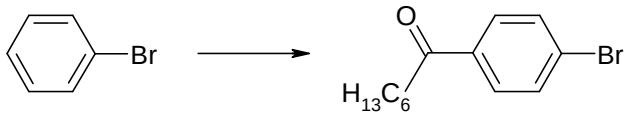
1-Bromo-4-hexyloxybenzene (9.952 g, 38.701 mmol,) in anhydrous diethylether (40 mL) was added to magnesium turnings (1.035 g, 42.571 mmol) in anhydrous diethylether (30 mL) at a sufficient rate as to maintain reflux. After addition the reaction mixture was heated to reflux for 2 hours. The solution was cooled and added dropwise to a solution of trimethylborate (8.043 g, 77.402 mmol, 8.8 mL) in anhydrous diethylether (20 mL) at -78°C. After addition the mixture was allowed to warm to ambient temperature over 12 hours before being quenched with dilute hydrochloric acid (1M, 100 mL) and stirred for 90 minutes. The crude product was extracted with dichloromethane (2x75 mL) and the organic layer washed with water (100 mL) and dried (Na_2SO_4). The solvent was removed under reduced pressure to afford the title compound as a white solid (6.806 g, 79%), m.p. 80-85, 89-91°C. δ_H (400 MHz, $CDCl_3$) 7.72 (2H, d, *J* 8.48), 6.93 (2H, d, *J* 8.48), 3.98 (2H, t, *J* 6.57), 1.78 (2H, m), 1.45 (2H, m), 1.32 (4H, m), 0.88 (3H, t, *J* 7.00).

4-Hexyloxyphenyl(trihydroxy)boronate sodium salt - 111:[122]



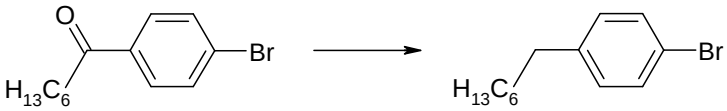
4-Hexyloxybenzeneboronic acid (5.013 g, 22.576 mmol) was dissolved in toluene (40 mL) with heating. The hot solution was filtered and saturated sodium hydroxide solution added dropwise until precipitation ceased. The precipitate was vacuum filtered through a sinter and dried in a desiccator over phosphorus pentoxide to afford the title compound as a white solid (5.524 g, 93%), m.p. >200°C. δ_H (400 MHz, D_3COD) 7.38 (2H, d, *J* 7.90), 6.72 (2H, d, *J* 7.90), 3.92 (2H, t, *J* 6.48), 1.73 (2H, m), 1.46 (2H, m), 1.35 (4H, m), 0.92 (3H, t, *J* 6.60).

1-Bromo-4-heptanoylbenzene - 113:[145]



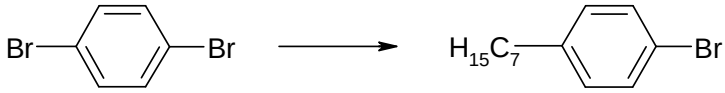
Heptanoyl chloride (25.153 g, 0.169 mol, 26.2 mL) was added dropwise to a stirred mixture of bromobenzene (75 mL) and aluminium chloride (24.788 g, 0.186 mol) at 0°C. The mixture was stirred at 0 °C for 1 hour before heating to 80°C for 2 hours, cooling and adding to hydrochloric acid (6M, 100 mL). The product was extracted into dichloromethane (2x30 mL) and the combined organic layers washed with water (2x30 mL), dried (Na_2SO_4) and the solvent removed under reduced pressure. Purification by distillation (b.p. 180-183°C, 20 mmHg) afforded the title compound as white plates (39.804 g, 87%), m.p. 69°C (lit. 69-72°C). δ_H (400 MHz, $CDCl_3$) 7.89 (2H, d, *J* 8.45), 7.60 (2H, d, *J* 8.45), 2.87 (2H, t, *J* 7.79), 1.75 (2H, m), 1.32 (6H, m), 0.93 (3H, t, *J* 6.97).

1-Bromo-4-heptylbenzene - 114:[145]



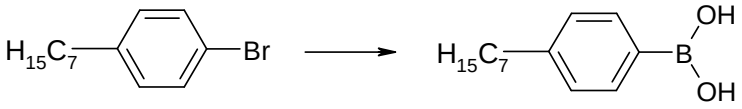
A mixture of 1-bromo-4-heptanoylbenzene (10.122 g, 0.0376 mmol), hydrazine monohydrate (5.648 g, 0.113 mol, 5.5 mL) and potassium hydroxide (6.751g, 0.120 mol) in diethylene glycol (50 mL) was heated to 130°C for 2 hours. The excess hydrazine was removed by distillation and the temperature raised to 200°C for 2 hours. The mixture was cooled and added to hydrochloric acid (6M, 100 mL). The product was extracted into diethyl ether (2x30 mL) and the combined organic layers washed with water (2x30 mL), dried (Na_2SO_4) and the solvent removed under reduced pressure. Purification by distillation (b.p. 146-149°C, 20 mmHg) afforded the title compound as a colourless oil (7.048 g, 73%). δ_H (400 MHz, $CDCl_3$) 7.39 (2H, d, *J* 8.31), 7.02 (2H, d, *J* 8.31), 2.49 (2H, t, *J* 7.76), 1.55 (2H, m), 1.27 (8H, m), 0.87 (3H, t, *J* 6.96).

1-Bromo-4-heptylbenzene - 114:[146]



1-Bromoheptane (27.225 g, 0.152 mol, 23.9 mL) in anhydrous diethylether (40 mL) was added to magnesium turnings (4.072 g, 0.167 mol) in anhydrous diethylether (60 mL) at a sufficient rate as to maintain reflux. After addition the reaction mixture was heated to reflux for 2 hours. The solution was then added dropwise to a solution of 1,4-dibromobenzene (35.859 g, 0.152 mol) and $PdCl_2$(dppf) (1.241 g, 1.520 mmol) in anhydrous diethylether (80 mL) at ambient temperature. The reaction mixture was heated to reflux for 24 hours before adding to water (100 mL) and filtering. The filtrate was extracted with diethylether (100 mL) and washed with water (100 mL), dried (Na_2SO_4) and the solvent removed under reduced pressure. Purification by distillation (b.p. 108-110°C, 0.8 mmHg) afforded the title compound as a colourless oil (22.698 g, 59%). δ_H (400 MHz, $CDCl_3$) 7.35 (2H, d, *J* 8.25), 7.01 (2H, d, *J* 8.25), 2.52 (2H, t, *J* 7.74), 1.56 (2H, m), 1.27 (8H, m), 0.87 (3H, t, *J* 6.94).

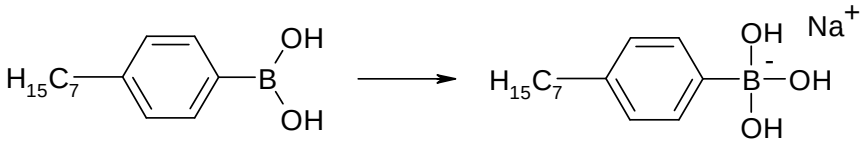
4-Heptylbenzeneboronic acid - 108:[208]



1-Bromo-4-heptylbenzene (9.995 g, 39.188 mmol,) in anhydrous diethyl ether (40 mL) was added to magnesium turnings (1.048 g, 43.107 mmol) in anhydrous diethyl ether (30 mL) at a sufficient rate as to maintain reflux. After addition the reaction mixture was heated to reflux for 2 hours. The solution was cooled and added dropwise to a solution of trimethylborate (8.144 g, 78.376 mmol, 8.9 mL) in anhydrous diethyl ether (20 mL) at -78°C. After addition the mixture was allowed to warm to ambient temperature over 12 hours before being quenched with dilute hydrochloric acid (1M, 100 mL) and stirred for 90 minutes. The crude product was extracted with dichloromethane (2x75 mL) and the organic layer washed with water (100 mL) and dried (Na_2SO_4). The solvent was removed under reduced pressure to afford the title compound as a white solid (6.229 g, 72%), m.p. 50-55, 67-70°C. δ_H

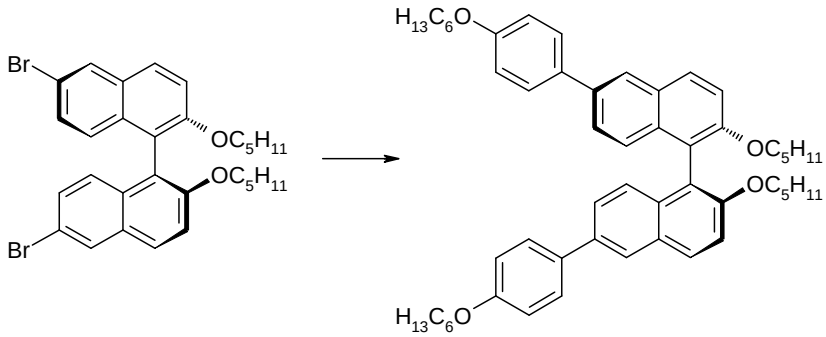
(400 MHz, $CDCl_3$) 8.13 (2H, d, *J* 7.64), 7.30 (2H, d, *J* 7.64), 2.67 (2H, t, *J* 7.71), 1.65 (2H, m), 1.35-1.24 (8H, m), 0.87 (3H, t, *J* 6.70).

4-Heptylphenyl(trihydroxy)boronate sodium salt - 116:[122]



4-Heptylbenzeneboronic acid (4.017 g, 18.252 mmol) was dissolved in toluene (50 mL) with heating. The hot solution was filtered and saturated sodium hydroxide solution added dropwise until precipitation ceased. The precipitate was vacuum filtered through a sinter and dried in a desiccator over phosphorus pentoxide to give the title compound as a white solid (4.534 g, 95%), m.p. >200°C. δ_H (400 MHz, D_3COD) 7.37 (2H, d, *J* 8.24), 6.70 (2H, d, *J* 8.24), 3.90 (2H, t, *J* 6.49), 3.29 (2H, m), 1.71 (2H, m), 1.45 (2H, m), 1.34 (4H, m), 0.90 (3H, t, *J* 6.84).

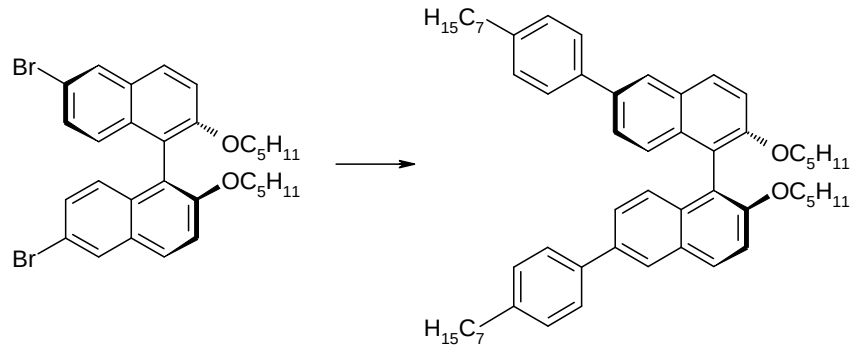
(S)-6,6'-Bis(4-hexyloxyphenyl)-2,2'-dipentoxy-1,1'-binaphthalene - 98:[122]



(*S*)-6,6'-Dibromo-2,2'-dipentoxy-1,1'-binaphthalene (0.206 g, 0.353 mmol), 4-hexyloxyphenyl(trihydroxy)boronate sodium salt (0.370 g, 1.410 mmol) and 2mol% $PdCl_2$(dppf) (5.766 mg, 7.060 µmol) were dissolved in toluene (10 mL) and the reaction mixture heated to reflux for 72 hours. The crude material was diluted with dichloromethane, filtered through celite and the solvent removed under reduced pressure. Purification by silica gel column chromatography (Hexane/DCM 4:1) afforded the *title compound* as a colourless oil (0.199 g, 71%), $[\alpha]_D^{25}$ 184.50 (*c* 0.08, chloroform). δ_H (400 MHz, $CDCl_3$) 8.02 (2H, s), 7.97 (2H, d, *J* 9.01), 7.61 (4H, d, *J* 8.58), 7.45 (4H, m), 7.26 (2H, d, *J* 8.58), 6.99 (4H, d, *J* 8.58), 3.99 (4H, t, *J* 6.51), 3.94 (4H, m), 1.81 (4H, m), 1.45 (8H, m), 1.35 (8H, m), 1.29 (4H, m), 1.02 (4H, m),

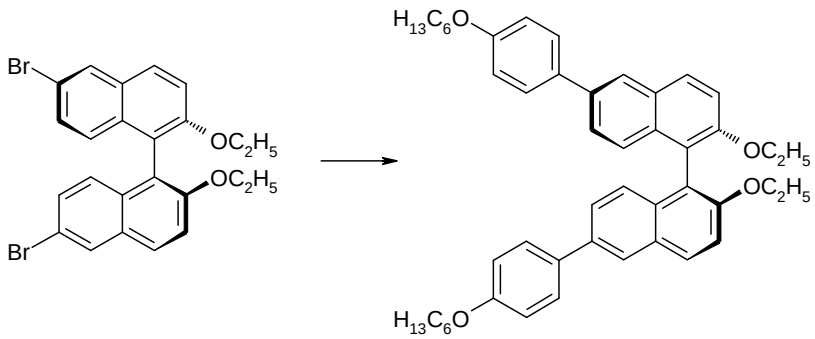
0.89 (6H, t, *J* 6.45), 0.653 (6H, t, *J* 7.08); δ_C (101 MHz, $CDCl_3$) 158.73, 154.72, 135.98, 133.86, 133.33, 129.78, 129.41, 128.33, 126.23, 125.87, 125.14, 120.80, 116.42, 114.99, 70.00, 68.29, 31.83, 29.521, 29.33, 28.10, 25.99, 22.81, 22.42, 14.35, 14.15; *m/z* (CI) 778.6 ($M+H^+$, 85%), 469.3 (21), 77.2 (24); HRMS: Found 778.4965 $C_{54}H_{67}O_4$ ($M+H^+$) Requires 778.4956.

(S)-6,6'-Bis(4-heptylphenyl)-2,2'-dipentoxy-1,1'-binaphthalene - 99:[122]



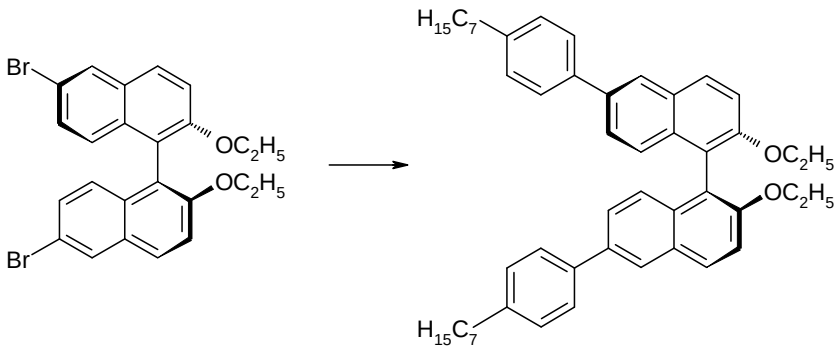
(*S*)-6,6'-Dibromo-2,2'-dipentoxy-1,1'-binaphthalene (0.426 g, 0.729 mmol), 4-heptylphenyl(trihydroxy)boronate sodium salt (0.619 g, 2.916 mmol) and 2mol% $PdCl_2$(dppf) (0.0119 g, 0.0146 mmol) were dissolved in toluene (10 mL) and the reaction mixture heated to reflux for 72 hours. The crude material was diluted with dichloromethane, filtered through celite and the solvent removed under reduced pressure. Purification by silica gel column chromatography (Hexane/DCM 9:1) afforded the *title compound* as a colourless oil (0.376 g, 67%), $[\alpha]_D^{24}$ 170.0 (*c* 0.001, chloroform). δ_H (400 MHz, $CDCl_3$) 8.04 (2H, d, *J* 1.79), 7.97 (2H, d, *J* 8.99), 7.59 (4H, d, *J* 8.09), 7.48 (2H, d, *J* 8.80, 1.79), 7.43 (2H, d, *J* 8.99), 7.25 (4H, d, *J* 8.09), 7.25 (2H, d, *J* 8.80), 3.96 (4H, m), 2.64 (4H, t, *J* 7.75), 1.64 (4H, m), 1.46-1.25 (20H, m), 1.01 (4H, m), 0.95-0.86 (10H, m), 0.64 (6H, t, *J* 7.18); δ_C (101 MHz, $CDCl_3$) 154.55, 141.74, 138.58, 136.00, 133.27, 129.46, 129.28, 128.79, 126.98, 125.96, 125.76, 125.36, 120.51, 116.14, 69.75, 35.62, 31.82, 31.53, 29.35, 29.20, 29.06, 27.84, 22.67, 22.17, 14.12, 13.92; *m/z* (CI) 792.6 ($M+NH_4^+$, 39%), 618.4 (100), 279.2 (36); HRMS: Found 792.5719 $C_{56}H_{74}NO_2$ ($M+NH_4^+$) Requires 792.5714.

(S)-6,6'-Bis(4-hexyloxyphenyl)-2,2'-diethoxy-1,1'-binaphthalene - 100:[122]



(*S*)-6,6'-Dibromo-2,2'-diethoxy-1,1'-binaphthalene (0.573 g, 1.146 mmol), 4-hexyloxyphenyl(trihydroxy)boronate sodium salt (1.201 g, 4.582 mmol) and 2mol% $PdCl_2$(dppf) (0.0187 g, 0.0229 mmol) were dissolved in toluene (20 mL) and the reaction mixture heated to reflux for 72 hours. The crude material was diluted with dichloromethane, filtered through celite and the solvent removed under reduced pressure. Purification by silica gel column chromatography (Hexane/DCM 4:1) afforded the *title compound* as colourless crystals (0.581 g, 76%), m.p. 98-100°C, $[\alpha]_D^{26}$ 131.63 (*c* 0.21, chloroform). δ_H (400 MHz, $CDCl_3$) 8.00 (2H, s), 7.97 (2H, d, *J* 9.21), 7.59 (4H, m), 7.44 (4H, m), 7.21 (2H, d, *J* 9.21), 6.97 (4H, m) 4.01 (8H, m), 1.78 (4H, m), 1.45 (4H, m), 1.30 (8H, m), 1.08 (6H, t, *J* 6.99), 0.90 (6H, t, *J* 6.97); δ_C (101 MHz, $CDCl_3$) 158.77, 154.47, 136.01, 133.78, 133.23, 129.72, 129.46, 128.38, 126.24, 125.96, 125.11, 120.71, 116.41, 115.06, 68.38, 65.41, 31.84, 29.52, 22.86, 15.23, 14.23; *m/z* (EI) 694.5 (M^+, 79%), 438.9 (16), 69.2 (35); HRMS: Found 694.9416 $C_{48}H_{55}O_4$ ($M+H^+$) Requires 694.9442.

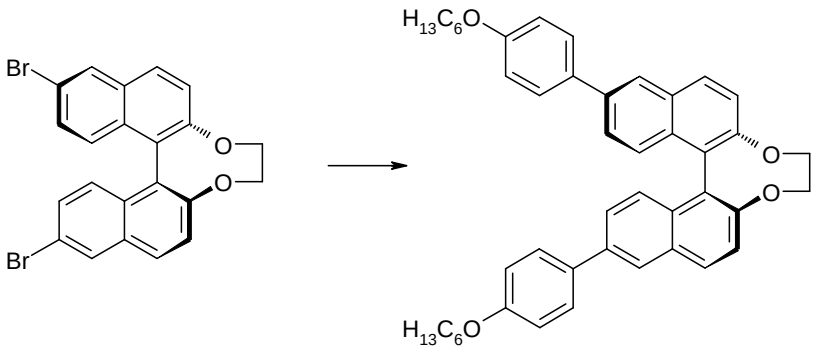
(S)-6,6'-Bis(4-heptylphenyl)-2,2'-diethoxy-1,1'-binaphthalene - 101:[122]



Optically pure (*S*)-6,6'-dibromo-2,2'-diethoxy-1,1'-binaphthalene (0.473 g, 0.946 mmol), 4-heptylphenyl(trihydroxy)boronate sodium salt (1.476 g, 5.674 mmol) and 2

mol% $PdCl_2$(dppf) (0.0155 g, 0.0189 mmol) were dissolved in toluene (30 mL) and the reaction mixture heated to reflux for 72 hours. The crude material was diluted with dichloromethane, filtered through celite and the solvent removed under reduced pressure. Purification by silica gel column chromatography (Hexane/DCM 1:1) afforded the *title compound* as a colourless crystals (0.492, 76%), m.p. 104-106°C, $[\alpha]_D^{26}$ -97.47 (*c* 0.21, chloroform). δ_H (400 MHz, $CDCl_3$) 8.09 (2H, s), 8.01 (2H, d, *J* 8.86), 7.63 (4H, d, *J* 8.27), 7.52 (2H, d, *J* 8.86), 7.47 (2H, d, *J* 9.04), 7.29 (4H, d, *J* 8.27), 7.27 (2H, d, *J* 8.75), 3.99 (4H, q, *J* 6.99), 2.56 (4H, t, *J* 7.74), 1.57 (4H, m), 1.24 (16H, m), 1.01 (6H, t, *J* 6.98), 0.80 (6H, t, *J* 6.81); δ_C (101 MHz, $CDCl_3$) 154.60, 142.06, 138.77, 136.31, 133.50, 129.75, 129.64, 129.08, 127.25, 126.25, 126.70, 125.65, 120.71, 116.40, 65.45, 35.88, 32.09, 31.78, 29.61, 29.47, 22.94, 15.27, 14.38; *m/z* (CI) 690.6 ($M+H^+$, 100%), 260.5 (61); HRMS: Found 690.4510 $C_{50}H_{59}O_2$ ($M+H^+$) Requires 690.4510.

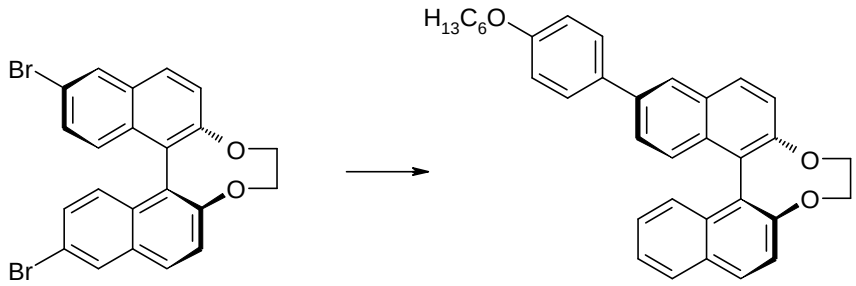
(S)-6,6'-Bis(4-hexyloxyphenyl)-2,2'-(ethylenedioxy)-1,1'-binaphthalene - 102:[122]



(*S*)-6,6'-Dibromo-2,2'-(ethylenedioxy)-1,1'-binaphthalene (0.352 g, 0.749 mmol), 4-hexyloxyphenyl(trihydroxy)boronate sodium salt (0.783 g, 2.988 mmol) and 2mol% $PdCl_2$(dppf) (0.0149 g, 0.0183 mmol) were dissolved in toluene (15 mL) and the reaction mixture heated to reflux for 72 hours. The crude material was diluted with dichloromethane, filtered through celite and the solvent removed under reduced pressure. Purification by silica gel column chromatography (Hexane/DCM 4:1) afforded the *title compound* as a colourless oil (0.421 g, 85%), $[\alpha]_D^{25}$ 466.74 (*c* 0.43, chloroform). δ_H (400 MHz, $CDCl_3$) 7.96 (2H, s), 7.92 (2H, d, *J* 8.80), 7.52 (4H, d, *J* 8.76), 7.40 (2H, dd, *J* 8.87, 1.85), 7.36 (2H, d, *J* 8.80), 7.26 (2H, d, *J* 8.87), 6.89 (4H, d, *J* 8.76), 4.32 (2H, d, *J* 8.95), 4.09 (2H, d, *J* 8.95 H), 3.90 (4H, t, *J* 6.58), 1.71 (4H, m), 1.38 (4H, m), 1.26 (8H, m), 0.82 (6H, t, *J* 7.04); δ_C (101 MHz, $CDCl_3$) 158.73, 156.36, 137.03, 133.02, 131.75, 131.29, 130.81, 128.17, 127.56, 125.75, 124.99,

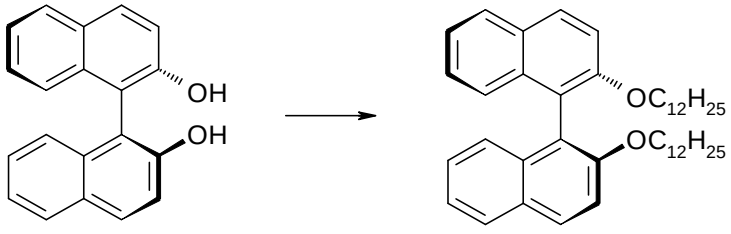
124.08, 122.81, 114.82, 72.99, 68.06, 31.58, 29.23, 25.71, 22.60, 14.04; *m/z* (CI) 665.5 ($M+H^+$, 31%), 664.4 (65), 43.2 (100); HRMS: Found 682.3890 $C_{56}H_{52}NO_4$ ($M+NH_4^+$) Requires 682.3891.

