Synthesis and Applications of New Poly(alkylene sulfide)s

A Thesis Submitted for the Degree of Doctor of Philosophy (PhD)

By

Asim Alaa Balakit

B.Sc. (Chemistry) 2000
M.Sc. (Chemistry) 2002

Cardiff School of Chemistry

Cardiff University

United Kingdom

2012

To the Memory of My Mother (Samira Balakit)

To My Father (Alaa Balakit)

To My Wife (Afrah Al-Zwaid)

To My Daughters (Usur and Fatima Balakit)

To My Brothers (Raeed and Mohammed Balakit)

To My Sisters (Suadad, Sura and Rana Balakit)

I sincerely dedicate this thesis

Asim A. Balakit

Acknowledgements

First and foremost, I thank the glorious creator of the universe, Allah almighty for granting me the ability and the strength to achieve this work.

I would like to express my sincere gratitude to my supervisor, Professor Keith Smith, for accepting me in his research group in Cardiff School of Chemistry, his supervision helped me to overcome the challenges and obstacles that I faced throughout my research work and writing up. He taught me how to be a researcher. Beside my supervisor, I would like to thank Professor Gamal El-Hiti, for teaching and supporting me in every step in my study, I will never forget his favours.

I would like to thank Dr Rob Jenkins, Mr Dave Walker and Mr Robin Hicks, Cardiff School of Chemistry, for their help in running mass spectra. Thanks to Dr Benson Kariuki, Cardiff School of Chemistry, for his assistance in the determination of the crystal structures.

I also wish to thank all to my friends and lab-mates, in particular Mansour, Ahmad, Ali, Alaa, Rhys, Heulyn, Mohammed and Basil for their support and the nice environment they created in the laboratory. Special thanks to Dr. Grazia Bezzu, Dr. Mariolino Carta, Dr. Yulia Rogan and Dr. Kadhum Msayib for their collaborations. Huge thanks to the academic, administrative and technical staff in Cardiff School of Chemistry.

Thanks to the Iraqi Government/Ministry of Higher Education and Scientific Research, for funding my scholarship and to the Iraqi Embassy in London/Cultural Attaché, for looking after me during my study.

I would like to express my sincere appreciation to my father (Alaa Balakit), my brothers (Raeed and Mohammed Balakit) and my sisters (Suadad, Sura and Rana Balakit), for their continuing support, patience and encouragement.

Very special thanks to my wife (Afrah Al-Zwaid) for her constant kind help, moral support and encouragement. Thanks also go to my daughters (Usur and Fatima) for pushing me in their own ways toward the success.

Last but not least, I thank everybody who supported me even with a single word.

Abbreviations

AIBN	2,2′-Azobis(isobutyronitrile)
app.	Apparent
BMS	Borane dimethyl sulfide
Boc	tert-Butoxycarbonyl
^{13}C NMR	Carbon nuclear magnetic resonance
calcd	Calculated
CI	Chemical ionization
d	Doublet
DCM	Dichloromethane
DCME	α,α-dichloromethyl ether
DEPT	Distortionless enhancement by polarization transfer
DMA	Dimethylacetamide
DMF	N,N-Dimethylformamide
DodSMe	Dodecyl methyl sulfide
EI	Electron impact
EI-MS	Electron impact - mass spectrometry
^{19}F NMR	Fluorine nuclear magnetic resonance
FT-IR	Fourier transform infrared spectroscopy
GC	Gas chromatography
GPC	Gel permeation chromatography
h	Hours
^{1}H NMR	Proton nuclear magnetic resonance
HDODA	1,6-Hexanediol diacrylate
HDODA-PS	1,6-Hexanediol diacrylate-cross-linked polystyrene
HRMS	High resolution mass spectrometry
HX	Hydrogen halide
IR	Infra red
J	Coupling constant
KOAc	Potassium acetate
LiTMP	Lithium 2,2,6,6-tetramethylpiperidide
m	Multiplet