(S)-6-(4-Hexyloxyphenyl)-2,2'-(ethylenedioxy)-1,1'-binaphthalene - 117:[122]



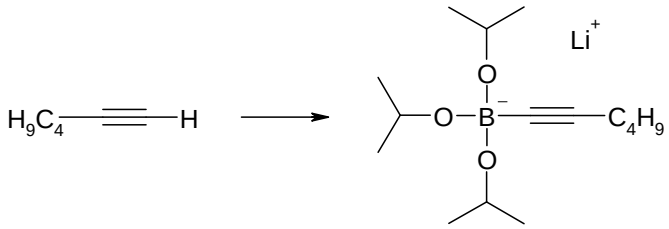
(*S*)-6,6'-Dibromo-2,2'-(ethylenedioxy)-1,1'-binaphthalene (0.322 g, 0.685 mmol), 4-hexyloxyphenyltrihydroxyboronate sodium salt (0.449 g, 1.712 mmol) and 2mol% $PdCl_2$(dppf) (0.0112 g, 0.0137 mmol) were dissolved in toluene (10 mL) and the reaction mixture heated to reflux for 72 hours. The crude material was diluted with dichloromethane, filtered through celite and the solvent removed under reduced pressure. Purification by silica gel column chromatography (Hexane/DCM 4:1) afforded the *title compound* as a colourless oil (0.164 g, 49%), $[\alpha]_D^{26}$ 934.58 (*c* 0.01, chloroform). δ_H (400 MHz, $CDCl_3$) 7.95 (1H, s), 7.91 (1H, d, *J* 8.45), 7.89 (1H, d, *J* 8.45), 7.81 (1H, d, *J* 8.12), 7.52 (2H, d, *J* 8.76), 7.39-7.34 (3H, m), 7.31 (1H, ddd, *J* 8.06, 6.67, 1.28), 7.24-7.13 (3H, m), 6.89 (2H, d, *J* 8.76), 4.20 (4H, m), 3.91 (2H, t, *J* 6.58), 1.71 (2H, qn, *J* 6.72), 1.39 (2H, m), 0.80 (3H, t, *J* 5.90); δ_C (101 MHz, $CDCl_3$) 158.74, 156.51, 156.36, 137.03, 133.03, 132.94, 131.75, 131.29, 130.94, 130.81, 130.72, 128.18, 128.02, 127.53, 127.09, 126.26, 126.21, 125.72, 125.00, 124.75, 124.18, 124.09, 122.79, 122.44, 114.83, 72.98, 68.08, 31.58, 29.24, 25.72, 22.60, 14.04; *m/z* (CI) 506.3 ($M+NH_4^+$, 100%), 100.2 (69); HRMS: Found 506.2698 $C_{34}H_{36}NO_3$ ($M+NH_4^+$) Requires 506.2690.

(S)-2,2'-Bis(dodecyloxy)-1,1'-binaphthalene - 119:[127]



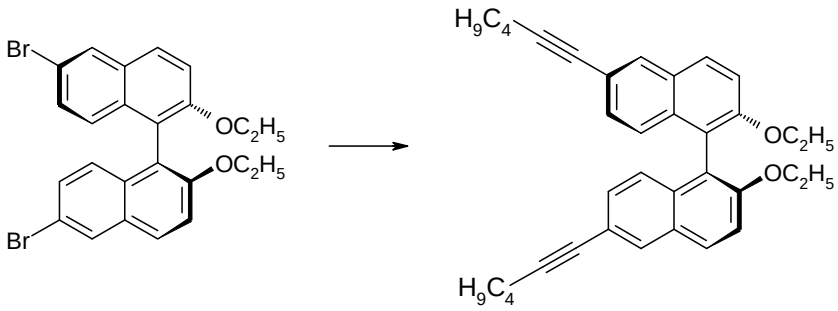
To a solution of optically pure (*S*)-1,1'-bi(2-naphthol) (0.519 g, 1.813 mmol) in acetone (30 mL) was added potassium carbonate (0.752 g, 5.439 mmol) and 1-bromododecane (2.712 g, 10.876 mmol, 2.6 mL). The mixture was heated to reflux for 48 hours monitoring the reaction by TLC. The reaction mixture was filtered, washed with acetone (50 mL) and the solvent removed under reduced pressure. The crude product was dissolved in dichloromethane (50 mL) and washed with dilute hydrochloric acid (1M, 25 mL), water (25 mL) and brine (25 ml). The solution was dried (Na_2SO_4) and the solvent removed under reduced pressure. Purification by silica gel column chromatography afforded the title compound as a colourless oil (1.002 g, 89%). δ_H (400 MHz, $CDCl_3$) 7.89 (2H, d, *J* 8.97), 7.81 (2H, d, *J* 8.08), 7.31 (2H, d, *J* 8.97), 7.27 (2H, ddd, *J* 8.08, 6.47, 1.47), 7.16 (2H, m), 7.12 (2H, d, *J* 8.08), 3.89 (4H, m), 1.39-0.91 (40H, m), 0.86 (6H, t, *J* 6.91).

Lithium 1-hexynyl(triisopropyl)borate - 126:[151]



n-Butyllithium (2.5M in hexanes 67.120 mmol, 26.8 mL) was added to a solution of 1-hexyne (5.012 g, 61.018 mmol) in anhydrous tetrahydrofuran (90 mL) at -78°C. The mixture was stirred for 1 hour before warming to 0°C and stirring for a further hour. After re-cooling to -78°C triisopropylborate (11.476 g, 61.018 mmol, 14.1 mL) was added dropwise, with vigorous stirring, and the mixture allowed to warm to room temperature over 12 hours. The solvent was removed under reduced pressure to afford the title compound as a white solid (11.121 g, 66%), m.p. >200°C. δ_H (400 MHz, $CDCl_3$) 3.92 (3H, sept, *J* 6.17), 2.16 (2H, t, *J* 6.58), 1.45 (4H, m), 1.15 (18H, d, *J* 6.17), 0.92 (3H, t, *J* 6.99).

(S)-6,6'-(1-Hexynyl)-2,2'-diethoxy-1,1'-binaphthalene - 120:



i) Using THF & 4 equivalents of 1-hexyne[209]

To a solution of (*S*)-6,6'-dibromo-2,2'-diethoxy-1,1'-binaphthalene (0.693 g, 1.386 mmol), copper(I) iodide (0.0396 g, 0.208 mmol), $PdCl_2(PPh_3)_2$ (0.0973 g, 0.139 mmol) and triethylamine (0.164 g, 2.772 mmol, 0.23 mL) in tetrahydrofuran (10 mL) was added 1-hexyne (0.455 g, 5.544 mmol, 0.64 mL) and the mixture heated to reflux for 48 hours. The cooled mixture was diluted with dichloromethane (20 mL) filtered through celite. The solution was washed with water (25 mL), brine (25 mL), dried (Na_2SO_4) and the solvent removed under reduced pressure. Purification by silica gel column chromatography (Hexane/DCM 4:1) afforded the mono-substituted derivative (0.0703 g, 12%).

ii) Using THF& 10 equivalents of 1-hexyne[209]

To a solution of (*S*)-6,6'-dibromo-2,2'-diethoxy-1,1'-binaphthalene (0.461 g, 0.922 mmol), copper(I) iodide (0.0263 g, 0.128 mmol), $PdCl_2(PPh_3)_2$ (0.0324 g, 0.0461 mmol) and triethylamine (0.109 g, 1.844 mmol, 0.15 mL) in tetrahydrofuran (10 mL) was added 1-hexyne (0.757 g, 9.220 mmol, 1.06 mL) and the mixture heated to reflux for 72 hours. The cooled mixture was diluted with dichloromethane (20 mL) and filtered through celite. The solution was washed with water (25 mL), brine (25 mL), dried (Na_2SO_4) and the solvent removed under reduced pressure. Purification by silica gel column chromatography (Hexane/DCM 4:1) afforded the mono-substituted derivative (0.105 g, 27%).

iii) Using Et_3N & 12 equivalents of 1-hexyne[150]

A solution of (*S*)-6,6'-dibromo-2,2'-diethoxy-1,1'-binaphthalene (0.374 g, 0.748 mmol), copper(I) iodide (0.0214 g, 0.112 mmol), $PdCl_2(PPh_3)_2$ (0.0262 g, 0.0374

mmol) in triethylamine (10 mL) was heated to 60 °C for 10 minutes before adding 1-hexyne (0.737 g, 8.976 mmol, 1.03 mL) and heating for a further 48 hours at 80°C. The cooled mixture was diluted with dichloromethane (20 mL) and filtered through celite. The solution was washed with water (25 mL), brine (25 mL), dried (Na_2SO_4) and the solvent removed under reduced pressure. Purification by silica gel column chromatography (Hexane/DCM 4:1) afforded the *title compound* as a yellow oil (0.0752 g, 20%) and the mono-substituted derivative (0.155 g, 49%).

iv) Using Et_3N & 15 equivalents of 1-hexyne[150]

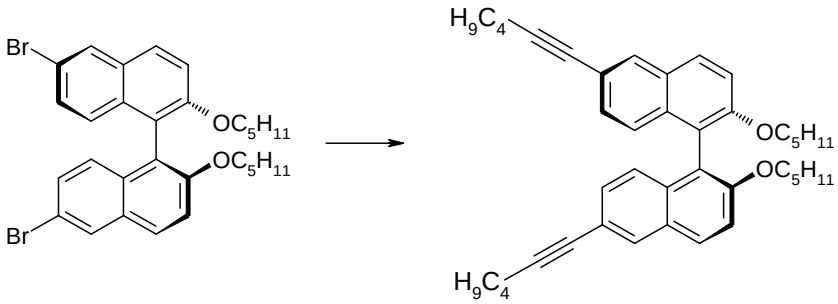
To a sealed tube was added (*S*)-6,6'-dibromo-2,2'-diethoxy-1,1'-binaphthalene (0.392 g, 0.784 mmol), copper(I) iodide (0.0224 g, 0.118 mmol), $PdCl_2(PPh_3)_2$ (0.0275 g, 0.0392 mmol) and triethylamine (10 mL). The mixture was heated to 60°C for 10 minutes before adding 1-hexyne (0.966 g, 11.760 mmol, 1.35 mL) and heating for a further 72 hours at 80°C. The mixture was diluted with dichloromethane (20 mL) and filtered through celite. The solution was washed with water (25 mL), brine (25 mL), dried (Na_2SO_4) and the solvent removed under reduced pressure. Purification by silica gel column chromatography (Hexane/DCM 4:1) afforded the *title compound* as a yellow oil (0.126 g, 32%) and the mono-substituted derivative (0.159 g, 48%).

v) Using lithium 1-hexynyl(triisopropoxy)borate salt[151]

To a mixture of lithium 1-hexynyl(triisopropoxy)borate (0.574 g, 2.079 mmol), copper(I) iodide (0.0497 g, 0.0261 mmol) and 5mol% $Pd(PPh_3)_4$ (0.0301 g, 0.0261 mmol) was added a solution of (*S*)-6,6'-dibromo-2,2'-diethoxy-1,1'-binaphthalene (0.261 g, 0.522 mmol) in anhydrous *N*,*N*-dimethylformamide (5 mL) and the reaction mixture heated to 90°C for 20 hours. The mixture was diluted with toluene (5 mL) and water (15 mL) and the layers separated. The organic layer was washed with water (2x25 mL), brine (2x25 mL), dried (Na_2SO_4) and the solvent removed under reduced pressure. Purification by silica gel column chromatography (Hexane/DCM 3:1) afforded the *title compound* as a yellow oil (0.211 g, 82%), $[\alpha]_D^{24}$ 51.1 (*c* 0.04, chloroform). δ_H (400 MHz, $CDCl_3$) 7.85 (2H. s), 7.78 (2H, d, *J* 9.04), 7.32 (2H, d, *J* 9.04), 7.11 (2H, d, *J* 8.77), 6.95 (2H, d, *J* 8.77), 3.96 (4H, m), 2.36 (4H, t, *J* 6.95), 1.40 (8H, m), 0.97 (6H, t, *J* 6.90), 0.88 (6H, t, *J* 7.22); δ_C (101 MHz, $CDCl_3$) 154.67, 133.12, 131.01, 128.94, 128.88, 128.75, 125.30, 120.15, 118.81,

115.96, 89.98, 80.99, 65.04, 30.92, 22.02, 19.20, 14.93, 13.66; *m/z* (CI) 520.3 ($M+NH_4^+$, 14%), 503.3 (34), 254.2 (100); HRMS: Found 520.3215 $C_{36}H_{42}NO_2$ ($M+NH_4^+$) Requires 520.3210.

(S)-6,6'-(1-Hexynyl)-2,2'-pentoxy-1,1'-binaphthalene – 121:



i) Using THF & 4 equivalents of 1-hexyne[209]

To a solution of (*S*)-6,6'-dibromo-2,2'-pentoxy-1,1'-binaphthalene (0.467 g, 0.815 mmol), copper(I) iodide (0.0233 g, 0.122 mmol), $PdCl_2(PPh_3)_2$ (0.0286 g, 0.0408 mmol) and triethylamine (0.0963 g, 1.630 mmol, 0.13 mL) in tetrahydrofuran (10 mL) was added 1-hexyne (0.268 g, 3.260 mmol, 0.37 mL) and the mixture heated to reflux for 48 hours. The cooled mixture was diluted with dichloromethane (20 mL) filtered through celite. The solution was washed with water (25 mL), brine (25 mL), dried (Na_2SO_4) and the solvent removed under reduced pressure. Purification by silica gel column chromatography (Hexane/DCM 6:1) afforded the mono-substituted derivative (0.0377 g, 9%).

ii) Using THF& 10 equivalents of 1-hexyne[209]

To a solution of (*S*)-6,6'-dibromo-2,2'-dipentoxy-1,1'-binaphthalene (0.299 g, 0.512 mmol), copper(I) iodide (0.0146 g, 0.768 mmol), $PdCl_2(PPh_3)_2$ (0.0179 g, 0.0256 mmol) and triethylamine (0.0605 g, 1.024 mmol, 0.08 mL) in tetrahydrofuran (10 mL) was added 1-hexyne (0.421 g, 5.120 mmol, 0.588 mL) and the mixture heated to reflux for 48 hours. The cooled mixture was diluted with dichloromethane (20 mL) and filtered through celite. The solution was washed with water (25 mL), brine (25 mL), dried (Na_2SO_4) and the solvent removed under reduced pressure. Purification by silica gel column chromatography (Hexane/DCM 6:1) afforded the *title compound* as a pale yellow oil (0.0279 g, 9%) and the mono-substituted derivative (0.126 g, 48%)

iii) Using Et_3N & 12 equivalents of 1-hexyne[150]

A solution of (*S*)-6,6'-dibromo-2,2'-dipentoxy-1,1'-binaphthalene (0.339 g, 0.580 mmol), copper(I) iodide (0.0166 g, 0.0870 mmol), $PdCl_2(PPh_3)_2$ (0.0203 g, 0.0290 mmol) in triethylamine (10 mL) was heated to 60 °C for 10 minutes before adding 1-hexyne (0.572 g, 6.960 mmol, 0.80 mL) and heating for a further 48 hours at 80 °C. The cooled mixture was diluted with dichloromethane (20 mL) and filtered through celite. The solution was washed with water (25 mL), brine (25 mL), dried (Na_2SO_4) and the solvent removed under reduced pressure. Purification by silica gel column chromatography (Hexane/DCM 6:1) afforded the *title compound* as a pale yellow oil (0.0561 g, 16%) and the mono-substituted derivative (0.157 g, 53%).

iv) Using Et_3N & 15 equivalents of 1-hexyne[150]

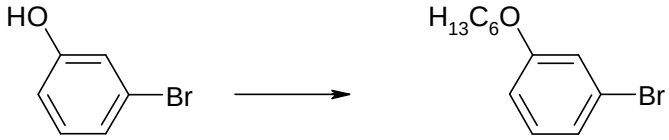
To a solution of (*S*)-6,6'-dibromo-2,2'-dipentoxy-1,1'-binaphthalene (0.371 g, 0.635 mmol) in triethylamine (10 mL) in a sealed tube was added copper(I) iodide (0.0181 g, 0.0952 mmol), $PdCl_2(PPh_3)_2$ (0.0223 g, 0.0318 mmol). The mixture was heated to 60°C for 10 minutes before adding 1-hexyne (0.782 g, 9.525 mmol, 1.09 mL) and heating for a further 72 hours at 80°C. The mixture was diluted with dichloromethane (20 mL) and filtered through celite. The solution was washed with water (25 mL), brine (25 mL), dried (Na_2SO_4) and the solvent removed under reduced pressure. Purification by silica gel column chromatography (Hexane/DCM 4:1) afforded the *title compound* as a yellow oil (0.146 g, 39%) and the mono-substituted derivative (0.136 g, 42%).

v) Using lithium 1-hexynyl(triisopropoxy)borate salt[151]

To a mixture of lithium 1-hexynyl(triisopropoxy)borate (0.551 g, 1.996 mmol), copper(I) iodide (4.742 mg, 0.0249 mmol) and 5mol% $Pd(PPh_3)_4$ (0.0301 g, 0.0249 mmol) was added a solution of (*S*)-6,6'-dibromo-2,2'-dipentoxy-1,1'-binaphthalene (0.292 g, 0.499 mmol) in anhydrous *N*,*N*-dimethylformamide (5 mL) and the reaction mixture was heated to 90°C for 20 hours. The mixture was diluted with toluene (5 mL) and water (15 mL) and the layers separated. The organic layer was washed with water (2x25 mL), brine (2x25 mL), dried (Na_2SO_4) and the solvent removed under reduced pressure. Purification by silica gel column chromatography (Hexane/DCM 3:1) afforded the *title compound* as a yellow oil (0.204 g, 69%), $[\alpha]_D^{25}$

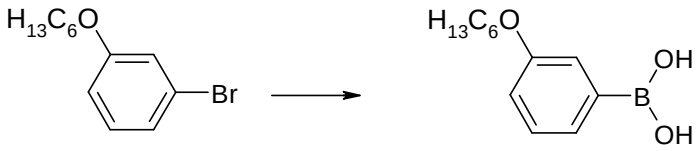
97.85 (*c* 0.15, chloroform). δ_H (400 MHz, $CDCl_3$) 7.91 (2H, s), 7.84 (2H, d, *J* 9.01), 7.37 (2H, d, *J* 9.01), 7.17 (2H, d, *J* 8.76), 7.03 (2H, d, *J* 8.76), 3.91 (4H, m), 2.43 (4H, t, *J* 7.01), 1.64-1.35 (12H, m), 1.05-0.86 (14H, m), 0.67 (6H, t, *J* 7.26); δ_C (101 MHz, $CDCl_3$) 154.90, 133.19, 130.97, 128.92, 128.79, 128.73, 125.29, 120.19, 118.75, 115.91, 88.86, 81.04, 69.53, 30.93, 28.97, 27.81, 22.13, 22.01, 19.20, 13.87, 13.66; *m/z* (CI) 587.6 ($M+H^+$, 46%), 586.6 (100); HRMS: Found 604.4141 $C_{42}H_{54}NO_2$ ($M+NH_4^+$) Requires 604.4149.

1-Bromo-3-hexyloxybenzene - 127:[208]



To a solution of 3-bromophenol (5.002 g, 28.914 mmol) in acetone (75 mL) was added dry potassium carbonate (7.992 g, 57.829 mol) and 1-bromohexane (9.546 g, 57.828 mol, 8.1 mL). The mixture was heated to reflux for 48 hours monitoring the reaction by TLC. The reaction mixture was filtered, washed with acetone and the solvent removed under reduced pressure. The crude product was dissolved in dichloromethane (100 mL) and the organic layer washed with water (50 mL), brine (50 mL), dried (Na_2SO) and the solvent removed under reduced pressure. Purification by distillation (96-98°C, 12 mmHg) afforded the title compound as a colourless oil (6.117 g, 82%). δ_H (400 MHz, $CDCl_3$) 7.41-7.27 (3H, m), 7.02 (1H, dd, *J* 8.16, 1.24), 4.09 (2H, t, *J* 6.96), 1.78 (2H, m), 1.37 (2H, m), 1.29 (4H, m), 0.82 (3H, t, *J* 7.12).

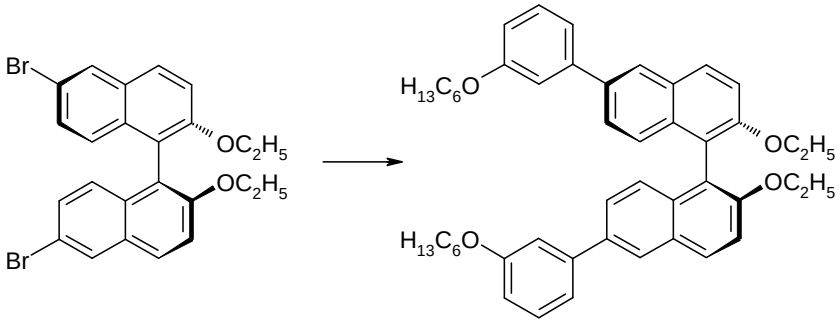
3-Hexyloxybenzeneboronic acid - 128:[208]



1-Bromo-3-hexyloxybenzene (5.111 g, 19.876 mmol,) in anhydrous diethylether (20 mL) was added to magnesium turnings (0.531 g, 21.863 mmol) in anhydrous diethylether (20 mL) at a sufficient rate as to maintain reflux. After addition the reaction mixture was heated to reflux for 2 hours. The solution was cooled and added dropwise to a solution of trimethylborate (4.131 g, 39.752 mmol, 4.5 mL) in

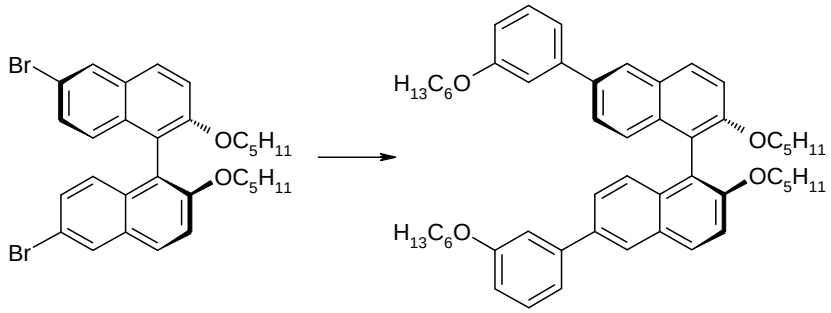
anhydrous diethylether (20 mL) at -78°C. After addition the mixture was allowed to warm to ambient temperature over 12 hours before being quenched with dilute hydrochloric acid (1M, 100 mL) and stirred for 90 minutes. The crude product was extracted with dichloromethane (2x75 mL) and the organic layer washed with water (100 mL) and dried (Na_2SO_4). The solvent was removed under reduced pressure to afford the title compound as a white solid (3.063 g, 69%), m.p. 78-82°C. δ_H (400 MHz, $CDCl_3$) 7.78 (1H, d, *J* 7.23), 7.70 (1H, d, *J* 2.61), 7.39 (1H, m), 7.10 (1H, ddd, 8.19, 2.61, 0.81), 4.04 (2H, t, *J* 6.56), 1.82 (2H, m), 1.49 (2H, m), 1.35 (4H, m), 0.92 (3H, t, *J* 7.09).

(S)-6,6'-Bis(3-hexyloxyphenyl)-2,2'-diethoxy-1,1'-binaphthalene - 129:



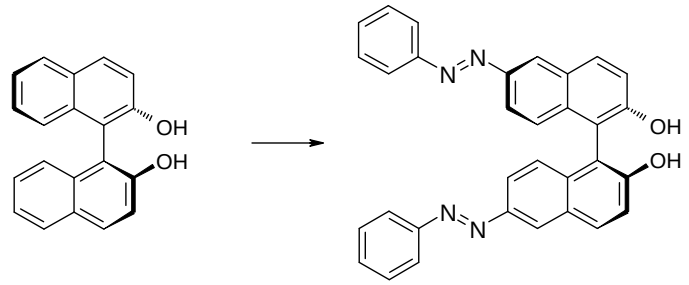
(*S*)-6,6'-Dibromo-2,2'-diethoxy-1,1'-binaphthalene (0.476 g, 0.951 mmol), 3-hexyloxybenzeneboronic acid (0.843 g, 3.796 mmol), caesium fluoride (0.576 g, 3.796 mmol) and 2mol% $PdCl_2$(dppf) (0.0155 g, 0.0190 mmol) were dissolved in toluene (20 mL) and the reaction mixture heated to reflux for 72 hours. The crude material was diluted with dichloromethane, filtered through celite and the solvent removed under reduced pressure. Purification by silica gel column chromatography (Hexane/DCM 4:1) afforded the *title compound* as white crystals (0.488 g, 77%), m.p. 108-110°C, $[\alpha]_D^{24}$ 79.4 (*c* 0.03, chloroform). δ_H (400 MHz, $CDCl_3$) 7.99 (2H, s), 7.92 (2H, d, *J* 9.08), 7.40 (2H, d, *J* 9.24), 7.26 (2H, m), 7.17 (4H, m), 7.14 (2H, s), 6.80 (2H, d, *J* 8.14), 4.00 (4H, m), 3.94 (4H, t, *J* 6.56), 1.73 (4H, m), 1.40 (4H, m), 1.26 (8H, m), 1.01 (6H, t, *J* 6.97), 0.82 (6H, t, *J* 6.37); δ_C (101 MHz, $CDCl_3$) 159.72, 154.68, 142.91, 136.22, 133.65, 129.91, 129.70, 129.59, 126.19, 126.06, 126.01, 120.57, 119.71, 116.35, 113.68, 113.20, 68.24, 65.39, 31.83, 29.52, 25.99, 22.85, 15.25, 14.29; *m/z* (CI) 712.6 ($M+NH_4^+$, 20%), 695.5 (100); HRMS: Found 712.4365 $C_{48}H_{58}NO_4$ ($M+NH_4^+$) Requires 712.4360.

(S)-6,6'-Bis(3-hexyloxyphenyl)-2,2'-dipentoxy-1,1'-binaphthalene - 130:



(*S*)-6,6'-Dibromo-2,2'-dipentoxy-1,1'-binaphthalene (0.616 g, 1.054 mmol), 3-hexyloxybenzeneboronic acid (1.045 g, 6.325 mmol), caesium fluoride (0.961 g, 6.325 mmol) and 2mol% $PdCl_2$(dppf) (0.0172 mg, 0.0211 mmol) were dissolved in toluene (15 mL) and the reaction mixture heated to reflux for 72 hours. The crude material was diluted with dichloromethane, filtered through celite and the solvent removed under reduced pressure. Purification by silica gel column chromatography (Hexane/DCM 3:1) afforded the *title compound* as a colourless oil (0.561 g, 68%), $[\alpha]_D^{24}$ 80.2 (*c* 0.04, chloroform). δ_H (400 MHz, $CDCl_3$) 7.98 (2H, s), 7.91 (2H, d, *J* 8.94), 7.41 (2H, d, *J* 8.86), 7.37 (2H, d, *J* 9.02), 7.37 (2H, m), 7.27 (6H, m), 6.80 (2H, d, *J* 8.07), 3.69-3.84 (8H, m), 1.73 (4H, m), 1.37 (8H, m), 1.27 (8H, m), 0.94 (4H, m), 0.88-0.80 (10H, m), 0.57 (6H, t, *J* 7.15); δ_C (101 MHz, $CDCl_3$) 159.70, 154.91, 142.99, 136.18, 133.70, 129.87, 129.61, 126.18, 126.00, 120.64, 119.71, 116.35, 113.67, 113.17, 69.93, 68.23, 31.81, 29.51, 29.27, 28.07, 25.97, 22.83, 22.39, 14.26, 14.15; *m/z* (CI) 780.6 ($M+H^+$, 15%), 779.5 (55), 778.5 (100), 207.1 (72); HRMS: Found 778.4952 $C_{54}H_{66}O_4$ (M^+) Requires 778.4956.

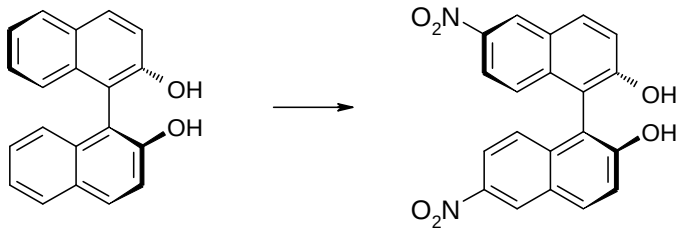
(S)-6,6'-bis(benzeneazo)-2,2'-dihydroxy-1,1'-binaphthalene - 135:[64]



A solution of aniline (4.656 g, 49.997 mmol) in water (20 mL) and aqueous tetrafluoroboric acid (50%, 17 mL) was cooled to 0°C and a solution of sodium

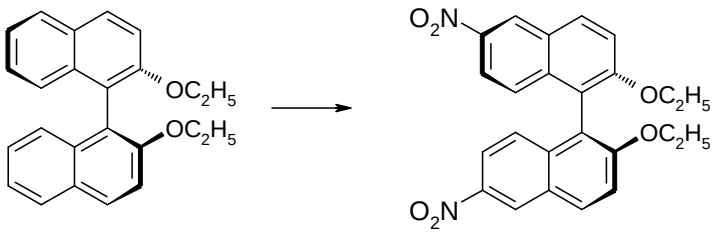
nitrite (3.455 g, 50.087 mmol) in water (8 mL) was added in two equal portions over 30 minutes. The crude precipitate was filtered and dissolved in acetone. The purified salt was collected by precipitation upon the addition of diethylether as a white solid. To a solution of (*S*)-1,1'-bi(2-naphthol) (0.258 g, 0.901 mmol) in anhydrous tetrahydrofuran (10 mL) was added potassium carbonate (0.373 g, 1.982 mmol) and pyridine (0.157 g, 1.982 mmol, 0.16 mL) under argon. The solution was cooled to -10°C and benzenediazonium tetrafluoroborate (0.380 g, 1.982 mmol) was added slowly in equal portions. The reaction mixture was stirred for 48 hours before diluting with diethylether (50 mL). The organic layer was washed with saturated ammonium chloride (25 mL), water (25 mL), brine (25 mL), dried (Na_2SO_4) and the solvent removed under reduced pressure. The title compound was not observed, with recovery of starting material.

(S)-6,6'-dinitro-2,2'-dihydroxy-1,1'-binaphthalene - 137:[159]



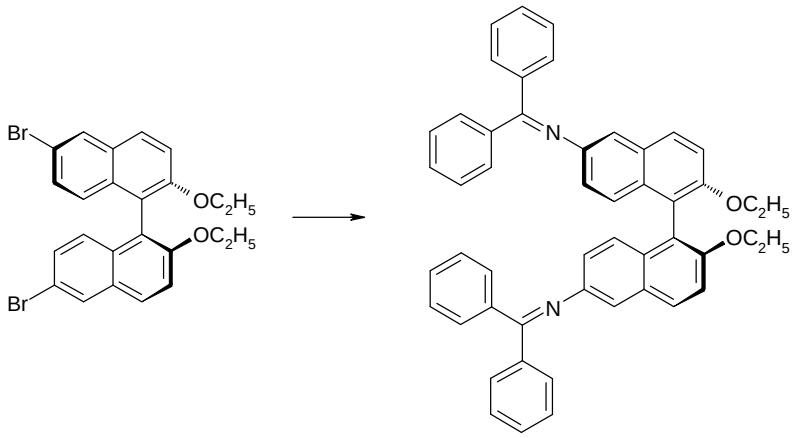
To a suspension of (*S*)-1,1'-bi(2-naphthol) (2.502 g, 8.738 mmol) in acetic acid (11 mL) and dichloromethane (11 mL) was added nitric acid (100%, 1.101 g, 17.476 mmol, 0.72 mL) in acetic acid (1 mL) dropwise. The mixture was stirred at ambient temperature for 16 hours. The mixture was added to ice/water (50 mL), filtered and washed with methanol and chloroform. Multiple nitrated products were detected in poor yield.

(S)-6,6'-dinitro-2,2'-diethoxy-1,1'-binaphthalene - 138:[143]



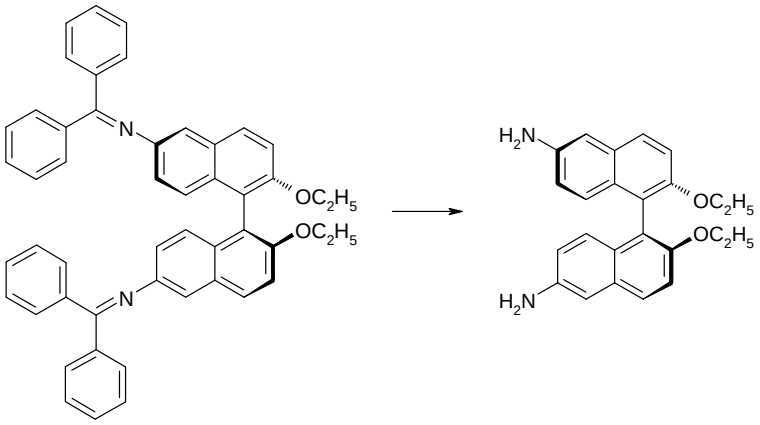
To a suspension of (*S*)-2,2'-diethoxy-1,1'-binaphthalene (0.947 g, 2.765 mmol) in acetic acid (7 mL) was added nitric acid (100%, 0.366 g, 5.807 mmol, 0.24 mL) in acetic acid (2 mL) dropwise. The mixture was stirred for 16 hours at ambient temperature before adding to water (30 mL) and extracting with dichloromethane (2x30 mL). The organic layer was washed with aqueous potassium hydroxide (1M, 25 mL), water (25 mL), brine (25 mL) and dried (Na_2SO_4). The solvent was removed under reduced pressure to afford multiple nitrated products in poor yield.

(S)-6,6'-Bis(benzophenoneimine)-2,2'-diethoxy-1,1'-binaphthalene - 140:[161]



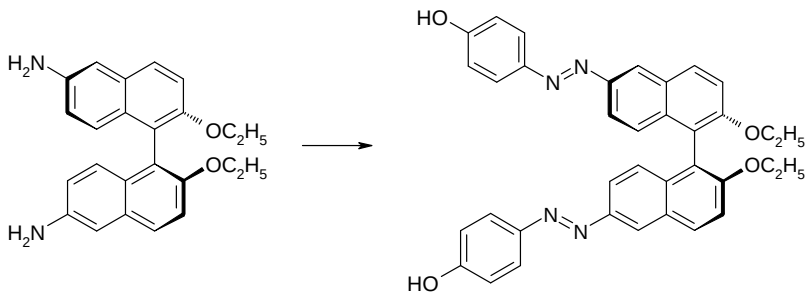
$Pd(OAc)_2$ (0.0141 g, 0.0628 mmol) and dppf (0.0523 g, 0.0943 mmol) were purged under an inert atmosphere. (*S*)-6,6'-dibromo-2,2'-diethoxy-1,1'-binaphthalene (0.786 g, 1.571 mmol), benzophenone imine (1.139 g, 6.284 mmol, 1.1 mL), sodium *tert*-butoxide (0.679 g, 7.069 mmol) and anhydrous, degassed toluene (5 mL) were added. The mixture was heated to 80°C until consumption of starting material was indicated by TLC. The mixture was cooled, diluted with ethyl acetate (30 mL) and filtered through celite. The filtrate was washed with water (30 mL), dried (Na_2SO_4) and the solvent removed under reduced pressure. Purification by silica gel column chromatography (Hexane/Ethyl Acetate 4:1) afforded the *title compound* as yellow crystals (0.797 g, 72%), m.p. 180-182°C, $[\alpha]_D^{24}$ 45.8 (*c* 0.23, chloroform). δ_H (400 MHz, $CDCl_3$) 7.72 (4H, dd, *J* 7.03, 1.56), 7.64 (2H, d, *J* 8.94), 7.43-7.35 (6H, m), 7.23 (2H, s), 7.19-7.09 (12H, m), 6.88 (2H, d, *J* 8.94), 6.62 (2H, dd, *J* 8.94, 2.15), 3.89 (4H, m), 0.91 (6H, t, *J* 6.99); δ_C (101 MHz, $CDCl_3$) 168.33, 153.57, 146.89, 140.15, 136.55, 131.07, 130.81, 129.85, 129.52, 128.38, 126.17, 126.11, 122.15, 120.85, 118.11, 116.34, 65.48, 15.26; *m/z* (CI) 701.3 ($M+H^+$, 100%), 537.3 (14), 332.3 (15); HRMS: Found 701.3153 $C_{50}H_{41}N_2O_2$ ($M+H^+$) Requires 701.3163.

(S)-6,6'-diamino-2,2'-diethoxy-1,1'-binaphthalene - 136:[161]



(*S*)-6,6'-bis(benzophenoneimine)-2,2'-diethoxy-1,1'-binaphthalene (0.462 g, 0.659 mmol) was dissolved in tetrahydrofuran (2.5 mL). Dilute hydrochloric acid (2M, 6 mL) was added and the solution stirred at ambient temperature until TLC indicated complete consumption of the starting material. The solution was diluted with ethyl acetate (30 mL) and dilute hydrochloric acid (1M, 30 mL) and the layers separated. The organic layer was washed with dilute hydrochloric acid (1M, 20 mL) and the aqueous layers combined. The aqueous layer was made basic with 10% sodium hydroxide and extracted with dichloromethane (2x30 mL). The solvent was removed under reduced pressure and the product purified by recrystallisation from isopropanol to afford the title compound as colourless crystals (0.230 g, 94%). δ_H (400 MHz, $CDCl_3$) 7.63 (2H, d, *J* 8.94), 7.28 (2H, d, *J* 8.94), 6.99 (2H, d, *J* 2.38), 6.96 (2H, d, *J* 8.94), 6.66 (2H, dd, *J* 8.94, 2.38), 3.92 (4H, m), 3.66 (4H, brs), 0.99 (6H, t, *J* 6.99).

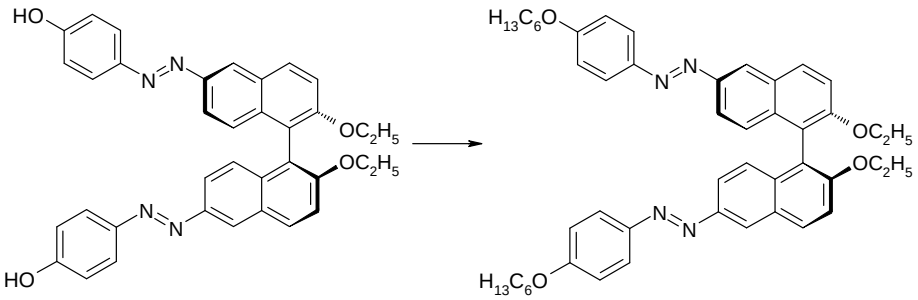
(S)-(E,E)-6,6-Bis(4-hydroxybenzeneazo)-2,2'-diethoxy-1,1'-binaphthalene - 141:[61]



(*S*)-6,6'-diamino-2,2'-diethhoxy-1,1'-binaphthalene (0.763 g, 2.049 mmol), was dissolved in mixture of water (10 mL) and concentrated hydrochloric acid (37%, 1.5

mL) and the solution cooled to 2°C. A solution of sodium nitrite (0.283 g, 4.098 mmol) in water (12 mL) was added dropwise over a period of 30 minutes and the mixture stirred for a further 15 minutes after addition. The resulting mixture was added dropwise to a cooled solution of phenol (0.424 g, 4.508 mmol) and sodium hydroxide (0.541 g, 13.524 mmol) in water (12 mL). The resulting suspension was made slightly acidic (pH ~ 5) with dilute hydrochloric acid and the precipitate was filtered and dried in a desiccator over phosphorus pentoxide. Purification by silica gel column chromatography (DCM/Ethanol 10:1) afforded the *title compound* as an orange/black solid (0.709 g, 59%). δ_H (400 MHz, $CDCl_3$) 8.36 (2H, d, *J* 1.92), 8.12 (2H, d, *J* 9.04), 7.78 (4H, d, *J* 8.96), 7.71 (2H, dd, *J* 9.24, 1.92), 7.54 (2H, d, *J* 9.04), 7.09 (2H, d, *J* 9.24), 6.87 (4H, d, *J* 8.94); δ_C (101 MHz, $CDCl_3$) 8.36 (2H, s), 8.05 (2H, d, *J* 9.14), 7.82 (4H, d, *J* 8.87), 7.72 (2H, d, *J* 9.14), 7.41 (2H, d, *J* 9.03), 6.87 (4H, d, *J* 8.87), 6.76 (2H, d, *J* 9.03), 5.09 (2H, s), 4.04 (4H, m), 1.03 (6H, t, *J* 6.87); δ_C (101 MHz, $CDCl_3$) 161.83, 157.11, 150.03, 147.66, 136.46, 131.98, 130.49, 130.43, 128.61, 127.32, 125.80, 121.43, 118.12, 116.72, 65.91, 15.35; *m/z* (CI) 582.2 ($M+H^+$, 49%), 332.3 (100), 271.2 (50); HRMS: Found 583.2330 $C_{36}H_{31}N_4O_4$ ($M+H^+$) Requires 583.2340.

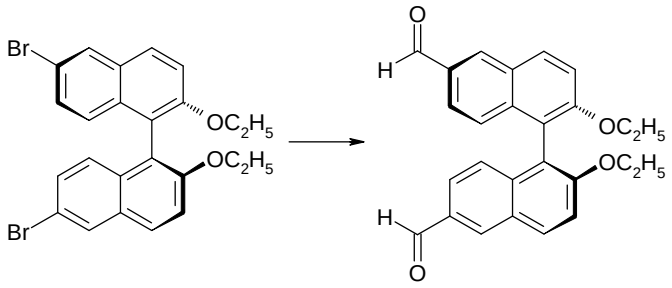
(S)-(E,E)-6,6'-Bis(4-hexyloxybenzeneazo)-2,2'-diethoxy-1,1'-binaphthalene – 142:[61]



To a solution of (*S*)-6,6'-bis(4-hydroxybenzeneazo)-2,2'-diethoxy-1,1'-binaphthalene (0.341 g, 0.585 mmol) in acetone (30 mL) was added potassium carbonate (0.243 g, 1.756 mmol) and 1-bromohexane (0.289 g, 1.756 mmol, 0.25 mL) and the mixture heated to reflux for 24 hours. The mixture was filtered, washed with acetone and the solvent removed under reduced pressure. The crude product was dissolved in dichloromethane and washed with dilute hydrochloric acid (1M, 30 mL), water (30 mL), brine (30 mL), dried (Na_2SO_4) and the solvent removed under

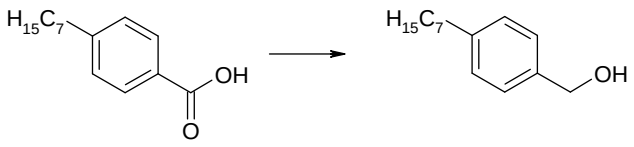
reduced pressure. Purification by silica gel column chromatography (Hexane/Ethyl Acetate 9:1) afforded the *title compound* as a yellow solid (0.204 g, 46%), $[\alpha]_D^{24}$ 148.1 (*c* 0.24, chloroform). δ_H (400 MHz, $CDCl_3$) 8.38 (2H, s), 8.05 (2H, d, 9.05), 7.87 (4H, d, *J* 8.95), 7.74 (2H, d, *J* 9.20), 7.41 (2H, d, *J* 9.05), 7.15 (2H, d, *J* 9.20), 6.93 (4H, d, *J* 8.95), 4.03 (4H, m), 3.97 (4H, t, *J* 6.53), 1.74 (4H m), 1.41 (4H, m), 1.28 (8H, m), 1.03 (6H, t, *J* 6.95), 0.79 (6H, t, *J* 6.76); δ_C (101 MHz, $CDCl_3$) 155.75, 148.80, 135.39, 124.65, 117.75, 115.83, 114.72, 114.51, 68.29, 64.93, 31.79, 31.44, 29.56, 29.22, 29.04, 27.84, 25.55, 22.54, 22.44, 14.75, 13.94, 13.86; *m/z* (CI) 751.4 ($M+H^+$, 100%), 391.3 (26); HRMS Found: 751.4210 $C_{48}H_{55}N_4O_4$ ($M+H^+$) Requires 751.4218.

(S)-2,2'-Diethoxy-1,1'-binaphthyl-6,6'-dicarbaldehyde - 146:[125]



n-Butyllithium (2.5M in hexanes, 3.2 mL, 8.092 mmol) was added to a solution of (*S*)-6,6'-dibromo-2,2'-diethoxy-1,1'-binaphthalene (0.920 g, 1.839 mmol) in anhydrous tetrahydrofuran (25 mL) at -78°C. After stirring for 4 hours anhydrous *N*,*N*-dimethylformamide (0.887 g, 12.138 mmol, 0.94 mL) was added dropwise. After stirring for 45 minutes the mixture was added to hydrochloric acid/ice (50:50) with vigorous stirring and allowed to warm to ambient temperature over 12 hours. The mixture was extracted into dichloromethane (100 mL) and the organic layer washed with water (2x50 mL), dried (Na_2SO_4) and the solvent removed under reduced pressure. Purification by recrystallisation from ethyl acetate/hexane gave the title compound as white crystals (0.613 g, 83%), m.p. 151°C (lit. 152°C). δ_H (400 MHz, $CDCl_3$) 10.06 (2H, s), 8.33 (2H, s), 8.09 (2H, d, *J* 9.03), 7.66 (2H, d, *J* 8.66), 7.47 (2H, d, *J* 9.03) 7.15 (2H, d, *J* 8.66), 4.08 (4H, m), 1.05 (6H, t, *J* 7.12).