MALDI-TOF	Matrix-assisted laser desorption/ionization-time-of-flight mass spectrometer.
min	Minutes
MMS	Methyl 6-morpholinohexyl sulfide
Mn	Number average molecular weight
Mp	Melting point
MS	Mass spectrometry
Mw	Weight average molecular weight
NBS	N-Bromosuccinimide
n-BuLi	*n*-Butyllithium
$Pd(OAc)_2$	Palladium acetate
$Pd_2dba_3 \bullet CHCl_3$	(dibenzylideneacetone)dipalladium(0)-chloroform adduct
PDI	Polydispersity index
PMMA	Poly(methyl methacrylate)
PnBMA	poly(n-butyl methacrylate)
RF	Response factor
R_f	Retardation factor
ROMP	Ring-opening metathesis polymerization
s	Singlet
Sia_2BH	Disiamylborane
t	Triplet
t-BuLi	*tert*-Butyllithium
TGA	Thermogravimetric analysis
THF	Tetrahydrofuran
TLC	Thin layer chromatography
TMEDA	Tetramethylethylenediamine
TMP	2,2,6,6-Tetramethylpiperidide

Summary

Two projects are involved in this thesis; both of them are about the synthesis and applications of new poly(alkylene sulfide)s. The objective of the first project is the development of new polymeric borane reagents. The goal of second project is to introduce a new strategy for the synthesis of novel photochromic poly(alkylene sulfide)s.

Chapter One

Chapter One is an introductory chapter about borane chemistry. It involves a definition of the borane reagents, their uses in the most important applications and their development. Generally, this chapter shows the importance of borane reagents and the needs to develop convenient ones.

Chapter Two

Chapter Two includes a brief introduction about methods of synthesis of poly(alkylene sulfide)s. It shows how by following the most convenient procedure a number of poly(alkylene sulfide)s have been produced and from those polymers a couple of borane complexes were prepared. It also shows the stability, uses in different applications (reduction, hydroboration-oxidation and more sophisticated reaction) and the recycling of the polymeric material. In this chapter we report new poly(propylene sulfide)–borane complexes as convenient and versatile reagents for organic synthesis.

Chapter Three

Chapter Three is about photochromism and diarylethenes. It shows the reported synthetic strategies for the production of diarylperfluorocyclopentenes and their uses in the production of the different types of photochromic polymers which are very interesting materials that are used in a wide range of advanced applications.

Chapter Four

Chapter Four describes our attempt to develop a new route for the production of poly(alkylene sulfide)s bearing photochromic units. It shows the synthesis of a novel photochromic diarylperfluorocyclopentene aldehyde and the use of such material in the production of a model that resembles the target polymers. The synthesis of a novel photochromic oligomeric material is presented in this chapter.

List of Publications

1. Balakit, A. A; Pardasani, R. T; El-Hiti, G. A.; Smith, K. New Polymeric Sulfide-Borane Complexes as Convenient Hydroborating and Reducing Agents, Poster (H26_P07) of Macro 2010: 43rd IUPAC World Polymer Congress; Polymer Science in Service of Society, Glasgow, United Kingdom, 11-16 July **2010**.

2. Balakit, A. A; Pardasani, R. T; El-Hiti, G. A.; Smith, K. A New Polymeric-Borane Adduct for the Hydroboration of Alkenes and Reduction of Carbonyl Compounds, Poster (Ic.003) of 3rd EuCheMS Chemistry Congress, Nurnberg, Germany, 29 August -2 September **2010**.

3. Smith, K.; Balakit, A.A.; Pardasani, R.T.; El-Hiti, G.A. New Polymeric Sulfide-Borane Complexes: Convenient Hydroborating and Reducing Reagents, *J. Sulfur Chem.* **2011**, *32*, 287–295.

4. Smith, K.; Balakit, A.A.; El-Hiti, G.A. Poly(propylene sulfide)-Borane: Convenient and Versatile Reagent for Organic Synthesis, *Tetrahedron* **2012**, *68*, 7834–7839.