4-Heptylbenzyl alcohol - 149:

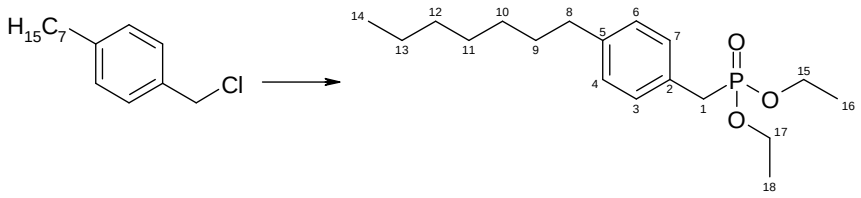


To a suspension of lithium aluminium hydride (2.332 g, 61.441 mmol) in anhydrous diethyl ether (60 mL) was added a solution of 4-heptylbenzoic acid (4.512 g, 20.480 mmol) in anhydrous tetrahydrofuran (20 mL) at such a rate as to maintain reflux. After the addition was complete the reaction mixture was left to stir at ambient temperature for 3 hours before cautiously adding water (20 mL) followed by aqueous sulphuric acid (30%, 20 mL). The mixture was filtered and the organic layer washed with dilute hydrochloric acid (1M, 200 mL) and dried (Na_2SO_4). The solvent was removed under reduced pressure to give the title compound as a colourless oil (4.196 g, 99%). δ_H (400 MHz, $CDCl_3$) 7.27 (2H, d, *J* 7.88), 7.18 (2H, d, *J* 7.88), 4.61 (2H, s), 2.62 (2H, t, *J* 7.72), 2.35 (1H, s), 1.63 (2H, m), 1.32 (H, m), 0.91 (3H, t, *J* 6.73).

4-Heptylbenzyl chloride - 150:

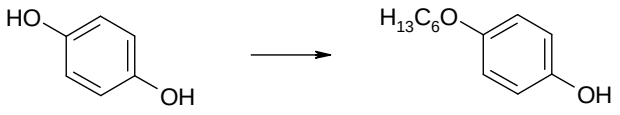
To a stirred solution of 4-heptylbenzyl alcohol (3.790 g, 18.371 mmol) in anhydrous dichloromethane (100 mL) was added thionyl chloride (10.928 g, 91.855 mmol, 6.7 mL) at ambient temperature. The reaction mixture was stirred for 12 hours before adding saturated sodium hydrogen carbonate solution (200 mL). The organic layer was washed with sodium hydrogen carbonate (100 mL), dilute hydrochloric acid (1M, 100 mL), water (100 mL) and dried (Na_2SO_4). The solvent was removed under reduced pressure to give the title compound as a colourless oil (3.554 g, 86%). δ_H (400 MHz, $CDCl_3$) 7.34 (2H, d, *J* 8.01), 7.21 (2H, d, *J* 8.01), 4.61 (2H, s), 2.65 (2H, t, *J* 7.73), 1.66 (2H, m), 1.36 (8H, m), 0.94 (3H, t, *J* 6.62).

(4-Heptylbenzyl)phosphonic acid diethyl ester - 147:[210]



To a solution of 4-heptylbenzyl chloride (3.491 g, 15.532 mmol) and potassium iodide (2.578 g, 15.532 mmol) in acetone (10 mL) and acetonitrile (6 mL) was added triethylphosphite (2.581 g, 15.532 mmol, 2.7 mL). The reaction mixture was stirred at room temperature for 3 hours and then for a further 12 hours at 50°C. The solvent was removed under reduced pressure and the crude product dissolved in dichloromethane, washed with water (2x50 mL), dried (Na_2SO_4) and the solvent removed under reduced pressure. Excess triethylphosphite was distilled off to afford the *title compound* as a pale yellow oil (5.018 g, 99%). δ_H (400 MHz, $CDCl_3$) 7.14 (2H, d, *J* 7.98, 3-H, 7-H), 7.05 (2H, d, *J* 7.98, 4-H, 6-H), 3.94 (4H, m, 15-H_2, 16-H_2), 3.05 (2H, d, $^2J_{PH}$ 21.42, 1-H_2), 2.51 (2H, t, *J* 8.12, 8-H_2), 1.52 (2H, m, 9-H_2), 1.23 (8H, m, 10-H_2, 11-H_2, 12-H_2, 13-H_2), 1.17 (6H, t, *J* 7.06, 16-H_3, 18-H_3), 0.81 (3H, t, *J* 7.08, 14-H_3); δ_C (101 MHz, $CDCl_3$) 129.44 (2-C), 129.38 (3-C, 7-C), 128.41 (5-C), 128.38 (4-C, 6-C) , 61.87 (d, $^2J_{PC}$ 6.85, 15-C, 17-C), 35.37 (8-C), 33.13 (d, $^1J_{PC}$ 138.6, 1-C), 31.65 (9-C), 31.27 (10-C), 29.04 (11-C), 28.99 (12-C), 22.48 (13-C), 16.18 (d, $^3J_{PC}$ 6.03, 16-C, 18-C), 13.92 (14-C); *m/z* (CI) 344.2 ($M+NH_4^+$, 22%), 327.2 (100); HRMS: Found 327.2082 $C_{18}H_{32}O_3P$ ($M+H^+$) Requires 327.2084.

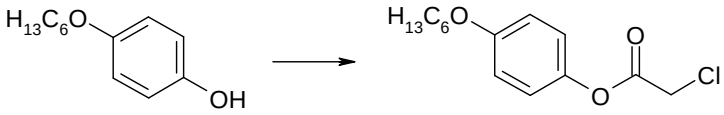
4-Hexyloxyphenol - 151:



To a solution of hydroquinone (5.068 g, 46.026 mmol) in acetone (200 mL) was added potassium carbonate (6.361 g, 46.026 mmol) and 1-bromohexane (7.598 g, 46.026 mmol, 6.5 mL). The solution was heated to reflux for 12 hours before cooling and filtering. The reaction mixture was filtered and the solvent removed

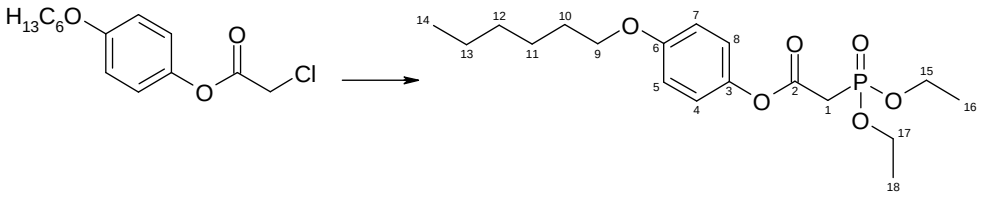
under reduced pressure. The crude product was taken up in dichloromethane (50 mL), washed with dilute hydrochloric acid (1M, 50 mL), water (50 mL), dried (Na_2SO_4) and the solvent removed under reduced pressure. Purification by silica gel column chromatography (Hexane/Ethyl acetate 10:1) afforded the title product as white crystals (4.576 g, 51%), m.p. 44-45°C (lit. 45-47°C). δ_H (400 MHz, $CDCl_3$) 6.74 (4H, m), 3.86 (2H, t, *J* 6.53), 1.72 (2H, m), 1.41 (2H, m), 1.29 (4H, m), 0.87 (3H, m).

4-Hexyloxyphenylacetyl chloride - 152:[211]



Chloroacetyl chloride was added dropwise to a cold (0°C), stirred solution of 4-hexyloxyphenol (2.014 g, 10.367 mmol) and triethylamine (1.44 mL, 10.367 mmol) in anhydrous diethylether (20 mL) under an inert atmosphere. The solution was allowed to warm to room temperature and was stirred for 1 hour. The reaction mixture was diluted with diethylether (50 mL) and washed with hydrochloric acid (1M, 2x50 mL), saturated sodium hydrogen carbonate (2x50 mL) and brine (2x50 mL). The organic layer was dried (Na_2SO_4) and the solvent removed under reduced pressure to give the *title compound* as a viscous colourless oil (2.704 g, 96%). δ_H (400 MHz, $CDCl_3$) 7.03 (2H, d, *J* 9.12), 6.88 (2H, d, *J* 9.12), 4.27 (2H, s), 3.93 (2H, t, *J* 6.54,), 1.77 (2H, m), 1.45 (2H, m), 1.33 (4H, m), 0.91 (3H, t, *J* 6.62); δ_C (101 MHz, $CDCl_3$) 166.46, 157.40, 143.81, 122.05, 115.28, 68.59, 41.11, 31.78, 29.40, 25.91, 22.82, 14.25; *m/z* (CI) 288.2 ($M+NH_4^+$, 43%), 254.3 (100), 194.2 (47), 110.1 (63); HRMS: Found 288.1361 $C_{14}H_{23}NO_3Cl$ ($M+NH_4^+$) Requires 288.1361.

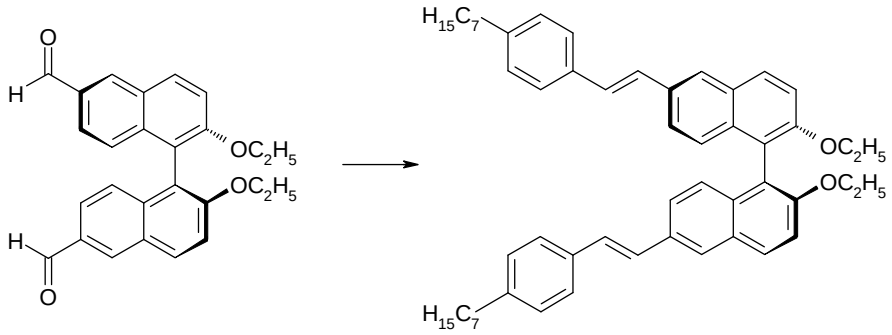
(4-Hexyloxyphenoxyacetyl)phosphonic acid diethyl ester - 148:[210]



To a solution of 4-hexyloxyphenylacetyl chloride (2.704 g, 9.988 mmol) and potassium iodide (1.658 g, 9.988 mmol) in acetone (6 mL) and acetonitrile (4 mL)

was added triethylphosphite (1.659 g, 9.988 mmol, 1.7 mL). The reaction mixture was stirred at room temperature for 3 hours and then for a further 12 hours at 50°C. The solvent was removed under reduced pressure and the crude product dissolved in dichloromethane, washed with water (2x50 mL), dried (Na_2SO_4) and the solvent removed under reduced pressure to give the *title compound* as a yellow oil (3.52 g, 95%). 6.95 (2H, d, *J* 8.82), 6.81 (2H, d, *J* 8.82), 4.17 (4H, m), 3.86 (2H, t, *J* 6.50), 3.12 (2H, d, $^2J_{PH}$ 21.65), 1.70 (2H, m), 1.38 (2H, m), 1.33-1.27 (10H, m), 0.84 (3H, t, *J* 6.36); δ_C (101 MHz, $CDCl_3$) 165.07 (d, $^2J_{PC}$ 6.70, 2-C), 157.25 (3-C), 143.98 (6-C), 122.23 (4-C, 8-C), 115.20 (5-C, 7-C), 68.54 (9-C), 63.10 (d, $^2J_{PC}$ 6.20, 15-C, 17-C), 34.63 (d, $^1J_{PC}$ 132.94, 1-C), 31.74 (10-C), 29.37 (11-C), 28.87 (12-C), 22.78 (13-C), 16.56 (d, $^3J_{PC}$ 6.20, 16-C, 18-C), 14.21 (14-C); *m/z* (CI) 390.3 ($M+NH_3$, 33%), 373.3 (36), 153.2 (100); HRMS: Found 373.1773 $C_{18}H_{30}O_6P$ ($M+H^+$) Requires 373.1775.

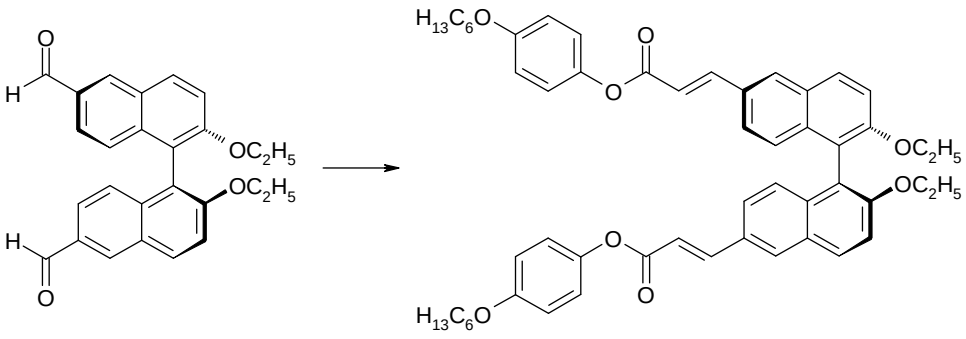
(S)-(E,E)-6,6'-bis[2-(4-heptylphenyl)-ethenyl]-2,2'-diethoxy-1,1'-binaphthalene - 153:[211]



To a 60% dispersion of sodium hydride in mineral oil (0.0537 g, 1.343 mmol) was added *n*-pentane (10 mL) under an inert atmosphere. The slurry was mixed thoroughly and the supernatant removed, drying the residue under reduced pressure. Anhydrous dimethoxyethane (15 mL) was added followed by the dropwise addition of (4-heptylbenzyl)phosphonic acid diethyl ester (0.438 g, 1.343 mmol). After hydrogen evolution had ceased, the reaction mixture was cooled to 0°C and a solution of (*S*)-2,2'-diethoxy-1,1'-binaphthyl-6,6'-dicarbaldehyde (0.214 g, 0.537 mmol) in anhydrous dimethoxyethane (10 mL) was added dropwise over a period of 5 minutes. The reaction mixture was stirred heated to 60°C for 16 hours before quenching with dilute hydrochloric acid (1M, 50 mL). The crude product was extracted with dichloromethane (2x50 mL) and the organic layer washed with water

(50 mL), brine (50 mL), dried (Na_2SO_4) and the solvent removed under reduced pressure. Purification by silica gel column chromatography (Hexane/Ethyl Acetate 15:1) afforded the *title compound* as white crystals (0.228 g, 57%), m.p. 172.5-174°C, $[\alpha]_D^{24}$ 412.1 (*c* 0.19, chloroform). δ_H (400 MHz, $CDCl_3$) 7.89 (2H, d, *J* 8.90), 7.83 (2H, d, *J* 1.49), 7.44-7.37 (8H, m), 7.19-7.04 (10H, m), 4.02 (4H, m), 2.57 (4H, t, *J* 7.69), 1.58 (4H, m), 1.26 (16H, m), 1.04 (6H, t, *J* 6.98), 0.84 (6H, t, *J* 6.98); δ_C (101 MHz, $CDCl_3$) 154.68, 142.62, 135.19, 133.85, 132.91, 129.58, 129.39, 128.92, 128.11, 126.66, 126.51, 126.07, 124.00, 120.85, 116.24, 65.37, 35.94, 32.03, 31.67, 31.15, 29.49, 29.40, 22.88, 15.22, 14.32; *m/z* (CI) 760.5 ($M+HH_4^+$, 29%), 350.2 (63), 327.2 (77), 217.2 (100); HRMS: Found 760.5090 $C_{54}H_{66}NO_2$ ($M+NH_4^+$) Requires 760.5088.

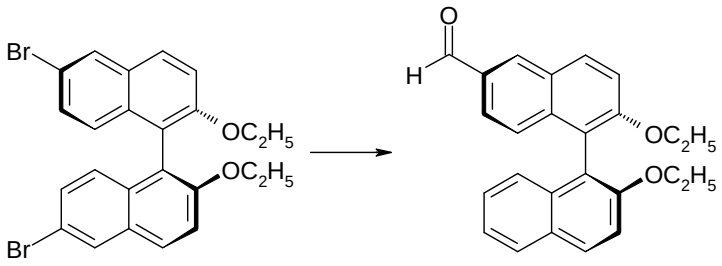
(S)-(E,E)-6,6'-bis[2-(4-hexyloxyphenoxycarbonyl)-ethenyl]-2,2'-diethoxy-1,1'-binaphthalene - 154:[211]



To a 60% dispersion of sodium hydride in mineral oil (0.059 g, 2.469 mmol) was added *n*-pentane (10 mL) under and inert atmosphere. The slurry was mixed thoroughly and the supernatant removed, drying the residue under reduced pressure. Anhydrous tetrahydrofuran (40 mL) was added followed by the dropwise addition of (4-hexyloxyphenoxyacetyl)phosphonic acid diethyl ester (0.919 g, 2.469 mmol). After hydrogen evolution had ceased, the reaction mixture was cooled to 0°C and a solution of (*S*)-2,2'-diethoxy-1,1'-binaphthyl-6,6'-dicarbaldehyde (0.412 g, 1.029 mmol) in anhydrous tetrahydrofuran (8 mL) was added dropwise over a period of 5 minutes. The reaction mixture was stirred at room temperature for 16 hours before quenching with water (100 mL). The crude product was extracted with dichloromethane (2x50 mL) and the organic layer washed with water (50 mL), brine (50 mL), dried (Na_2SO_4) and the solvent removed under reduced pressure. Purification by silica gel column chromatography (Hexane/Ethyl acetate 4:1)

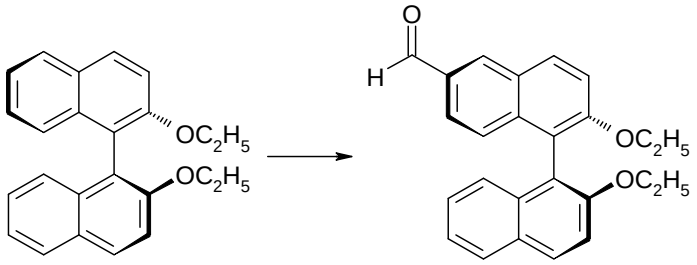
afforded the *title compound* as white crystals (0.554 g, 64%), m.p. 166.5-168°C, $[\alpha]_D^{24}$ 219.0 (*c* 0.02, chloroform). δ_H (400MHz, acetone-d_6) 8.27 (2H, d, *J* 1.47), 8.15 (2H, d, *J* 8.95), 7.98 (2H, d, *J* 15.99), 7.70 (2H, dd, *J* 8.95, 1.47), 7.65 (2H, d, *J* 9.15), 7.14 (2H, d, *J* 9.15), 7.10 (2H, d, *J* 9.17), 6.96 (2H, d, *J* 9.17), 6.75 (2H, d, *J* 15.99), 4.17 (4H, q, *J* 6.97), 3.99 (4H, t, *J* 6.49), 1.77 (4H, m), 1.48 (4H, m), 1.35 (8H, m), 1.09 (6H, t, *J* 6.97), 0.90 (6H, t, *J* 7.07); δ_C (101MHz, $CDCl_3$) 166.19, 156.89, 155.81, 146.66, 144.26, 135.24, 130.83, 130.38, 129.51, 128.85, 126.15, 123.88, 122.37, 120.08, 116.27, 115.86, 115.07, 68.35, 64.86, 31.45, 29.10, 25.58, 22.46, 14.72, 13.87; *m/z* (CI) 835.5 ($M+H^+$, 80%), 791.5 (100); HRMS: Found 835.4179 $C_{48}H_{59}O_8$ ($M+H^+$) Requires 835.4204.

(S)-2,2'-Diethoxy-1,1'-binaphthyl-6-carbaldehyde - 156:[125]



n-Butyllithium (2.5M in hexanes, 1.8 mL, 4.416 mmol) was added to a solution of (*S*)-6,6'-dibromo-2,2'-diethoxy-1,1'-binaphthalene (1.004 g, 2.007 mmol) in anhydrous tetrahydrofuran (100 mL) at -78°C. After stirring for 4 hours anhydrous *N*,*N*-dimethylformamide (0.176 g, 2.408 mmol, 0.19 mL) was added dropwise. The reaction mixture was stirred for 45 minutes before adding to hydrochloric acid/ice (50:50) with vigorous stirring and allowing to warm to ambient temperature over 12 hours. The mixture was extracted into dichloromethane (150 mL) and the organic layer washed with water (2x50 mL), dried (Na_2SO_4) and the solvent removed under reduced pressure. Purification by silica gel column chromatography (Hexane/DCM 3:1) afforded the title compound as a white solid (0.0178 g, 2%), m.p. 70-71°C, (lit. 69-70°C). δ_H (400 MHz, $CDCl_3$) 10.06 (1H, s), 8.33 (1H, s), 8.07 (1H, d, *J* 9.04), 7.93 (1H, d, *J* 9.04) 7.85 (1H, d, *J* 8.05), 7.64 (1H, d, *J* 8.80), 7.47 (1H, d, *J* 9.04), 7.40 (1H, d, *J* 9.04), 7.30 (1H, m), 7.18 (2H, m), 7.06 (1H, d, *J* 8.56), 4.06 (4H, m), 1.05 (3H, t, *J* 6.96), 1.02 (3H, t, *J* 6.96).

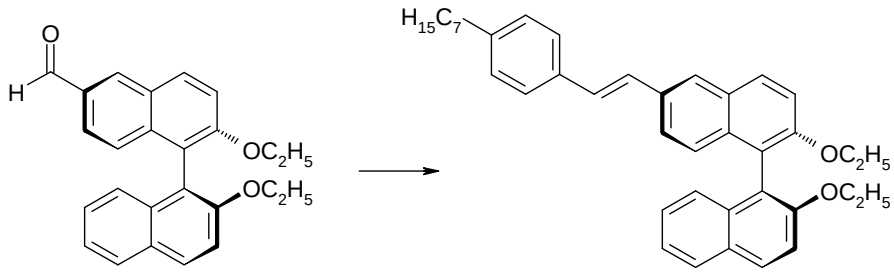
(S)-2,2'-Diethoxy-1,1'-binaphthyl-6-carbaldehyde - 156:[125, 168]



A solution of bromine (3.628 g, 22.708 mmol, 1.2 mL) in dichloromethane (40 mL) was added dropwise to a stirred solution of (*S*)-2,2'-diethoxy-1,1'-binaphthalene (3.534 g, 10.321 mmol) in dichloromethane (200 mL) at -10°C with streaming N_2. The reaction was monitored by TLC until consumption of starting material was observed. Sodium metabisulphite solution (10%, 50 mL) was added and the layers separated. The organic layer was dried (Na_2SO_4) and the solvent removed under reduced pressure. The resulting, approximately 50:50, mixture of mono/dibrominated product was dissolved in anhydrous tetrahydrofuran (120 mL) and *n*-butyllithium (2.5 M in hexanes, 13.4 mL, 33.603 mmol) was added dropwise at -78°C. After stirring for 4 hours anhydrous *N*,*N*-dimethylformamide (3.685 g, 50.413 mmol, 3.9 mL) was added dropwise. The mixture was stirred for a further 45 minutes before the mixture was added to hydrochloric acid/ice (50:50) with vigorous stirring and allowed to warm to ambient temperature over 12 hours. The mixture was extracted into dichloromethane (2x75 mL) and the organic layer washed with water (2x50 mL), dried (Na_2SO_4) and the solvent removed under reduced pressure. Purification by silica gel column chromatography (Hexane/Ethyl acetate 8:1) afforded the title compound as white crystals (1.578 g, 41%), m.p. 69-71°C (lit. 69-70°C). δ_H (400 MHz, $CDCl_3$) 10.06 (1H, s), 8.32 (1H, d, *J* 1.61), 8.07 (1H, d, *J* 9.03), 7.93 (1H, d, *J* 9.03) 7.84 (1H, d, *J* 8.08), 7.64 (1H, dd, *J* 8.84, 1.61), 7.47 (1H, d, *J* 9.03), 7.40 (1H, d, *J* 9.03), 7.30 (1H, m), 7.19 (2H, m), 7.06 (1H, d, *J* 8.52), 4.05 (4H, m), 1.07 (3H, t, *J* 6.98), 1.02 (3H, t, *J* 6.98).

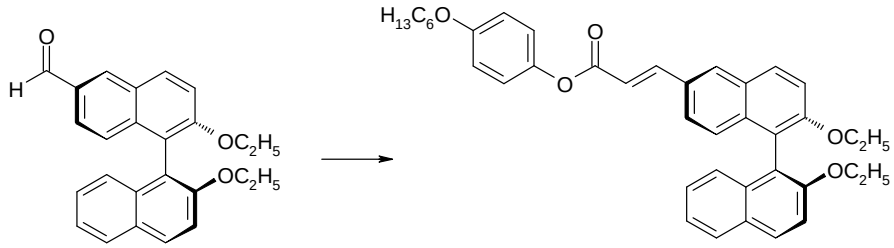
Column chromatography also yielded the 6,6'-dicarbaldehyde as white crystals (1.658 g, 40%), m.p. 151-152°C (lit. 152°C). δ_H (400 MHz, $CDCl_3$) 10.06 (2H, s), 8.33 (2H, s), 8.09 (2H, d, *J* 9.05), 7.66 (2H, d, *J* 8.61), 7.47 (2H, d, *J* 9.05) 7.14 (2H, d, *J* 8.61), 4.07 (4H, m), 1.05 (6H, t, *J* 7.06).

(S)-(E)-6-[2-(4-heptylphenyl)-ethenyl]-2,2'-diethoxy-1,1'-binaphthalene - 157:[211]



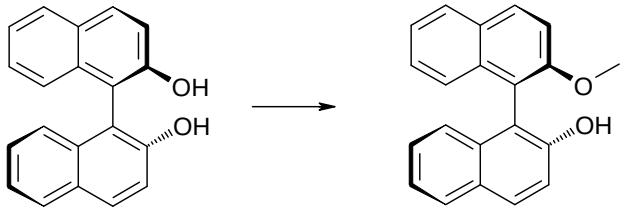
To a 60% dispersion of sodium hydride in mineral oil (0.0589 g, 1.474 mmol) was added *n*-pentane (10 mL) under an inert atmosphere. The slurry was mixed thoroughly and the supernatant removed, drying the residue under reduced pressure. Anhydrous dimethoxyethane (15 mL) was added followed by the dropwise addition of (4-heptylbenzyl)phosphonic acid diethyl ester (0.481 g, 1.474 mmol). After hydrogen evolution had ceased, the reaction mixture was cooled to 0°C and a solution of (*S*)-2,2'-diethoxy-1,1'-binaphthyl-6-carbaldehyde (0.364 g, 1.474 mmol) in anhydrous dimethoxyethane (10 mL) was added dropwise over a period of 5 minutes. The reaction mixture was heated to 60°C for 16 hours before quenching with dilute hydrochloric acid (1M, 50 mL). The crude product was extracted with dichloromethane (2x50 mL) and the organic layer washed with water (50 mL), brine (50 mL), dried (Na_2SO_4) and the solvent removed under reduced pressure. Purification by silica gel column chromatography (Hexane/Ethyl Acetate 12:1) afforded the *title compound* as white crystals (0.507 g, 63%), m.p. 76-79°C, $[\alpha]_D^{24}$ 20.9 (*c* 0.18, chloroform). δ_H (400 MHz, Acetone-d6) 8.01-7.96 (3H, m), 7.89 (1H, d, *J* 8.76), 7.56-7.48 (5H, m), 7.33-7.17 (6H, m), 7.06 (1H, d, *J* 8.56), 7.02 (1H, d, *J* 8.76), 4.07 (4H, m), 2.59 (2H, t, *J* 7.76), 1.59 (2H, m), 1.33-1.24 (8H, m), 1.05-0.99 (6H, m), 0.85 (3H, t, *J* 6.90); δ_C (101 MHz, $CDCl_3$) 154.62, 154.41, 142.49, 135.09, 134.21, 133.78, 132.76, 129.48, 129.30, 129.20, 129.17, 128.77, 128.01, 127.97, 127.84, 126.48, 126.36, 126.14, 125.96, 125.52, 123.81, 123.49, 120.85, 120.61, 116.11, 115.91, 65.19, 65.10, 35.62, 31.70, 31.32, 29.16, 29.06, 22.52, 14.88, 14.82, 13.94; *m/z* (CI) 560.4 ($M+NH_4^+$, 100%), 543.3 (39); HRMS: Found 560.3516 $C_{39}H_{46}NO_2$ ($M+NH_4^+$) Requires 560.3523.

(S)-(E)-6-[2-(4-hexyloxyphenoxycarbonyl)-ethenyl]-2,2'-diethoxy-1,1'-binaphthalene - 158:[211]



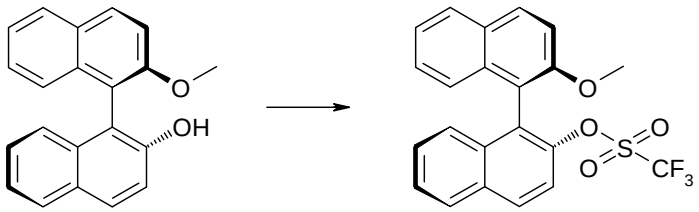
To a 60% dispersion of sodium hydride in mineral oil (0.0415 g, 1.037 mmol) was added *n*-pentane (10 mL) under and inert atmosphere. The slurry was mixed thoroughly and the supernatant removed, drying the residue under reduced pressure. Anhydrous dimethoxyethane (15 mL) was added followed by the dropwise addition of (4-hexyloxyphenoxyacetyl)phosphonic diethyl ester (0.386 g, 1.037 mmol). After hydrogen evolution had ceased, the reaction mixture was cooled to 0°C and a solution of (*S*)-2,2'-diethoxy-1,1'-binaphthyl-6,6'-dicarbaldehyde (0.307 g, 0.829 mmol) in anhydrous dimethoxyethane (10 mL) was added dropwise over a period of 5 minutes. The reaction mixture was stirred at room temperature for 16 hours before quenching with dilute hydrochloric (1M, 50 mL). The crude product was extracted with dichloromethane (2x50 mL) and the organic layer washed with water (50 mL), brine (50 mL), dried (Na_2SO_4) and the solvent removed under reduced pressure. Purification by silica gel column chromatography (Hexane/Ethyl Acetate 15:1) afforded the *title compound* as white crystals (0.307 g, 66%), m.p. 99-101°C, $[\alpha]_D^{24}$ 27.3 (*c* 0.24, chloroform). δ_H (400 MHz, $CDCl_3$) 7.93-7.87 (4H, m), 7.80 (1H, d, *J* 8.04), 7.39-7.34 (3H, m), 7.25 (1H, ddd, *J* 8.04, 6.73, 1.26), 7.15 (1H, ddd, *J* 8.04, 6.73, 1.26), 7.08 (1H, d, *J* 8.90), 7.04 (1H, d, *J* 8.45), 6.99 (2H, d, *J* 9.04), 6.83 (2H, d, *J* 9.04), 6.52 (1H, d, *J* 15.96), 4.00 (4H, m), 3.87 (2H, t, *J* 6.56), 1.70 (2H, m), 1.38 (2H, m), 1.26 (4H, m), 1.00 (6H, m), 0.83 (3H, t, *J* 7.04); δ_C (101 MHz, $CDCl_3$) 166.33, 156.96, 155.97, 154.46, 146.91, 144.38, 135.56, 134.18, 130.99, 130.26, 129.57, 129.53, 129.41, 128.98, 128.12, 126.57, 126.43, 125.41, 123.83, 123.72, 122.55, 120.94, 120.06, 116.26, 116.16, 115.83, 115.23, 68.59, 65.35, 65.12, 31.80, 29.45, 25.93, 22.83, 15.21, 15.09, 14.27; *m/z* (CI) 606.3 ($M+NH_4^+$, 12%), 589.3 (100); HRMS: Found 589.2844 $C_{39}H_{41}O_5$ ($M+H^+$) Requires 589.2949.

(R)-2-Methoxy-2'-hydroxy-1,1'-binaphthalene:[127]



To a solution of (*R*)-1,1'-bi(2-naphthol) (1.013 g, 3.538 mmol) in acetone (50 mL) was added potassium carbonate (0.538 g, 3.892 mmol) and iodomethane (0.552 g, 3.892 mmol, 0.24 mL). The reaction mixture was heated to reflux for 6 hours monitoring the reaction by TLC. The solvent was removed under reduced pressure and the crude product dissolved in dichloromethane (50 mL), washed with dilute hydrochloric acid (1M, 50 mL), water (50 mL) and brine (50 mL). The organic layer was dried (Na_2SO_4) and the solvent removed under reduced pressure. Purification by silica gel column chromatography gave the title compound as white crystals (0.503 g, 47%), m.p. 150-151°C (lit. 152-153°C). δ_H (400 MHz, $CDCl_3$) 8.03 (1H, d, *J* 8.98), 7.89 (1H, d, *J* 8.98), 7.88 (1H, dd, *J* 8.09, 0.60), 7.84 (1H, dd, *J* 8.09, 0.60), 7.45 (1H, d, *J* 9.05), 7.37-7.15 (6H, m), 7.05 (1H, m), 5.26 (1H, s), 3.77 (3H, s).

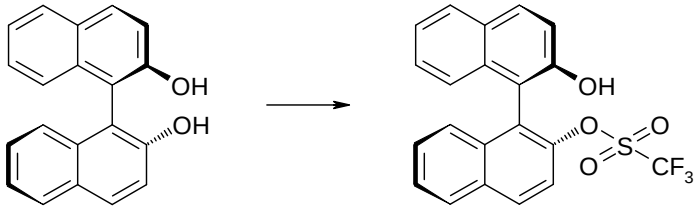
(R)-2-Methoxy-2'-(trifluoromethanesulphonyl)oxy-1,1'-binapthalene:



To a solution of (R)-2-methoxy-2'-hydroxy-1,1'-binaphthalene (0.401 g, 1.335 mmol) in anhydrous dichloromethane (25 mL) was added pyridine (0.158 g, 2.003 mmol, 0.16 mL) and the solution cooled to 0°C. Triflic anhydride (0.565 g, 2.003 mmol, 0.34 mL) was added dropwise and the mixture was allowed to cool to room temperature over 12 hours. The mixture was diluted with ethyl acetate (50 mL) and washed with dilute hydrochloric acid (1M, 100 mL), saturated sodium hydrogen carbonate (100 mL), brine (100 mL), dried (Na_2SO_4) and the solvent removed under reduced pressure. Purification by silica gel column chromatography (Hexane/DCM 3:1) afforded the title compound as a pale brown solid (0.556 g, 96%), m.p. 98.5-

100°C (lit. 99-101°C). δ_H (400 MHz, $CDCl_3$) 8.06 (1H, d, *J* 9.04), 7.95 (1H, d, *J* 8.27), 7.90 (1H, d, *J* 9.04), 7.84 (1H, d, *J* 8.09), 7.54 (2H, m), 7.40 (2H, m), 7.33-7.20 (3H, m), 6.99 (1H, d, *J* 8.40 Hz), 4.94 (3H, s).

(R)-2-(Trifluoromethanesulphonyloxy)-2'-hydroxy-1,1'-binaphthalene:



i) Using triflic anhydride

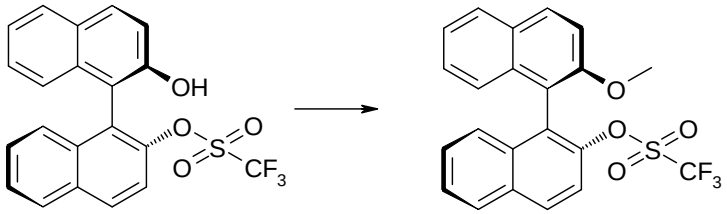
To a solution of (*R*)-1,1'-bi(2-naphthol) (1.934 g, 6.754 mmol) in anhydrous dichloromethane (40 mL) was added pyridine (0.586 g, 7.429 mmol, 6.0 mL) and the solution cooled to 0°C. Triflic anhydride (2.096 g, 7.429 mmol, 1.3 mL) was added dropwise and the mixture was allowed to cool to room temperature over 12 hours. The mixture was diluted with ethyl acetate (50 mL) and washed with dilute hydrochloric acid (1M, 100 mL), saturated sodium hydrogen carbonate (100 mL), brine (100 mL), dried (Na_2SO_4) and the solvent removed under reduced pressure. Purification by silica gel column chromatography (Hexane/DCM 1:1) afforded the title compound as a pale brown solid (1.371 g, 49%), m.p. 118-119°C. δ_H (400 MHz, $CDCl_3$) 8.04 (1H, d, *J* 9.06), 7.95 (1H, d, *J* 8.27), 7.92 (1H, d, *J* 8.99), 7.84 (1H, d, *J* 8.06), 7.54 (2H, m), 7.41 (2H, m), 7.33-7.21 (3H, m), 6.99 (1H, d, *J* 8.56), 4.93 (1H, s).

ii) Using N-phenyl-bis(trifluoromethane)sulphonimide[173]

To a solution of (*R*)-1,1'-bi(2-naphthol) (0.999 g, 3,489 mmol) in anhydrous dichloromethane (16 mL) was added 2,4,6-collidine (0.423 g, 3.489 mmol), dimethylaminopyridine (0.0512 g, 0.419 mmol) and *N*-phenyl bis-trifluoromethane sulphonimide (1.246 g, 3.489 mmol). The mixture was heated to reflux for 12 hours and the solvent removed under reduced pressure. Purification by silica gel column chromatography (Toluene) afforded the title compound as a pale brown solid (1.112 g, 76%), m.p. 118-119°C. δ_H (400 MHz, $CDCl_3$) 8.05 (1H, d, *J* 9.07), 7.95 (1H, d, *J*

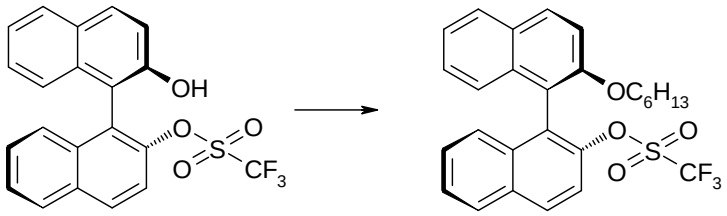
8.27), 7.92 (1H, d, *J* 8.97), 7.83 (1H, d, *J* 8.09), 7.54 (2H, m), 7.39 (2H, m), 7.33-7.22 (3H, m), 6.99 (1H, d, *J* 8.40 Hz), 4.93 (3H, s).

(R)-2-Methoxy-2'-(trifluoromethanesulphonyl)oxy-1,1'-binaphthalene:



To a solution of (*R*)-2-hydroxy-2'-(trifluoromethanesulphonyl)oxy-1,1'-binaphthalene (1.051 g, 2.512 mmol) in acetone (50 mL) was added potassium carbonate (0.694 g, 5.024 mmol) and iodomethane (0.713 g, 5.024 mmol). The solution was heated to reflux for 24 hours monitoring the reaction by TLC. The reaction mixture was filtered and the solvent removed under reduced pressure. The crude product was dissolved in dichloromethane (25 mL) and washed with dilute hydrochloric acid (1M, 50 mL), water (50 mL) and brine (50 mL). The solution was dried (Na_2SO_4) and the solvent removed under reduced pressure. Purification by silica gel column chromatography (Hexane/DCM 3:1) gave the title compound as a white solid (0.983 g, 91%), m.p. 99-100.5°C (lit. 99-101°C). δ_H (400 MHz, $CDCl_3$) 7.97 (1H, d, *J* 9.05 Hz), 7.96 (1H, d, *J* 9.07 Hz), 7.89 (1H, d, *J* 8.18 Hz), 7.81 (1H, d, *J* 8.11 Hz), 7.48 (1H, d, *J* 9.05 Hz), 7.45 (1H, dd, *J* 8.13, 6.47 Hz), 7.37 (1H, d, *J* 9.11 Hz), 7.26 (3H, m), 7.17 (1H, m), 6.92 (1H, d, *J* 8.49 Hz), 3.74 (3H, s).

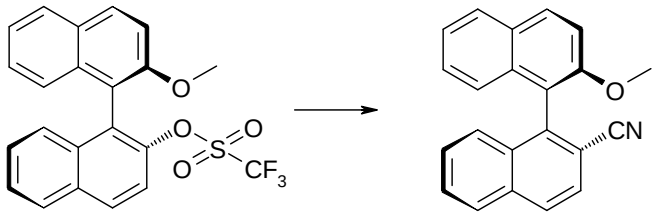
(R)-2-Hexyloxy-2'-(trifluoromethanesulphonyl)oxy-1,1'-binaphthalene:



To a solution of (*R*)-2-hydroxy-2'-(trifluoromethanesulphonyl)oxy-1,1'-binaphthalene (0.783 g, 2.114 mmol) in acetone (50 mL) was added potassium carbonate (0.584 g, 4.227 mmol) and 1-bromohexane (0.698 g, 4.227 mmol). The solution was heated to reflux for 24 hours monitoring the reaction by TLC. The reaction mixture was filtered and the solvent removed under reduced pressure. The

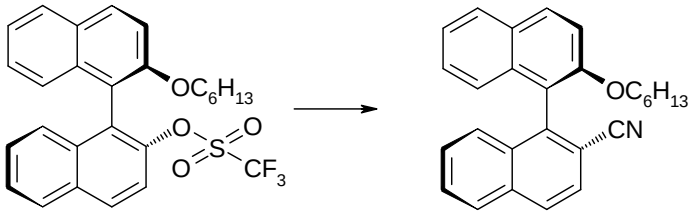
crude product was dissolved in dichloromethane (25 mL) and washed with dilute hydrochloric acid (1M, 50 mL), water (50 mL) and brine (50 mL). The solution was dried (Na_2SO_4) and the solvent removed under reduced pressure. Purification by silica gel column chromatography (Hexane/DCM 5:1) gave the title compound as a colourless oil (0.989 g, 93%). δ_H (400 MHz, $CDCl_3$) 7.97 (1H, d, *J* 9.05 Hz), 7.96 (1H, d, *J* 9.07 Hz), 7.89 (1H, d, *J* 8.18 Hz), 7.81 (1H, d, *J* 8.11 Hz), 7.48 (1H, d, *J* 9.05 Hz), 7.45 (1H, dd, *J* 8.13, 6.47 Hz), 7.37 (1H, d, *J* 9.11 Hz), 7.26 (3H, m), 7.17 (1H, m), 6.92 (1H, d, *J* 8.49 Hz), 3.74 (3H, s).

(R)-2-Cyano-2'-methoxy-1,1'-binaphthalene - 170:[174]



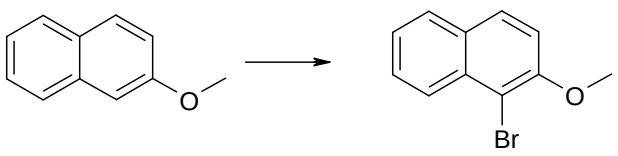
To a solution of (*R*)-2-methoxy-2'-(trifluoromethanesulphonyl)oxy-1,1'-binaphthalene (0.196 g, 0.453 mmol) in anhydrous *N*,*N*-dimethylformamide (10 mL) was added 4mol% $Pd_2(dba)_3$ (0.0159 g, 0.0174 mmol) and 15mol% dppf (0.0377 g, 0.0680 mmol) and the mixture was heated to 70°C under argon. Zinc cyanide (0.0638 g, 0.544 mmol) was added over 2 hours in 10 equal portions and after addition was complete the mixture was heated for a further 2 hours at 70°C. The mixture was diluted with dichloromethane (25 mL) and washed with water (4x25 mL), dried (Na_2SO_4) and the solvent removed under reduced pressure. Purification by silica gel column chromatography (Hexane/DCM 6:1) afforded the title compound as white crystals (0.0468 g, 31%), m.p. 155°C (lit. 145-147°C), $[\alpha]_D^{24}$ -85.5 (*c* 0.25, chloroform). δ_H (400 MHz, $CDCl_3$) 8.09 (1H, d, *J* 8.86), 7.99 (2H, m), 7.91 (1H, d, *J* 7.92), 7.80 (1H, d, *J* 8.08), 7.60 (1H, m), 7.49 (1H, d, *J* 8.86), 7.36 (3H, m), 7.26 (1H, dd, *J* 6.92), 6.93 (1H, d, *J* 7.92), 3.85 (3H, s).

(R)-2-Cyano-2'-hexyloxy-1,1'-binaphthalene - 171:[174]



To a solution of (*R*)-2-hexyloxy-2'-(trifluoromethanesulphonyl)oxy-1,1'-binaphthalene (0.127 g, 0.253 mmol) in anhydrous *N*,*N*-dimethylformamide (10 mL) was added 4mol% $Pd_2(dba)_3$ (9.267 mg, 0.0101 mmol) and 15mol% dppf (0.0210 g, 0.0380 mmol) and the mixture was heated to 70°C under an inert atmosphere. Zinc cyanide (0.0357 g, 0.304 mmol) was added over 2 hours in 10 equal portions. After the addition was complete the mixture was heated for a further 2 hours at 70°C. The mixture was diluted with dichloromethane (25 mL) and washed with water (4x25 mL), dried (Na_2SO_4) and the solvent removed under reduced pressure. Purification by silica gel column chromatography (Hexane/DCM 5:1) afforded the title compound as a pale brown solid (0.0263 g, 27%), m.p. 67.5-68.5°C, $[\alpha]_D^{24}$ -33.2 (*c* 0.22, chloroform). δ_H (400 MHz, $CDCl_3$) 8.02 (1H, d, *J* 9.05 Hz) 7.99 (1H, d, *J* 8.90 Hz), 7.96 (1H, d, *J* 8.51 Hz), 7.89 (1H, d, *J* 8.16 Hz), 7.78 (1H, d, *J* 8.47 Hz), 7.59 (1H, m), 7.45 (1H, d, *J* 9.08 Hz), 7.33 (3H, m), 7.23 (1H, m), 6.95 (1H, d, *J* 7.99 Hz), 4.04 (2H, m), 1.45 (2H, m), 1.01 (6H, m), 0.73 (3H, t, *J* 6.87 Hz); δ_C (101 MHz, $CDCl_3$) 154.44, 146.51, 142.09, 134.78, 133.44, 132.46, 130.97, 128.87, 128.50, 128.43, 128.22, 128.15, 127.36, 127.27, 126.99, 126.79, 124.34, 123.72, 118.73, 114.61, 111.82, 69.30, 31.19, 29.10, 25.27, 22.40, 13.86; *m/z* (CI) 397.3 ($M+NH_4^+$, 100%), 100.1 (24), 52.2 (42); HRMS: Found 397.2271 $C_{27}H_{29}N_2O$ ($M+NH_4^+$) Requires 397.2274.