Contents

Chapter Four

Synthesis of Poly(alkylene sulfide)s Bearing Photochromic Units

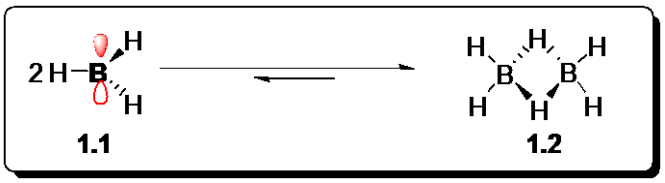
Chapter One

Introduction to Borane and Its Reagents

Introduction to Borane and Its Reagents

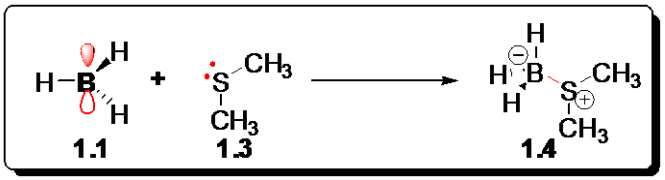
1.1 Introduction

Boron is the element with atomic number 5 in the Periodic Table, located at the top of group 13. It has only three electrons in the *2p* orbital therefore it forms three conventional two-centre two-electron bonds with other atoms (hydrogen atoms in the case of BH_3) in a planar structure leaving a an empty *p* orbital which is perpendicular to the plane. Borane (BH_3; **1.1**) represents the simplest boron hydride; it dimerizes to diborane (B_2H_6; **1.2**) in an equilibrium in which the diborane side is favoured under normal conditions (Scheme 1.1).[1]



Scheme 1.1

The vacant *p* orbital makes borane (BH_3) and its derivatives electrophilic (Lewis acids); therefore they react easily with electron-rich species (Lewis bases) forming a Lewis acid-base complex. For example, borane-dimethyl sulfide (BH_3•SMe_2, BMS; **1.4**) is a complex that results from the interaction of the vacant *p* orbital of BH_3 with the lone pair of the sulfur atom in the dimethyl sulfide molecule (**1.3**; Scheme 1.2).[2]



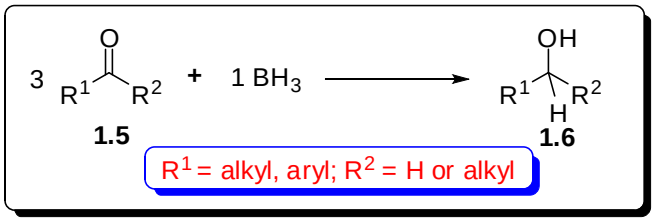
Scheme 1.2

Borane complexes are highly versatile reagents with numerous applications in organic syntheses and industrial processes. In the following sections we will highlight these applications as well as the efforts made by researchers to afford convenient borane complexes.

1.2 Borane-Complexes as Reducing Agents

Borane reagents offer interesting applications in the reduction of different functional groups (*e.g.* aldehydes, ketones, carboxylic acids, esters, amides and epoxides),[3] in this section we will discuss some of these applications.

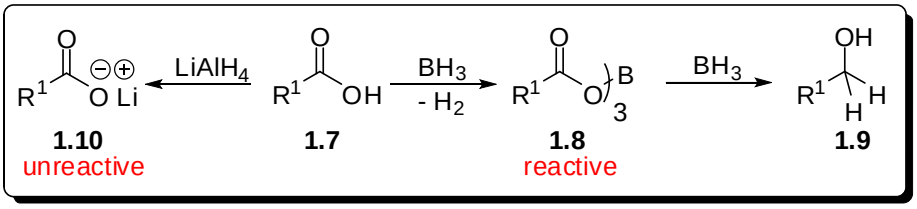
Primary and secondary alcohols can be prepared by the reduction of aldehydes and ketones, respectively. Borane dimethyl-sulfide (BH_3•SMe_2) and borane-tetrahydrofuran (BH_3•THF) are the most commonly used borane complexes as reducing agents for such reactions.[4] In 1970 Brown *et al.*[5] studied the reaction of borane in THF with different carbonyl compounds, including aldehydes and ketones. The study revealed that the aldehydes and ketones examined all consumed one hydride from borane to produce to the corresponding alcohols (Scheme 1.3).