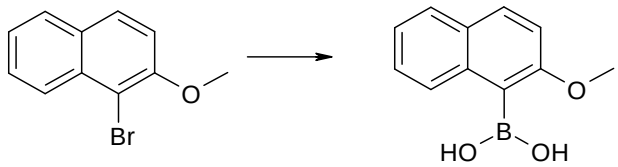
1-Bromo-2-methoxynaphthalene - 174:[181]



2-Methoxynaphthalene (30.135 g, 0.190 mol) was dissolved in acetic acid (300 mL) and aqueous hydrobromic acid (48% solution, 150 mL) was added whilst stirring.

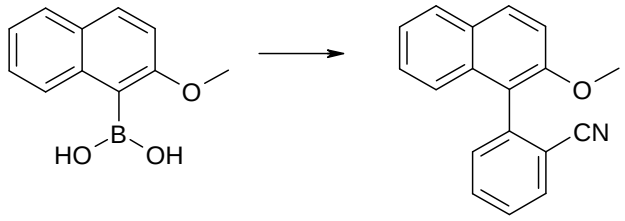
Dimethylsulphoxide (150 mL, 2.114 mol) was added dropwise at room temperature and the reaction monitored by TLC to completion. The reaction mixture was diluted with diethylether (300 mL) and the organic layer collected. The aqueous layer was extracted with diethylether (2x50 mL) and the organic layers combined. The combined organic layers were washed with water (4x100 mL), dried (Na_2SO_4) and the solvent removed under reduced pressure. Purification by silica gel column chromatography (Hexane/Ethyl Acetate 5:1) afforded the title compound as white crystals (42.626 g, 94%), m.p. 81-82 °C (lit. 80-83°C). δ_H (400 MHz, $CDCl_3$) 8.15 (1H, d, *J* 8.61), 7.75 (1H, d, *J* 9.03), 7.71 (1H, d, *J* 8.06), 7.49 (1H, dd, *J* 8.61, 7.06), 7.32 (1H, dd, *J* 8.06, 6.89), 7.20 (1H, d, *J* 9.03).

2-Methoxynaphthaleneboronic acid - 175:[212]



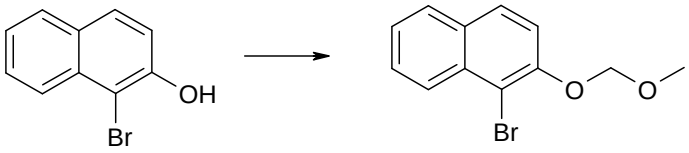
1-Bromo-2-methoxynaphthalene (2.056 g, 8.671 mmol) in anhydrous diethylether (50 mL) was added to magnesium turnings (0.232 g, 9.543 mmol) under an inert atmosphere at a sufficient rate as to maintain reflux. After addition the reaction mixture was refluxed for a further 3 hours. The solution was then added dropwise to a cooled (-78°C) solution of trimethylborate (1.808 g, 17.400 mmol, 2.0 mL) in anhydrous diethylether (25 mL). The reaction mixture was warmed to room temperature and stirred for 12 hours before adding dilute hydrochloric acid (1M, 100 mL) and stirring for a further 3 hours. The aqueous layer was extracted with diethylether and the combined organic layers dried (Na_2SO_4) and the solvent removed under reduced pressure to afford the title compound as a white solid (1.454 g, 83%), m.p. 107-111°C (lit. 109-112°C). δ_H (400 MHz, $CDCl_3$) 7.86 (1H, d, *J* 9.11 Hz), 7.78 (1H, d, *J* 9.11 Hz), 7.52 (1H, d, *J* 8.12 Hz), 7.41 (2H, m), 7.28 (1H, d, *J* 9.11 Hz), 5.10 (2H, s), 3.89 (3H, s).

1-(2-Cyanophenyl)-2-methoxynaphthalene - 176:



To a solution of 1-bromobenzonitrile (0.199 g, 1.094 mmol) in anhydrous toluene (10 mL) was added 2-methoxynaphthaleneboronic acid (0.442 g, 2.188 mmol), tripotassium phosphate (0.464 g, 2.188 mmol) and 2mol% $PdCl_2$(dppf) (17.87 mg, 21.88 μmol). The reaction mixture was heated to reflux for 48 hours before diluting with dichloromethane (50 mL). The crude product was passed through celite and the solvent removed under reduced pressure. Purification by silica gel column chromatography (Hexane/DCM 3:1) gave the *title compound* as colourless crystals (0.0971 g, 34%), m.p. 153-154°C. δ_H (400 MHz, $CDCl_3$) 7.96 (1H, d, *J* 9.11 Hz), 7.84 (2H, m), 7.71 (1H, dd, *J* 7.68 Hz), 7.52 (1H, dd, *J* 7.68 Hz), 7.46 (1H, d, *J* 7.73 Hz), 7.40 (1H, d, *J* 9.11 Hz), 7.36 (2H, m), 7.28 (1H, m), 3.92 (3H, s); δ_C (101 MHz, $CDCl_3$) 154.72, 140.97, 133.09, 132.45, 132.22, 130.89, 129.10, 128.30, 127.72, 127.07, 124.15, 123.83, 120.86, 120.17, 118.33, 115.01, 113.30, 56.46; *m/z* (CI) 277.2 ($M+NH_4^+$, 100%), 52.2 (17); HRMS: Found 277.1336 $C_{18}H_{17}N_2O$ ($M+NH_4^+$) Requires 277.1335.

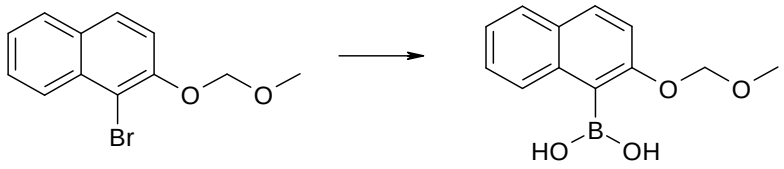
1-Bromo-2-methoxymethyloxynaphthalene - 178:[213]



To a solution of dimethoxymethane (10.356 g, 0,136 mol) in anhydrous toluene (35 mL) was added 0.01mol% zinc acetate (0.249 g, 1.36 mmol). The mixture was stirred at ambient temperature and acetyl chloride (10.676 g, 0.136 mol, 9.7 mL) was added dropwise over 5 minutes under an inert atmosphere. The mixture was warmed to 45°C over 15 minutes, cooled to ambient temperature and stirred until consumption of dimethoxymethane was complete to afford an approximately 2 M solution of methoxymethylchloride in toluene. To the toluene solution of

methoxymethyl chloride (~2 M, 43 mL) at ambient temperature and under an inert atmosphere, 1-bromo-2-naphthol (10.106 g, 45.304 mmol) and *N*,*N*-diisopropylethylamine (8.783 g, 67.953 mmol, 11.8 mL) were added sequentially. The reaction mixture was stirred for 16 hours before diluting with ethyl acetate (50 mL). Saturated ammonium chloride (100 mL) was added and the mixture stirred vigorously for 10 minutes. The organic layer was separated and washed with saturated sodium hydrogen carbonate (50 mL), brine (50 mL), dried (Na_2SO_4) and the solvent removed under reduced pressure Purification by distillation (140°C, 1 mmHg) afforded the title compound as a yellow oil (11.403 g, 94%). δ_H (400 MHz, $CDCl_3$) 8.21 (1H, d, *J* 8.67 Hz), 7.72 (1H, d, *J* 8.67 Hz), 7.71 (1H, d, *J* 9.05 Hz), 7.52 (1H, ddd, *J* 8.21, 6.81, 1.12 Hz), 7.39 (1H, d, *J* 9.05 Hz), 7.37 (1H, ddd, *J* 8.21, 6.81, 1.12 Hz), 5.31 (2H, s), 3.53 (3H, s).

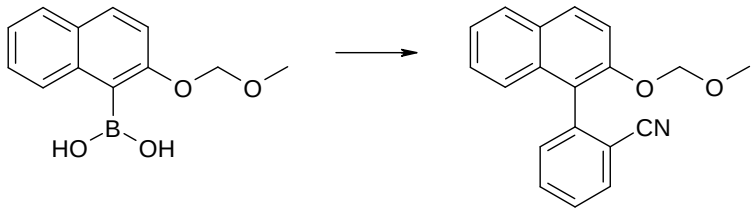
2-Methoxymethyloxynaphthaleneboronic acid - 179:[212]



n-Butyllithium (2.5M in hexanes, 32.132 mmol, 12.9 mL) was added to a stirred solution of 1-bromo-2-methoxymethyloxynaphthalene (7.802 g, 29.211 mmol) in anhydrous diethylether (90 mL) at -78°C. The solution was allowed to warm to ambient temperature and stirred for 2 hours. After re-cooling to -78°C trimethylborate (3.339 g, 32.132 mmol, 3.7 mL) was added dropwise and the mixture allowed to warm to ambient temperature over 12 hours. Saturated ammonium chloride (100 mL) was added and the mixture stirred for 90 minutes. The layers were separated and the aqueous layer extracted with diethyl ether (50 mL). The combined organic layers were dried (Na_2SO_4) and the solvent removed under reduced pressure. Purification by recrystallisation from dichloromethane/hexane afforded the *title compound* as white needles (4.236 g, 63%), m.p. 93-94°C. δ_H (400 MHz, $CDCl_3$) 8.09 (1H, d, *J* 8.61 Hz), 7.90 (1H, d, *J* 9.05 Hz), 7.79 (1H, d, *J* 8.08 Hz), 7.51 (1H, ddd, *J* 8.61, 6.81, 1.38 Hz), 7.39 (1H, m), 7.38 (1H, d, *J* 9.05 Hz), 6.40 (2H, s), 5.34 (2H, s), 3.52 (3H, s); δ_C (101 MHz, $CDCl_3$) 160.67, 137.56,

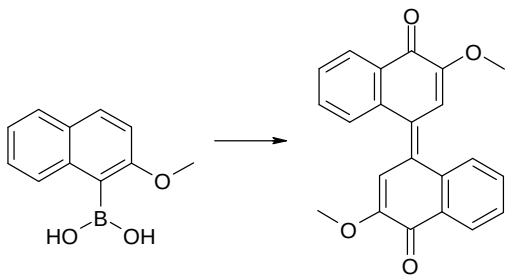
133.19, 130.30, 128.43, 128.31, 127.22, 124.56, 116.06, 96.15, 56.94; HRMS: Found 231.0877 $C_{12}H_{12}BO_4$ ($M+H^-$) Requires 231.0834.

1-(2-Cyanophenyl)-2-methoxymethyloxynaphthalene - 180:



1-Bromo-2-methoxymethyloxynaphthaleneboronic acid (0.866 g, 3.733 mmol), 2-bromobenzonitrile (0.453 g, 2.489 mmol), caesium fluoride (0.605 g, 3.982 mmol) and 2mol% $PdCl_2$(dppf) (0.0407 g, 0.0497 mmol) were dissolved in dimethoxyethane (20 mL) and the reaction mixture heated to reflux for 72 hours. The crude mixture was diluted with dichloromethane, filtered through celite and the solvent removed under reduced pressure. Purification by silica gel column chromatography (Hexane/DCM 2:1) afforded the *title compound* as colourless crystals (0.344 g, 48%), m.p. 133-134.5°C. δ_H (400 MHz, $CDCl_3$) 7.92 (1H, d, *J* 8.94 Hz), 7.90-7.98 (2H, m), 7.70 (1H, m), 7.57 (1H, d, *J* 9.12 Hz), 7.52 (1H, m), 7.46 (1H, m), 7.40-7.34 (2H, m), 7.28 (1H, m), 5.25 (1H, d, *J* 6.94 Hz), 5.15 (1H, d, *J* 6.94 Hz), 3.38 (3H, s); δ_C (101 MHz, $CDCl_3$) 152.33, 141.07, 132.07, 132.60, 132.31, 130.99, 129.80, 128.40, 127.97, 127.15, 124.56, 124.42, 122.21, 118.49, 116.41, 115.03, 95.55, 56.39; *m/z* (CI) 307.2 ($M+NH_4^+$, 100%), 289.2 (10), 45.1 (15); HRMS: Found 307.1440 $C_{19}H_{19}N_2O_2$ Requires 307.1441.

3,3'-Dimethoxy-1,1'-binaphthylidene-4,4'-dione - 182:



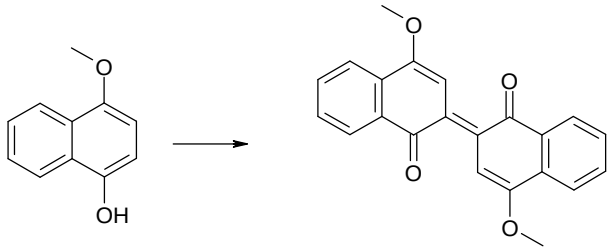
i) In presence of $Pd(OAc)_2$

To a solution of 2-methoxynaphthaleneboronic acid (0.311 g, 1.539 mmol) in a toluene/H_2O/ethanol (3:1:3, 15 mL) mixture was added $Pd(OAc)_2$ (6.914 mg, 0.0308 mmol) and barium hydroxide octahydrate (0.971 g, 3.078 mmol). The mixture was stirred at ambient temperature and open to the atmosphere for 24 hours. The mixture was diluted with dichloromethane and filtered through celite. The filtrate was washed with water (3x25 mL), brine (25 mL), dried (Na_2SO_4) and the solvent removed under reduced pressure. Purification by silica gel column chromatography (Hexane/DCM 1:1) afforded the title compound as a shimmering dark purple solid (0.261 g, 98%). δ_H (400 MHz, $CDCl_3$) 8.37 (2H, m), 7.91 (2H, m), 7.61 (4H, m), 7.29 (2H, s), 3.99 (4H, s).

ii) In absence of $Pd(OAc)_2$

To a solution of 2-methoxynaphthaleneboronic acid (0.421 g, 2.084 mmol) in a toluene/H_2O/ethanol (3:1:3, 15 mL) mixture was added barium hydroxide octahydrate (1.315 g, 4.168 mmol). The mixture was stirred at ambient temperature and open to the atmosphere for 24 hours. The mixture was diluted with dichloromethane and washed with water (2x25 mL), brine (25 mL), dried (Na_2SO_4) and the solvent removed under reduced pressure to afford the title compound as a shimmering dark purple solid (0.358 g, 99%). δ_H (400 MHz, $CDCl_3$) 8.38 (2H, m), 7.90 (2H, m), 7.60 (4H, m), 7.33 (2H, s), 4.01 (4H, s).

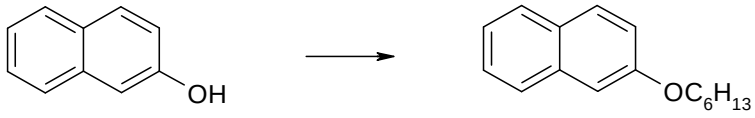
4,4'-Dimethoxy-2,2'-binaphthylidene-1,1'-dione - 188:



To a solution of 4-methoxy-1-naphthol (0.215 g, 1.234 mmol), in a toluene/water/ethanol mixture (3:1:3, 10 mL) was added barium hydroxide octahydrate (0.779 g, 2.469 mmol) and the mixture stirred at ambient temperature, open to the atmosphere, until TLC indicated consumption of starting material. The mixture was washed with water (2x25 mL), brine (25 mL), dried (Na_2SO_4) and the

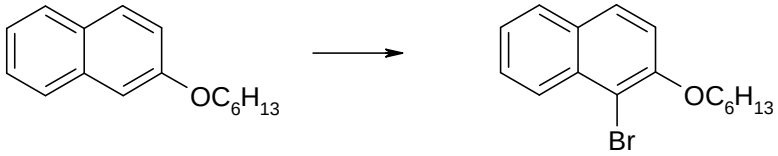
solvent removed under reduced pressure to afford the title compound as a dark blue solid (4.217 g, 99%). δ_H (400 MHz, $CDCl_3$) 8.38 (2H, s), 8.13 (2H, d, *J* 7.75), 7.76 (2H, d, *J* 7.75), 7.58 (2H, m), 7.45 (2H, m), 4.04 (6H, s).

2-Hexyloxynaphthalene - 190:



To a solution of 1-naphthol (29.984 g, 0.2084 mol) in acetone (300 mL) was added potassium carbonate (57.489 g, 0.416 mol) and 1-bromohexane (68.666 g, 0.416 mol, 58.4 mL). The reaction mixture was heated to reflux for 48 hours before filtering and removing the solvent under reduced pressure. The crude product was dissolved in dichloromethane (150 mL) and washed with dilute hydrochloric acid (1M, 100 mL), water (100 mL), brine (100 mL) and dried (Na_2SO_4). Purification by distillation (160-162°C, 1.5 mmHg) afforded the title compound as a yellow oil (42.570 g, 90%). δ_H (400 MHz, $CDCl_3$) 7.68 (1H, d, *J* 8.06), 7.65 (1H, d, *J* 8.96), 7.37 (1H, ddd, *J* 8.06, 6.93, 1.12), 7.26 (1H, ddd, *J* 8.06, 6.93, 1.12), 7.11 (1H, d, *J* 8.96), 7.03 (1H, s), 3.94 (2H, t, *J* 6.55), 1.75 (2H, m), 1.42 (2H, m), 1.30 (4H, m), 0.89 (3H, t, *J* 6.65).

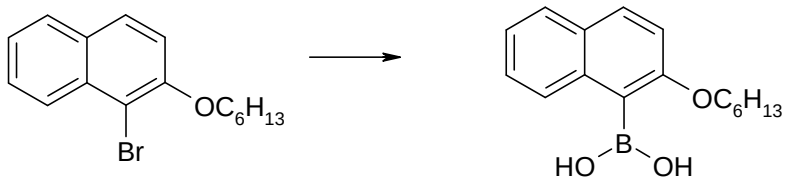
1-Bromo-2-hexyloxynaphthalene - 191:[181]



To a solution of 2-hexyloxynaphthalene (19.666 g, 86.137 mol) in acetic acid (200 mL) was added an aqueous solution of hydrobromic acid (48%, 100 mL) followed by the dropwise addition of dimethylsulphoxide (1.409 mol, 100 mL). The reaction mixture was stirred until TLC confirmed completion of the reaction. The reaction was cautiously quenched with saturated sodium hydrogen carbonate and extracted into diethylether (200 mL). The aqueous layer was extracted with diethyl ether (2x50 mL) and the combined organic layers washed with water (2x100 mL), brine (100 mL), dried (Na_2SO_4) and the solvent removed under reduced pressure. Recrystallisation from ethanol afforded the title compound as white crystals (23.813

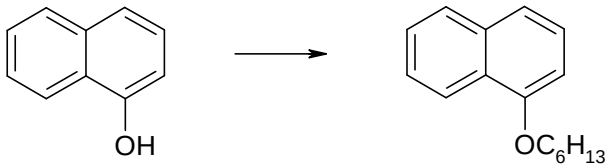
g, 90%), m.p. 59°C (lit. 59°C). δ_H (400 MHz, $CDCl_3$) 8.21 (1H, d, *J* 8.60), 7.76 (1H, d, *J* 9.10), 7.75 (1H, d, *J* 8.16), 7.54 (1H, ddd, *J* 8.16, 6.88, 1.19), 7.37 (1H, ddd, *J* 8.01, 6.88, 1.06), 7.23 (1H, d, *J* 9.10), 4.15 (2H, t, *J* 6.52), 1.86 (2H, m), 1.54 (2H, m), 1.36 (4H, m), 0.91 (3H, t, *J* 7.05).

2-Hexyloxy-1-naphthalene boronic acid - 192:[212]



n-Butyllithium (2.5M in hexanes, 25.093 mmol, 10.0 mL) was added to a stirred solution of 1-bromo-2-hexyloxynaphthalene (7.008 g, 22.812 mmol) in anhydrous diethyl ether (90 mL) at -78°C. The solution was allowed to warm to ambient temperature and stirred for 2 hours. After re-cooling to -78°C trimethylborate (2.607 g, 25.093 mmol, 2.8 mL) was added dropwise and the mixture allowed to warm to ambient temperature over 12 hours. Dilute hydrochloric acid (1M, 100 mL) was added and the mixture stirred for 90 minutes. The layers were separated and the aqueous layer extracted with diethyl ether (50 mL). The organic layer was dried (Na_2SO_4) and the solvent removed under reduced pressure. Purification by recrystallisation from diethylether/hexane afforded the title compound as white crystals (4.840 g, 77%). δ_H (400 MHz, $CDCl_3$) 8.93 (1H, d, *J* 8.68), 7.91 (1H, d, *J* 9.05), 7.77 (1H, d, *J* 8.09), 7.50 (1H, m), 7.36 (1H, m), 7.25 (1H, d, *J* 9.05), 6.68 (2H, s), 4.20 (2H, t, *J* 6.64), 1.88 (2H, m), 1.50 (2H, m), 1.36 (4H, m), 0.92 (3H, t, *J* 6.88).

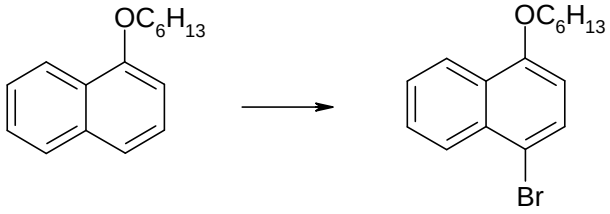
1-Hexyloxynaphthalene - 193:



To a solution of 1-naphthol (30.775 g, 0.214 mol) in acetone (300 mL) was added potassium carbonate (59.015 g, 0.427 mol) and 1-bromohexane (70.477 g, 0.427 mol, 59.9 mL). The reaction mixture was heated to reflux for 48 hours before

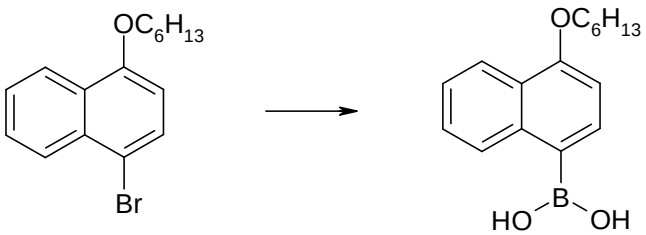
filtering and removing the solvent under reduced pressure. The crude product was dissolved in dichloromethane (150 mL) and washed with hydrochloric acid (1M, 100 mL), water (100 mL), brine (100 mL) and dried (Na_2SO_4). Purification by distillation (178-180°C, 3 mmHg) afforded the title compound as a colourless oil (43.016 g, 88%). δ_H (400 MHz, $CDCl_3$) 8.31 (1H, m), 7.79 (1H, m), 7.51-7.34 (4H, m), 6.79 (1H, dd, *J* 7.36, 0.98), 4.12 (2H, t, *J* 6.42), 1.93 (2H, m), 1.57 (2H, m), 1.39 (4H, m), 0.94 (3H, t, *J* 7.03).

1-Bromo-4-hexyloxynaphthalene - 194:[214, 215]



To a solution of 1-hexyloxynaphthalene (20.722 g, 88.792 mol) in acetonitrile (300 mL) was added *N*-bromosuccinimide (17.385 g, 97.671 mol). The reaction mixture was stirred at ambient temperature for 32 hours before filtering the precipitate. The crude product was dissolved in dichloromethane (150 mL) and washed with saturated sodium hydrogen carbonate (100 mL). Precipitation by addition of ethanol followed by recrystallisation from ethanol afforded the title compound as white crystals (23.802 g, 87%), m.p. 41-42°C (lit. 41°C). δ_H (400 MHz, $CDCl_3$) 8.21 (1H, d, *J* 8.31), 8.06 (1H, d, *J* 8.43), 7.53 (1H, d, *J* 8.20), 7.50 (1H, m), 7.42 (1H, m), 6.54 (1H, d, *J* 8.20), 3.98 (2H, t, *J* 6.40), 1.81 (2H, m), 1.45 (2H, m), 1.28 (4H, m), 0.83 (3H, t, *J* 6.42).