Scheme 1.3

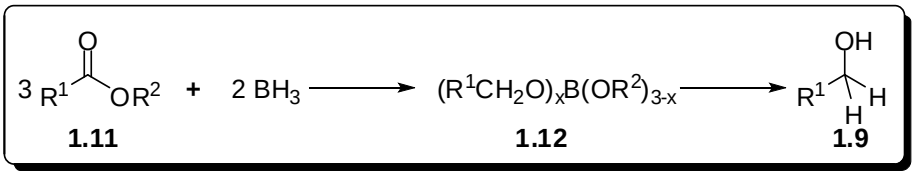
Borane is considered to be the best reagent for the reduction of carboxylic acids **1.7** to the corresponding primary alcohols **1.9**.[6] It was found that three hydrides of the borane were consumed, one for the formation of triacyloxyboranes **1.8** with evolution of hydrogen gas, one for cleavage of the acyl-oxygen bond, and the third for reduction of the carbonyl group.[5]

In triacyloxyboranes **1.8** the oxygen next to the boron shares its lone pair of electrons between the carbonyl group and the boron's empty *p* orbital; consequently, triacyloxyboranes are more reactive than normal esters, or than the lithium carboxylates **1.10** formed from the reaction of carboxylic acids with $LiAlH_4$. Therefore, triacyloxyboranes, which are formed in the first step of the reaction, can be converted into the alcohol in a fast step (Scheme 1.4).[6]



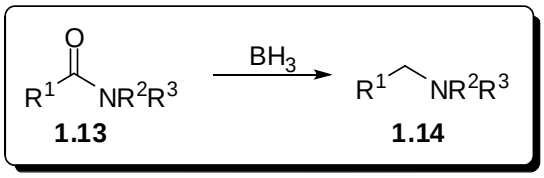
Scheme 1.4

Other carboxylic acid derivatives such as esters **1.11** and amides **1.13** can also be reduced using borane reagents to the corresponding alcohols **1.9** and amines **1.14**, respectively.[3,4] Reduction of aliphatic and aromatic carboxylic esters with 0.67 molar equivalents of BMS (Scheme 1.5) was reported by Brown and Choi and the products were obtained in high (89–97 %) yields.[7]



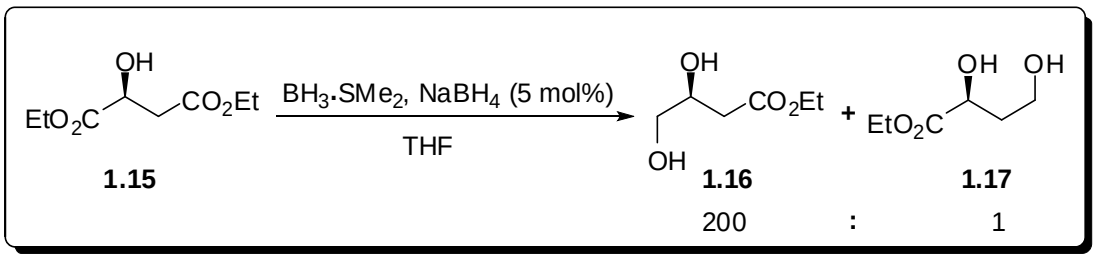
Scheme 1.5

Primary, secondary and tertiary amides (aliphatic and aromatic) can be converted to the corresponding amines using excess diborane in THF (Scheme 1.6). In practice, early reports showed that 2.33, 2.0 and 1.67 molar equivalents of borane are required for the reduction of the primary, secondary and tertiary amides, respectively.[8] It was reported that primary amines could be reduced with 1.33 molar equivalents of BMS to the corresponding primary amine using an improved procedure.[9]



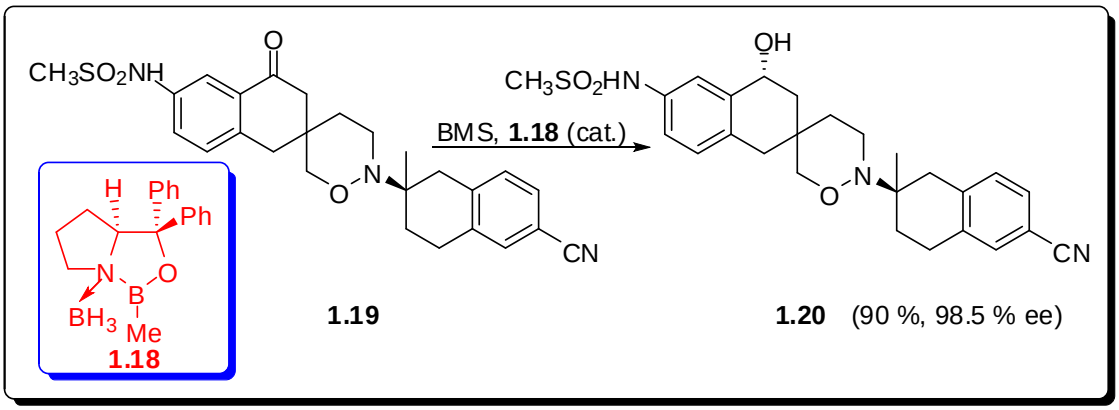
Scheme 1.6

Borane reagents are widely used for chemo- and stereo-selective reductions.[4,10] Saito *et al.*[11] have demonstrated the use of borane-dimethyl sulfide complex (BMS) with a catalytic amount of sodium borohydride ($NaBH_4$) for the chemo-selective reduction of the ester group α to the hydroxyl group in diethyl (*S*)-malate (**1.15**; Scheme 1.7).



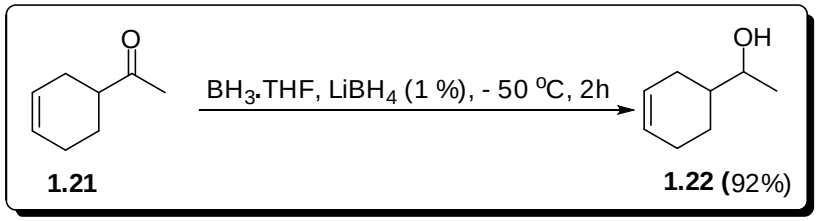
Scheme 1.7

In the presence of oxazaborolidine **1.18** as catalyst, BMS has been used for the asymmetric reduction of ketones.[12] For example, Cai *et al.*[13] have used the BH_3-oxazaborolidine system for the reduction of the carbonyl group in compound **1.19** to the corresponding alcohol **1.20** (Scheme 1.8), which represents both a chemo-selective and a stereo-selective reaction.



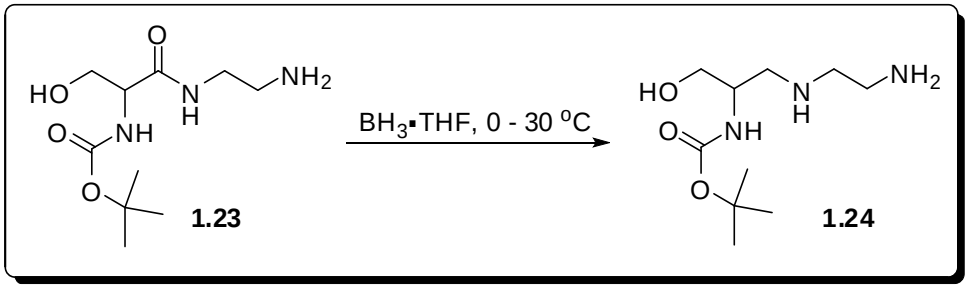
Scheme 1.8

Another example for chemo-selective reduction using borane was reported by Arase *et al.*[14] They have presented a method for the selective reduction of the carbonyl group of conjugated and unconjugated alkenones with borane in tetrahydrofuran (THF) in the presence of lithium borohydride as catalyst (*e.g.* Scheme 1.9).



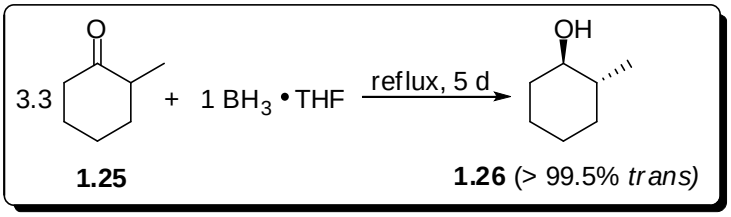
Scheme 1.9

Amedia *et al.*[15] have reported a chemo-selective reduction of amide groups using BH_3•THF and have developed optimized conditions for reduction of the amide carbonyl group of compound **1.23** without affecting the Boc protecting group (Scheme 1.10).