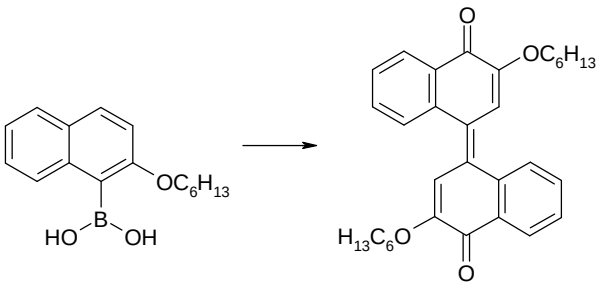
4-Hexyloxy-1-naphthalene boronic acid - 195:[214]



1-Bromo-4-hexyloxynaphthalene (5.311 g, 17.288 mmol) in anhydrous diethylether (40 mL) was added to magnesium turnings (0.462 g, 19.017 mmol) in anhydrous diethylether (25 mL) at a sufficient rate as to maintain reflux. After addition the

reaction mixture was heated to reflux for 2 hours. The solution was cooled and added dropwise to a solution of trimethylborate (2.695 g, 25.936 mmol, 2.9 mL) in anhydrous diethyl ether (20 mL) at -78°C. After addition the mixture was allowed to warm to ambient temperature over 12 hours before being quenched with dilute hydrochloric acid (1M, 100 mL) and stirred for 90 minutes. The crude product was extracted with dichloromethane (2x75 mL) and the organic layer washed with water (100 mL), dried (Na_2SO_4) and the solvent removed under reduced pressure to afford the title compound as a white solid (3.161 g, 67%). δ_H (400 MHz, $CDCl_3$) 8.31 (1H, d *J* 8.66), 7.93 (1H, d, *J* 9.06), 7.69-7.58 (3H, m), 6.94 (1H, d, *J* 8.20), 6.49 (2H, brs), 4.18 (2H, t, *J* 6.72), 1.92 (2H, m), 1.49 (2H, m), 1.33 (4H, m), 0.99 (3H, t, *J* 6.76).

3,3'-Dihexyloxy-1,1'-binaphthylidene-4,4'-dione - 196:



i) Using $Ba(OH)_2$

To a solution of 2-hexyloxynaphthaleneboronic acid (0.454 g, 1.668 mmol) in a toluene:H_2O:ethanol mixture (3:1:3, 40 mL) was added barium hydroxide octahydrate (1.053 g, 3.337 mmol) and the mixture was stirred at ambient temperature, open to the atmosphere until TLC indicated complete reaction of starting material. The mixture was diluted with dichloromethane and washed with water (3x30 mL), brine (30 mL), dried (Na_2SO_4) and the solvent removed under reduced pressure to afford the *title compound* as a dark purple solid (0.401 g, 99%). δ_H (400 MHz, $CDCl_3$) 8.35 (2H, m), 7.93 (2H, m), 7.59 (4H, m), 7.29 (2H, s), 3.98 (4H, t, *J* 7.26), 1.79 (4H, m), 1.46-1.91 (12H, m), 0.82 (6H, t, *J* 6.72). δ_C (101 MHz, $CDCl_3$) 186.51, 184.77, 183.84, 183.76, 136.17, 133.60, 132.08, 131.32, 128.83, 127.39, 63.31, 32.97, 31.83, 25.61, 22.83, 14.24; *m/z* (EI) 484.3 (M^+, 10%), 55.2 (100); HRMS: Found: 484.2603 $C_{32}H_{36}O_4$ (M^+) Requires 484.2608.

ii) Using NaOH

To a solution of 2-hexyloxynaphthaleneboronic acid (0.379 g, 1.393 mmol) in a toluene:H_2O:ethanol mixture (3:1:3, 25 mL) was added solid sodium hydroxide (0.111 g, 2.786 mmol) and the mixture was stirred at ambient temperature, open to the atmosphere until TLC indicated complete reaction of starting material. TLC indicated no oxidative dimerised product with possible product degradation.

iii) Using KOH

To a solution of 2-hexyloxynaphthaleneboronic acid (0.960 g, 3.528 mmol) in a toluene:H_2O:ethanol mixture (3:1:3, 40 mL) was added solid potassium hydroxide (0.396 g, 7.056 mmol) and the mixture was stirred at ambient temperature, open to the atmosphere until TLC indicated complete reaction of starting material. TLC indicated no oxidative dimerised product with possible product degradation.

iii) Using K_2CO_3

To a solution of 2-hexyloxynaphthaleneboronic acid (0.471 g, 1.731 mmol) in a toluene:H_2O:ethanol mixture (3:1:3, 40 mL) was added potassium carbonate (0.478 g, 3.462 mmol) and the mixture was stirred at ambient temperature, open to the atmosphere. No reaction occurred with complete recovery of starting material.

iii) Using K_3PO_4

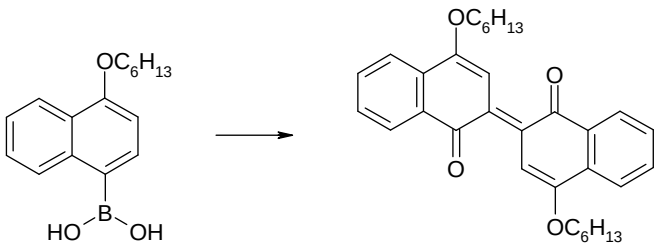
To a solution of 2-hexyloxynaphthaleneboronic acid (0.502 g, 1.845 mmol) in a toluene:H_2O:ethanol mixture (3:1:3, 40 mL) was added tripotassium phosphate (0.783 g, 3.689 mmol) and the mixture was stirred at ambient temperature, open to the atmosphere. The mixture was diluted with dichloromethane and washed with water (2x30 mL), brine (30 mL), dried (Na_2SO_4) and the solvent removed under reduced pressure to afford the *title compound* as a dark purple solid (0.443 g, 99%). δ_H (400 MHz, $CDCl_3$) 8.34 (2H, m), 7.94 (2H, m), 7.59 (4H, m), 7.31 (2H, s), 4.00 (4H, t, *J* 7.26), 1.77 (4H, m), 1.48-1.90 (12H, m), 0.77 (6H, t, *J* 6.72).

iv) Using $Ba(OH)_2$ in DCM:H_2O:Ethanol

To a solution of 2-hexyloxynaphthaleneboronic acid (0.312 g, 1.147 mmol) in a dichloromethane:H_2O:ethanol mixture (3:1:3, 20 mL) was added barium hydroxide

octahydrate (0.723 g, 2.293 mmol) and the mixture was stirred at ambient temperature, open to the atmosphere until TLC indicated complete reaction of starting material. The mixture was diluted with dichloromethane and washed with water (3x30 mL), brine (30 mL), dried (Na_2SO_4) and the solvent removed under reduced pressure to afford the *title compound* as a shimmering dark purple solid (0.276 g, 99%). δ_H (400 MHz, $CDCl_3$) 8.35 (2H, m), 7.95 (2H, m), 7.60 (4H, m), 7.33 (2H, s), 4.01 (4H, t, *J* 6.94), 1.76 (4H, m), 1.50-1.94 (12H, m), 0.79 (6H, t, *J* 6.76).

4,4'-Dihexyloxy-2,2'-binaphthylidene-1,1'-dione - 197:



i) Using $Ba(OH)_2$

To a solution of 4-hexyloxynaphthaleneboronic acid (1.019 g, 3.979 mmol) in a toluene:H_2O:ethanol mixture (3:1:3, 40 mL) was added barium hydroxide octahydrate (2.510 g, 7.957 mmol) and the mixture was stirred at ambient temperature, open to the atmosphere until TLC indicated complete reaction of starting material. The mixture was diluted with dichloromethane and washed with water (3x30 mL), brine (30 mL), dried (Na_2SO_4) and the solvent removed under reduced pressure to afford the *title compound* as a dark blue-black solid (0.958 g, 99%). δ_H (400 MHz, $CDCl_3$) 8.35 (2H, s), 8.11 (2H, d, *J* 7.79), 7.76 (2H, d, *J* 7.79), 7.59 (2H, m), 7.43 (2H, m), 4.01 (4H, t, *J* 6.76), 1.69 (4H, m), 1.41-1.89 (12H, m), 0.79 (6H, t, *J* 6.94).

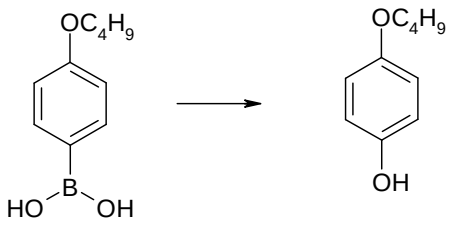
ii) Using NaOH

To a solution of 4-hexyloxynaphthaleneboronic acid (0.526 g, 1.933 mmol) in a toluene:H_2O:ethanol mixture (3:1:3, 40 mL) was added solid sodium hydroxide (0.155 g, 3.866 mmol) and the mixture was stirred at ambient temperature, open to the atmosphere until TLC indicated complete reaction of starting material. TLC indicated no oxidative dimerised product with possible product degradation.

iii) Using KOH

To a solution of 4-hexyloxynaphthaleneboronic acid (1.069 g, 4.174 mmol) in a toluene:H_2O:ethanol mixture (3:1:3, 40 mL) was added solid potassium hydroxide (0.468 g, 8.348 mmol) and the mixture was stirred at ambient temperature, open to the atmosphere until TLC indicated complete reaction of starting material. TLC indicated no oxidative dimerised product with possible product degradation.

4-Butyloxyphenol - 203:



i) Using $Ba(OH)_2$ at ambient temperature

To a solution of 4-butyloxybenzeneboronic acid (0.159 g, 0.819 mmol) in a toluene:H_2O:ethanol mixture (3:1:3, 15 mL) was added barium hydroxide octahydrate (0.517 g, 1.639 mmol) and the mixture was stirred at ambient temperature open to the atmosphere for 96 hours. Complete recovery of starting material was observed.

ii) Using $Ba(OH)_2$ at 60°C

To a solution of 4-butyloxybenzeneboronic acid (0.228 g, 1.175 mmol) in a toluene:H_2O:ethanol mixture (3:1:3, 20 mL) was added barium hydroxide octahydrate (0.741 g, 2.350 mmol) and the mixture was stirred at 60°C open to the atmosphere for 120 hours. The cooled mixture was diluted with dichloromethane and washed with water (3x30 mL), brine (30 mL), dried (Na_2SO_4) and the solvent removed under reduced pressure. Partial conversion to the title compound was observed by ^{1}H NMR.

iii) Using KOH at ambient temperature

To a solution of 4-butyloxybenzeneboronic acid (0.208 g, 1.072 mmol) in a toluene:H_2O:ethanol mixture (3:1:3, 15 mL) was added solid potassium hydroxide

(0.120 g, 2.144 mmol) and the mixture was stirred at ambient temperature open to the atmosphere for 96 hours. Complete recovery of starting material was observed.

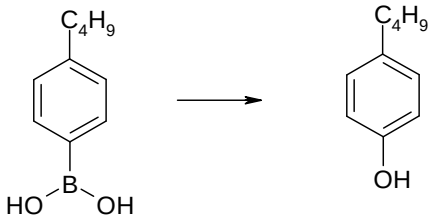
iv) Using KOH at 60°C

To a solution of 4-butyloxybenzeneboronic acid (0.197 g, 1.015 mmol) in a toluene:H_2O:ethanol mixture (3:1:3, 20 mL) was added solid potassium hydroxide (0.641 g, 2.031 mmol) and the mixture was stirred at 60°C open to the atmosphere for 24 hours. The cooled mixture was diluted with dichloromethane and washed with water (3x30 mL), brine (30 mL), dried (Na_2SO_4) and the solvent removed under reduced pressure. Partial conversion to the title compound was observed by ^{1}H NMR.

v) Using $Ba(OH)_2$ at 100°C

To a solution of 4-butyloxybenzeneboronic acid (0.222 g, 1.144 mmol) in a toluene:H_2O:ethanol mixture (3:1:3, 20 mL) was added barium hydroxide octahydrate (0.722 g, 2.289 mmol) and the mixture was stirred at 100°C open to the atmosphere for 120 hours. The cooled mixture was diluted with dichloromethane and washed with water (3x30 mL), brine (30 mL), dried (Na_2SO_4) and the solvent removed under reduced pressure. Partial conversion to the title compound was observed by ^{1}H NMR.

4-Butylphenol - 206:



i) Using $Ba(OH)_2$ at ambient temperature

To a solution of 4-butylbenzeneboronic acid (0.251 g, 1.409 mmol) in a toluene:H_2O:ethanol mixture (3:1:3, 25 mL) was added barium hydroxide octahydrate (0.889 g, 2.819 mmol) and the mixture was stirred at ambient temperature open to the atmosphere for 120 hours. Complete recovery of starting material was observed.

ii) Using $Ba(OH)_2$ at 60°C

To a solution of 4-butylbenzeneboronic acid (0.106 g, 0.546 mmol) in a toluene:H_2O:ethanol mixture (3:1:3, 15 mL) was added barium hydroxide octahydrate (0.304 g, 1.092 mmol) and the mixture was stirred at 60°C open to the atmosphere for 120 hours. Complete recovery of starting material was observed.

iii) Using $Ba(OH)_2$ at 100°C

To a solution of 4-butylbenzeneboronic acid (0.215 g, 1.207 mmol) in a toluene:H_2O:ethanol mixture (3:1:3, 15 mL) was added barium hydroxide octahydrate (0.762 g, 2.416 mmol) and the mixture was stirred at 100°C open to the atmosphere for 120 hours. Complete recovery of starting material was observed.

iv) Using KOH at 60°C

To a solution of 4-butylbenzeneboronic acid (0.177 g, 0.994 mmol) in a toluene:H_2O:ethanol mixture (3:1:3, 15 mL) was added barium hydroxide octahydrate (0.627 g, 1.989 mmol) and the mixture was stirred at 60°C open to the atmosphere for 120 hours. Complete recovery of starting material was observed.

v) Using KOH at 100°C

To a solution of 4-butylbenzeneboronic acid (0.250 g, 1.404 mmol) in a toluene:H_2O:ethanol mixture (3:1:3, 15 mL) was added barium hydroxide octahydrate (0.158 g, 2.808 mmol) and the mixture was stirred at 100°C open to the atmosphere for 120 hours. Complete recovery of starting material was observed.

Chapter 4

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Appendix 1

X-ray Crystal Structure Data

Crystal structure analysis of (*S*)-2,2'-diethoxy-6,6'-bis(m-hexyloxyphenyl)-1,1'-binaphthyl - 128

Crystal data: $C_{48}H_{54}O_4$, M = 694.9. Monoclinic, space group $P2_1$ (no. 4), a = 11.8078(12), b = 7.6226(8), c = 21.7245(19) Å, β = 91.263(8) °, V = 1954.9(3) $Å^3$. Z = 2, Dc = 1.181 g cm^{-3}, F(000) = 748, T = 140(1) K, μ(Mo-Kα) = 0.7 cm^{-1}, λ(Mo-Kα) = 0.71069 Å.

Crystals are colourless needles. One, *ca* 0.50 x 0.08 x 0.05 mm, was mounted in oil on a glass fibre and fixed in the cold nitrogen stream on an Oxford Diffraction Xcalibur-3 CCD diffractometer equipped with Mo-Kα radiation and graphite monochromator. Intensity data were measured by thin-slice ω- and φ-scans. Total no. of reflections recorded, to θ_{max} = 22.5°, was 19974 of which 5081 were unique (Rint = 0.102); 2967 were 'observed' with $I > 2\sigma_I$.

Data were processed using the CrysAlisPro-CCD and -RED (1) programs. The structure was determined by the direct methods routines in the SHELXS program (2A) and refined by full-matrix least-squares methods, on F^2's, in SHELXL (2B). The non-hydrogen atoms were refined with anisotropic thermal parameters. Hydrogen atoms were included in idealised positions and their Uiso values were set to ride on the Ueq values of the parent carbon atoms. At the conclusion of the refinement, wR_2 = 0.095 and R_1 = 0.099 (2B) for all 5081 reflections weighted $w = [\sigma^2(F_o^2) + (0.0345P)^2]^{-1}$ with $P = (F_o^2 + 2F_c^2)/3$; for the 'observed' data only, R_1 = 0.054.

In the final difference map, the highest peak (*ca* 0.16 $eÅ^{-3}$) was close to H(23a).

Scattering factors for neutral atoms were taken from reference (3). Computer programs used in this analysis have been noted above, and were run through WinGX (4) on a Dell Precision 370 PC at the University of East Anglia.

References

(1) Programs CrysAlisPro-CCD and -RED, Oxford Diffraction Ltd., Abingdon, UK (2008).

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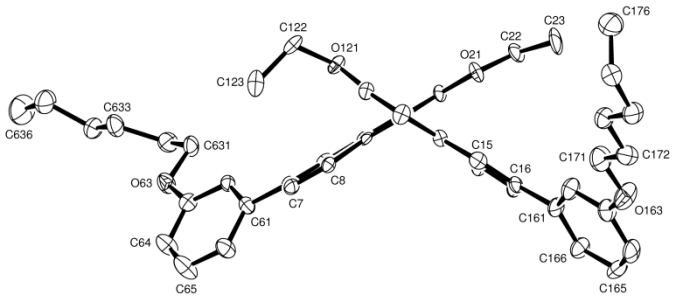
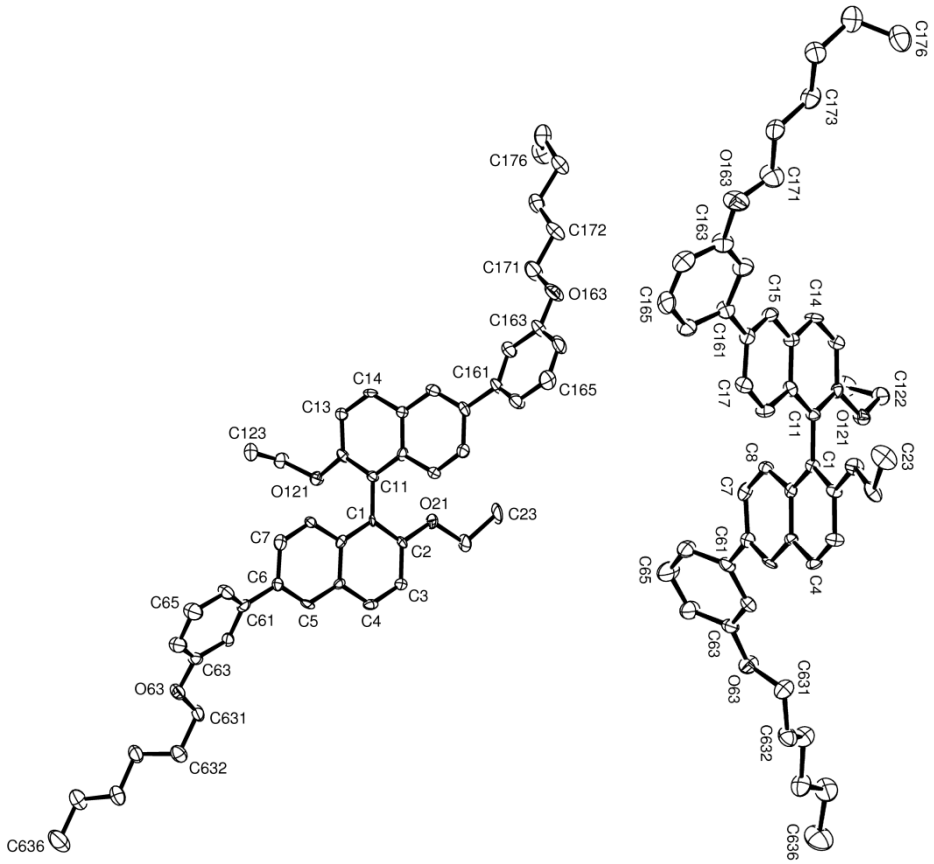
Legends for Figures

Figure 1. Views of a molecule of 2,2'-diethoxy-6,6'-bis(m-hexyloxy-phenyl)-1,1'-binaphthyl, indicating the atom numbering scheme. Hydrogen atoms have been omitted for clarity. Thermal ellipsoids are drawn at the 50% probability level.

Notes on the structure





Crystal structure refinement data for (*S*)-2,2'-diethoxy-6,6'-bis(m-hexyloxyphenyl)-1,1'-binaphthyl – 128

Identification code	chriss3 (CS02)
Elemental formula	C48 H54 O4
Formula weight	694.9
Crystal system	Monoclinic
Space group	$P2_1$ (no. 4)
Unit cell dimensions	a = 11.8078(12) Å α = 90 °
	b = 7.6226(8) Å β = 91.263(8) °
	c = 21.7245(19) Å γ = 90 °
Volume	1954.9(3) $Å^3$
No. of formula units, Z	2
Calculated density	1.181 Mg/m^3
F(000)	748
Absorption coefficient	0.073 mm^{-1}
Temperature	140(1) K
Wavelength	0.71073 Å
Crystal colour, shape	colourless needle
Crystal size	0.50 x 0.08 x 0.05 mm
Crystal mounting	on a glass fibre, in oil, fixed in cold N_2 stream
On the diffractometer:	
Theta range for data collection	3.5 to 22.5 °
Limiting indices	-12<=h<=12, -8<=k<=8, -23<=l<=23
Completeness to theta = 22.5	99.5 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	1.057 and 0.912
Reflections collected (not including absences)	19974
No. of unique reflections	5081 [R(int) for equivalents = 0.102]
No. of 'observed' reflections ($I > 2\sigma_I$)	2967
Structure determined by:	direct methods, in SHELXS
Refinement:	Full-matrix least-squares on F^2, in SHELXL
Data / restraints / parameters	5081 / 1 / 469
Goodness-of-fit on F^2	0.829
Final R indices ('observed' data)	$R_1 = 0.054$, $wR_2 = 0.086$
Final R indices (all data)	$R_1 = 0.099$, $wR_2 = 0.095$
Reflections weighted:	$w = [\sigma^2(Fo^2)+(0.0345P)^2]^{-1}$
	where $P=(Fo^2+2Fc^2)/3$
Absolute structure parameter	0.0(17)
Largest diff. peak and hole	0.16 and -0.16 $e.Å^{-3}$
Location of largest difference peak	near H(23a)

Table 1. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^4). U(eq) is defined as one third of the trace of the orthogonalized Uij tensor. E.s.ds are in parentheses.

	x	y	z	U(eq)
C(1)	5451(4)	6171(5)	3678.6(18)	129(11)
C(2)	6512(4)	6724(6)	3870.2(19)	169(12)
O(21)	7380(3)	6406(4)	3485.9(12)	241(8)
C(22)	8463(4)	7113(6)	3644(2)	275(13)
C(23)	9201(4)	6908(6)	3093(2)	404(15)
C(3)	6676(4)	7590(6)	4437.7(18)	213(12)
C(4)	5792(4)	7895(5)	4814.8(19)	203(12)
C(5)	3750(4)	7667(5)	5024.3(18)	176(11)
C(6)	2686(4)	7152(6)	4858.8(19)	181(12)
C(7)	2519(4)	6376(5)	4273.0(19)	228(12)
C(8)	3407(4)	6065(5)	3897.8(19)	166(11)
C(9)	4535(4)	6503(5)	4065.7(19)	156(12)
C(10)	4681(4)	7363(5)	4640.8(18)	148(11)
C(61)	1726(4)	7395(6)	5272(2)	208(11)
C(62)	1867(4)	7209(5)	5907.7(19)	198(11)
C(63)	967(4)	7371(6)	6291(2)	230(12)
C(64)	-98(4)	7765(6)	6052(2)	336(14)
C(65)	-254(4)	7968(7)	5426(2)	409(15)
C(66)	653(4)	7801(6)	5037(2)	289(13)
O(63)	1016(2)	7198(4)	6918.8(13)	296(8)
C(631)	2094(4)	7163(7)	7219.1(17)	281(13)
C(632)	1920(4)	7516(6)	7896.3(19)	326(13)
C(633)	1251(4)	6125(7)	8231.5(19)	337(13)
C(634)	1001(4)	6679(6)	8890(2)	357(14)
C(635)	574(5)	5211(6)	9291(2)	433(15)
C(636)	224(5)	5873(7)	9932(2)	604(18)
C(11)	5278(4)	5216(6)	3087.5(18)	161(11)
C(12)	4931(4)	3465(6)	3094(2)	176(12)
O(121)	4857(2)	2710(4)	3659.0(13)	241(8)
C(122)	4321(4)	1015(6)	3720(2)	273(13)
C(123)	3056(4)	1137(6)	3649(2)	378(14)
C(13)	4715(3)	2553(6)	2546.8(18)	199(12)
C(14)	4892(4)	3343(5)	1995.4(19)	211(12)
C(15)	5527(4)	5869(6)	1388(2)	220(12)
C(16)	5908(4)	7584(6)	1350.9(19)	204(12)
C(17)	6012(4)	8541(6)	1904(2)	231(12)
C(18)	5819(4)	7798(6)	2464.2(19)	223(12)
C(19)	5461(4)	6013(6)	2514(2)	178(11)
C(20)	5292(4)	5069(6)	1959.0(19)	179(12)
C(161)	6175(4)	8407(6)	754(2)	256(13)
C(162)	6549(4)	7420(7)	261.6(19)	310(13)
C(163)	6779(4)	8188(7)	-288(2)	335(14)
C(164)	6662(4)	10023(7)	-355(2)	362(14)
C(165)	6293(4)	10982(6)	120(2)	355(14)
C(166)	6049(4)	10212(6)	677(2)	300(13)
O(163)	7157(3)	7382(5)	-808.1(14)	453(10)
C(171)	7189(5)	5511(7)	-824(2)	444(16)
C(172)	7537(4)	5052(6)	-1476(2)	353(15)
C(173)	7575(4)	3085(6)	-1586(2)	361(14)
C(174)	7986(4)	2653(6)	-2228(2)	378(14)
C(175)	8064(4)	666(6)	-2359(2)	440(16)
C(176)	8879(4)	-278(7)	-1939(2)	512(16)

Table 2. Molecular dimensions. Bond lengths are in Angstroms, angles in degrees. E.s.ds are in parentheses.

C(1)-C(11)	1.486(5)	C(11)-C(12)	1.396(5)
C(1)-C(2)	1.378(5)	C(11)-C(19)	1.408(5)
C(1)-C(9)	1.407(5)	C(12)-O(121)	1.360(5)
C(2)-O(21)	1.358(5)	C(12)-C(13)	1.395(5)
C(2)-C(3)	1.408(5)	O(121)-C(122)	1.446(5)
O(21)-C(22)	1.423(5)	C(122)-C(123)	1.501(6)
C(22)-C(23)	1.504(5)	C(13)-C(14)	1.361(5)
C(3)-C(4)	1.362(5)	C(14)-C(20)	1.401(5)
C(4)-C(10)	1.416(5)	C(15)-C(16)	1.385(6)
C(5)-C(6)	1.357(5)	C(15)-C(20)	1.415(5)
C(5)-C(10)	1.413(5)	C(16)-C(161)	1.482(5)
C(6)-C(61)	1.473(6)	C(16)-C(17)	1.410(6)
C(6)-C(7)	1.413(5)	C(17)-C(18)	1.365(5)
C(7)-C(8)	1.363(5)	C(18)-C(19)	1.430(6)
C(8)-C(9)	1.414(5)	C(19)-C(20)	1.413(5)
C(9)-C(10)	1.418(5)	C(161)-C(162)	1.387(6)
C(61)-C(62)	1.394(5)	C(161)-C(166)	1.393(6)
C(61)-C(66)	1.390(6)	C(162)-C(163)	1.362(5)
C(62)-C(63)	1.370(5)	C(163)-O(163)	1.370(5)
C(63)-O(63)	1.370(4)	C(163)-C(164)	1.413(6)
C(63)-C(64)	1.384(5)	C(164)-C(165)	1.345(6)
C(64)-C(65)	1.377(6)	C(165)-C(166)	1.380(6)
C(65)-C(66)	1.384(6)	O(163)-C(171)	1.427(5)
O(63)-C(631)	1.418(5)	C(171)-C(172)	1.524(6)
C(631)-C(632)	1.514(5)	C(172)-C(173)	1.519(6)
C(632)-C(633)	1.518(6)	C(173)-C(174)	1.523(5)
C(633)-C(634)	1.527(5)	C(174)-C(175)	1.544(6)
C(634)-C(635)	1.512(6)	C(175)-C(176)	1.496(6)
C(635)-C(636)	1.546(6)		

C(2)-C(1)-C(9)	118.0(4)	C(13)-C(14)-C(20)	121.6(4)
C(2)-C(1)-C(11)	121.2(4)	C(16)-C(15)-C(20)	121.8(4)
C(9)-C(1)-C(11)	120.8(4)	C(15)-C(16)-C(161)	121.7(4)
O(21)-C(2)-C(1)	116.9(4)	C(15)-C(16)-C(17)	117.5(4)
C(1)-C(2)-C(3)	121.0(4)	C(17)-C(16)-C(161)	120.8(4)
O(21)-C(2)-C(3)	122.1(4)	C(18)-C(17)-C(16)	122.1(4)
C(2)-O(21)-C(22)	118.0(3)	C(17)-C(18)-C(19)	121.2(4)
O(21)-C(22)-C(23)	107.6(3)	C(11)-C(19)-C(18)	121.9(4)
C(4)-C(3)-C(2)	120.9(4)	C(11)-C(19)-C(20)	120.9(4)
C(3)-C(4)-C(10)	120.6(4)	C(20)-C(19)-C(18)	117.1(4)
C(6)-C(5)-C(10)	121.6(4)	C(14)-C(20)-C(15)	121.8(4)
C(5)-C(6)-C(61)	121.5(4)	C(14)-C(20)-C(19)	118.1(4)
C(5)-C(6)-C(7)	118.0(4)	C(19)-C(20)-C(15)	120.1(4)
C(7)-C(6)-C(61)	120.5(4)	C(162)-C(161)-C(16)	121.5(4)
C(8)-C(7)-C(6)	121.2(4)	C(166)-C(161)-C(16)	119.9(4)
C(7)-C(8)-C(9)	122.5(4)	C(162)-C(161)-C(166)	118.6(5)
C(1)-C(9)-C(8)	122.4(4)	C(163)-C(162)-C(161)	121.0(5)
C(1)-C(9)-C(10)	122.0(4)	C(162)-C(163)-O(163)	127.2(5)
C(8)-C(9)-C(10)	115.6(4)	C(162)-C(163)-C(164)	119.7(5)
C(5)-C(10)-C(4)	121.6(4)	O(163)-C(163)-C(164)	113.1(4)
C(4)-C(10)-C(9)	117.5(4)	C(65)-C(64)-C(63)	119.7(5)
C(5)-C(10)-C(9)	121.0(4)	C(64)-C(65)-C(66)	120.3(5)
C(62)-C(61)-C(6)	120.9(4)	C(65)-C(66)-C(61)	120.5(4)
C(66)-C(61)-C(6)	120.7(4)	C(63)-O(63)-C(631)	118.5(3)

C(66)-C(61)-C(62)	118.4(4)	O(63)-C(631)-C(632)	107.7(4)
C(63)-C(62)-C(61)	121.0(4)	C(631)-C(632)-C(633)	115.2(4)
O(63)-C(63)-C(62)	125.5(4)	C(632)-C(633)-C(634)	111.7(4)
C(62)-C(63)-C(64)	120.2(4)	C(635)-C(634)-C(633)	114.1(4)
O(63)-C(63)-C(64)	114.4(4)	C(634)-C(635)-C(636)	112.1(4)
C(12)-C(11)-C(1)	119.6(4)	C(165)-C(164)-C(163)	119.4(5)
C(19)-C(11)-C(1)	122.2(4)	C(164)-C(165)-C(166)	121.2(5)
C(12)-C(11)-C(19)	118.2(4)	C(165)-C(166)-C(161)	120.1(5)
O(121)-C(12)-C(11)	116.0(4)	C(163)-O(163)-C(171)	118.5(4)
C(13)-C(12)-C(11)	121.0(4)	O(163)-C(171)-C(172)	105.0(4)
O(121)-C(12)-C(13)	123.0(4)	C(173)-C(172)-C(171)	112.5(4)
C(12)-O(121)-C(122)	119.8(3)	C(172)-C(173)-C(174)	111.7(4)
O(121)-C(122)-C(123)	111.8(4)	C(173)-C(174)-C(175)	113.7(4)
C(14)-C(13)-C(12)	120.0(4)	C(176)-C(175)-C(174)	113.6(4)

Table 3. Anisotropic displacement parameters ($Å^2$ x 10^3) for the expression:
Exp {$-2\Pi^2$ ($h^2a^{*2}U_{11}$ + ... + 2hka*b*U_{12})} E.s.ds are in parentheses

	U11	U22	U33	U23	U13	U12
C(1)	14(3)	12(3)	13(3)	3(2)	6(2)	-5(2)
C(2)	16(3)	21(3)	14(3)	-2(2)	8(2)	0(2)
O(21)	13(2)	31(2)	29.3(19)	-4.9(17)	5.2(16)	-4.0(16)
C(22)	18(3)	27(3)	39(3)	-4(3)	14(2)	4(2)
C(23)	26(3)	45(4)	52(3)	-4(3)	27(3)	-8(3)
C(3)	21(3)	24(3)	19(3)	-6(3)	4(2)	-5(3)
C(4)	35(3)	14(3)	11(3)	2(2)	-5(3)	-3(3)
C(5)	31(3)	11(3)	11(3)	-4(2)	7(3)	4(3)
C(6)	20(3)	16(3)	18(3)	3(2)	2(2)	-2(2)
C(7)	20(3)	25(3)	23(3)	9(3)	-3(3)	-2(2)
C(8)	21(3)	16(3)	13(3)	0(2)	3(2)	-1(2)
C(9)	18(3)	9(3)	20(3)	5(2)	-3(2)	-3(2)
C(10)	19(3)	10(3)	15(3)	0(2)	-2(2)	-3(2)
C(61)	18(3)	17(3)	27(3)	-7(3)	1(2)	-2(2)
C(62)	19(3)	16(3)	24(3)	-2(2)	6(2)	0(2)
C(63)	29(3)	20(3)	20(3)	-4(3)	2(3)	0(3)
C(64)	22(3)	48(4)	31(3)	-8(3)	-1(3)	4(3)
C(65)	22(3)	66(4)	34(3)	-9(3)	-1(3)	5(3)
C(66)	25(3)	42(3)	20(3)	-2(3)	4(3)	5(3)
O(63)	24(2)	43(2)	22.5(18)	0.5(18)	5.3(16)	1.4(18)
C(631)	24(3)	39(3)	22(3)	7(3)	5(2)	-4(3)
C(632)	33(3)	33(3)	32(3)	-1(3)	9(3)	6(3)
C(633)	27(3)	46(4)	29(3)	3(3)	7(2)	-2(3)
C(634)	35(4)	40(3)	32(3)	11(3)	6(3)	1(3)
C(635)	47(4)	45(4)	38(4)	7(3)	12(3)	2(3)
C(636)	75(5)	62(4)	46(4)	-1(4)	27(3)	5(4)
C(11)	22(3)	14(3)	13(3)	0(2)	2(2)	-1(2)
C(12)	21(3)	19(3)	13(3)	6(2)	3(2)	5(2)
O(121)	34(2)	14.0(19)	23.8(19)	1.4(17)	2.3(15)	-3.2(16)
C(122)	42(4)	14(3)	26(3)	6(2)	0(3)	-4(3)
C(123)	39(4)	38(3)	37(3)	-1(3)	12(3)	-14(3)
C(13)	23(3)	18(3)	19(3)	-2(3)	4(2)	-2(3)
C(14)	31(3)	20(3)	12(3)	-8(2)	2(2)	-4(2)
C(15)	23(3)	28(3)	15(3)	-2(2)	0(2)	2(3)
C(16)	16(3)	27(3)	18(3)	3(3)	7(2)	2(3)
C(17)	26(3)	19(3)	24(3)	0(3)	4(2)	-4(2)
C(18)	27(3)	25(3)	15(3)	-2(2)	3(2)	-6(3)
C(19)	19(3)	12(3)	22(3)	2(2)	2(2)	-3(2)
C(20)	17(3)	21(3)	16(3)	-2(2)	1(2)	-2(2)
C(161)	31(3)	29(3)	18(3)	5(3)	11(2)	2(3)

C(162)	39(3)	33(3)	22(3)	4(3)	5(2)	-4(3)
C(163)	35(4)	43(4)	23(3)	3(3)	14(3)	2(3)
C(164)	38(4)	47(4)	23(3)	11(3)	8(3)	-6(3)
C(165)	44(4)	25(3)	37(3)	12(3)	1(3)	1(3)
C(166)	40(4)	30(3)	20(3)	3(3)	6(3)	0(3)
O(163)	71(3)	41(2)	24(2)	3(2)	18.2(19)	-2(2)
C(171)	47(4)	49(4)	38(4)	1(3)	16(3)	2(3)
C(172)	37(4)	48(4)	21(3)	7(3)	8(3)	12(3)
C(173)	35(4)	43(4)	30(3)	11(3)	5(3)	0(3)
C(174)	43(4)	42(4)	29(3)	6(3)	13(3)	6(3)
C(175)	32(4)	46(4)	54(4)	9(3)	4(3)	-1(3)
C(176)	51(4)	48(4)	55(4)	5(3)	12(3)	10(3)

Table 4. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$ x 10^3). All hydrogen atoms were included in idealised positions with U(iso)'s set at 1.2*U(eq) or, for the methyl groups, 1.5*U(eq) of the parent carbon atom

	x	y	z	U(iso)
H(22A)	8790	6491	3995	33
H(22B)	8395	8343	3752	33
H(23A)	9940	7375	3187	61
H(23B)	8870	7532	2750	61
H(23C)	9264	5687	2991	61
H(3)	7399	7958	4557	26
H(4)	5918	8458	5190	24
H(5)	3870	8232	5399	21
H(7)	1791	6072	4141	27
H(8)	3265	5545	3517	20
H(62)	2584	6971	6074	24
H(64)	-707	7892	6313	40
H(65)	-971	8218	5263	49
H(66)	544	7961	4615	35
H(63A)	2582	8053	7047	34
H(63B)	2447	6027	7165	34
H(63C)	1531	8630	7936	39
H(63D)	2656	7632	8099	39
H(63E)	1678	5038	8240	40
H(63F)	543	5911	8009	40
H(63G)	1688	7155	9078	43
H(63H)	440	7609	8877	43
H(63I)	1163	4332	9342	52
H(63J)	-73	4658	9087	52
H(63K)	-48	4905	10170	91
H(63L)	-365	6733	9884	91
H(63M)	867	6391	10139	91
H(12A)	4514	528	4121	33
H(12B)	4609	226	3410	33
H(12C)	2731	-10	3689	57
H(12D)	2862	1606	3250	57
H(12E)	2767	1894	3961	57
H(13)	4451	1405	2559	24
H(14)	4744	2722	1634	25
H(15)	5422	5226	1027	26
H(17)	6219	9717	1888	28
H(18)	5922	8464	2820	27
H(162)	6645	6216	308	37
H(164)	6839	10563	-725	43
H(165)	6200	12186	72	43
H(166)	5801	10899	1001	36
H(17A)	6451	5023	-737	53

H(17B)	7736	5062	-524	53
H(17C)	7004	5580	-1767	42
H(17D)	8278	5546	-1550	42
H(17E)	6824	2597	-1537	43
H(17F)	8077	2546	-1282	43
H(17G)	8728	3173	-2279	45
H(17H)	7474	3182	-2530	45
H(17I)	7318	150	-2318	53
H(17J)	8294	497	-2781	53
H(17K)	8875	-1505	-2037	77
H(17L)	8658	-120	-1520	77
H(17M)	9627	187	-1990	77

Table 5. Torsion angles, in degrees. E.s.ds are in parentheses

C(2)-C(1)-C(11)-C(12)	113.7(5)
C(9)-C(1)-C(11)-C(12)	-64.9(6)
C(9)-C(1)-C(2)-O(21)	-179.3(4)
C(11)-C(1)-C(2)-O(21)	2.0(6)
C(9)-C(1)-C(2)-C(3)	0.3(6)
C(11)-C(1)-C(2)-C(3)	-178.4(4)
C(1)-C(2)-O(21)-C(22)	174.0(4)
C(3)-C(2)-O(21)-C(22)	-5.5(6)
C(2)-O(21)-C(22)-C(23)	-168.4(4)
O(21)-C(2)-C(3)-C(4)	179.9(4)
C(1)-C(2)-C(3)-C(4)	0.4(7)
C(2)-C(3)-C(4)-C(10)	-0.7(7)
C(10)-C(5)-C(6)-C(7)	-3.2(6)
C(10)-C(5)-C(6)-C(61)	177.1(4)
C(5)-C(6)-C(7)-C(8)	3.4(6)
C(61)-C(6)-C(7)-C(8)	-176.8(4)
C(6)-C(7)-C(8)-C(9)	-0.4(7)
C(2)-C(1)-C(9)-C(8)	176.8(4)
C(11)-C(1)-C(9)-C(8)	-4.5(6)
C(2)-C(1)-C(9)-C(10)	-0.7(6)
C(11)-C(1)-C(9)-C(10)	178.0(4)
C(7)-C(8)-C(9)-C(1)	179.6(4)
C(7)-C(8)-C(9)-C(10)	-2.7(6)
C(6)-C(5)-C(10)-C(4)	-179.8(4)
C(6)-C(5)-C(10)-C(9)	-0.1(6)
C(3)-C(4)-C(10)-C(5)	-180.0(4)
C(3)-C(4)-C(10)-C(9)	0.3(6)
C(1)-C(9)-C(10)-C(5)	-179.4(4)
C(8)-C(9)-C(10)-C(5)	3.0(6)
C(1)-C(9)-C(10)-C(4)	0.4(6)
C(8)-C(9)-C(10)-C(4)	-177.3(4)
C(5)-C(6)-C(61)-C(66)	144.5(4)
C(7)-C(6)-C(61)-C(66)	-35.2(6)
C(5)-C(6)-C(61)-C(62)	-36.0(6)
C(7)-C(6)-C(61)-C(62)	144.2(4)
C(66)-C(61)-C(62)-C(63)	1.9(7)
C(6)-C(61)-C(62)-C(63)	-177.6(4)
C(61)-C(62)-C(63)-O(63)	179.4(4)
C(61)-C(62)-C(63)-C(64)	-1.5(7)
O(63)-C(63)-C(64)-C(65)	-179.9(4)
C(62)-C(63)-C(64)-C(65)	0.9(7)
C(63)-C(64)-C(65)-C(66)	-0.8(8)
C(64)-C(65)-C(66)-C(61)	1.2(8)
C(62)-C(61)-C(66)-C(65)	-1.7(7)

C(6)-C(61)-C(66)-C(65)	177.8(4)
C(62)-C(63)-O(63)-C(631)	12.2(7)
C(64)-C(63)-O(63)-C(631)	-166.9(4)
C(63)-O(63)-C(631)-C(632)	163.2(4)
O(63)-C(631)-C(632)-C(633)	64.8(5)
C(631)-C(632)-C(633)-C(634)	-173.6(4)
C(632)-C(633)-C(634)-C(635)	-167.1(4)
C(633)-C(634)-C(635)-C(636)	-174.4(4)
C(2)-C(1)-C(11)-C(19)	-65.8(6)
C(9)-C(1)-C(11)-C(19)	115.6(5)
C(19)-C(11)-C(12)-O(121)	174.7(4)
C(1)-C(11)-C(12)-O(121)	-4.8(6)
C(19)-C(11)-C(12)-C(13)	-3.2(6)
C(1)-C(11)-C(12)-C(13)	177.3(4)
C(13)-C(12)-O(121)-C(122)	-12.9(6)
C(11)-C(12)-O(121)-C(122)	169.3(4)
C(12)-O(121)-C(122)-C(123)	-74.1(5)
O(121)-C(12)-C(13)-C(14)	-174.7(4)
C(11)-C(12)-C(13)-C(14)	3.0(7)
C(12)-C(13)-C(14)-C(20)	0.1(7)
C(20)-C(15)-C(16)-C(17)	-2.5(6)
C(20)-C(15)-C(16)-C(161)	178.7(4)
C(15)-C(16)-C(17)-C(18)	4.1(7)
C(161)-C(16)-C(17)-C(18)	-177.1(4)
C(16)-C(17)-C(18)-C(19)	-2.2(7)
C(12)-C(11)-C(19)-C(20)	0.3(6)
C(1)-C(11)-C(19)-C(20)	179.8(4)
C(12)-C(11)-C(19)-C(18)	-179.9(4)
C(1)-C(11)-C(19)-C(18)	-0.4(7)
C(17)-C(18)-C(19)-C(11)	178.8(4)
C(17)-C(18)-C(19)-C(20)	-1.4(7)
C(13)-C(14)-C(20)-C(19)	-2.9(7)
C(13)-C(14)-C(20)-C(15)	177.1(4)
C(11)-C(19)-C(20)-C(14)	2.6(6)
C(18)-C(19)-C(20)-C(14)	-177.2(4)
C(11)-C(19)-C(20)-C(15)	-177.3(4)
C(18)-C(19)-C(20)-C(15)	2.9(6)
C(16)-C(15)-C(20)-C(14)	179.1(4)
C(16)-C(15)-C(20)-C(19)	-0.9(6)
C(15)-C(16)-C(161)-C(162)	-29.2(7)
C(17)-C(16)-C(161)-C(162)	152.1(5)
C(15)-C(16)-C(161)-C(166)	150.6(5)
C(17)-C(16)-C(161)-C(166)	-28.1(7)
C(166)-C(161)-C(162)-C(163)	-0.7(8)
C(16)-C(161)-C(162)-C(163)	179.1(4)
C(161)-C(162)-C(163)-O(163)	179.6(5)
C(161)-C(162)-C(163)-C(164)	1.6(8)
C(162)-C(163)-C(164)-C(165)	-2.0(8)
O(163)-C(163)-C(164)-C(165)	179.7(4)
C(163)-C(164)-C(165)-C(166)	1.5(8)
C(164)-C(165)-C(166)-C(161)	-0.5(8)
C(162)-C(161)-C(166)-C(165)	0.1(7)
C(16)-C(161)-C(166)-C(165)	-179.7(4)
C(162)-C(163)-O(163)-C(171)	8.8(8)
C(164)-C(163)-O(163)-C(171)	-173.1(4)
C(163)-O(163)-C(171)-C(172)	174.9(4)
O(163)-C(171)-C(172)-C(173)	-177.9(4)
C(171)-C(172)-C(173)-C(174)	-176.9(4)
C(172)-C(173)-C(174)-C(175)	178.8(4)
C(173)-C(174)-C(175)-C(176)	-61.4(6)