Scheme 1.10

Cha *et. al.*[16] have reported the use of BH_3•THF as a stereo-selective reducing agent for the reduction of cyclic ketones to the thermodynamically more stable alcohols. 2-Methylcyclohexanone (**1.25**) was one of the examples studied (Scheme 1.11).



Scheme 1.11

In the literature there are more different publications about reduction reactions in which borane reagents were used.[17] Very recently Shi *et al.*[18] have reported a selective and convenient procedure for the reduction of aldehydes and ketones to the corresponding alcohols using borane-ammonia complex in neat water.

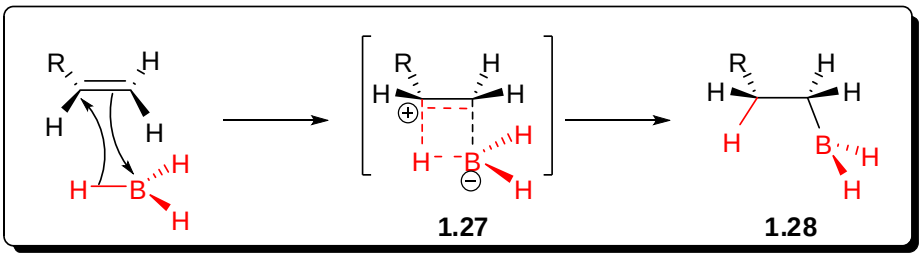
1.3 The Chemistry of Hydroboration

The term hydroboration refers to the addition of the boron–hydrogen bond to carbon–carbon multiple bonds (double and triple). In 1956, Brown's research group reported the first example of hydroboration, and since that time this reaction has found diverse applications in organic synthesis. It is used for the formation of organoboranes, which are versatile synthetic intermediates that can be converted into a variety of functional groups. Herbert C. Brown (1912-2004) was awarded the Nobel Prize in

Chemistry in 1979 as a recognition of his work in hydroboration and associated areas of reactivity.[19,20]

1.3.1 Mechanism and Stereochemistry of Hydroboration

In the proposed mechanism for the hydroboration, an addition product is formed through a four–atom transition state **1.27** formed when π electrons of the alkene add to the vacant *p* orbital of the borane. In such a transition state the boron atom is partially bonded to the less substituted carbon atom of the double bond (in the case of unsymmetrical alkenes) and one of the hydrogen atoms is partially bonded to the other carbon atom in a concerted addition (both new bonds are formed more or less at the same time). It is clear from the mechanism that both the boron and the hydrogen atoms add to the same face of the double bond which determines a stereo controlled *syn*-addition (Scheme 1.12).[6,19,21]



Scheme 1.12

Both steric and electronic factors play roles in the regioselectivity of the hydroboration reaction. Because of the steric effect, attachment of the borane moiety takes place preferably to the less hindered carbon of the double bond on the unsymmetrical alkene, and due to the shifting of the π electrons toward the boron atom away from the carbon atom; a partial positive charge is developed on that carbon atom. The presence of electron releasing groups such as alkyl groups stabilizes that positive charge in the transition state, again encouraging attachment of the hydrogen atom to the more substituted carbon atom.[22] In other words the hydroboration is an *anti*-Markonikov regioselective addition reaction. However, hydroborations of alkenes containing electron withdrawing substituents, such as styrene (**1.30**), allyl chloride (**1.31**) and 3,3,3-trifluoropropene (**1.32**), give significant amounts of Markonikov addition products (Figure 1.1).[23]

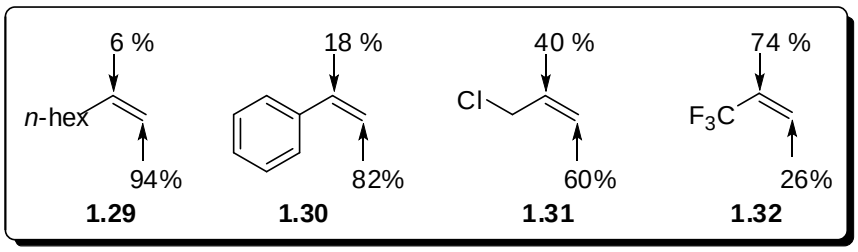
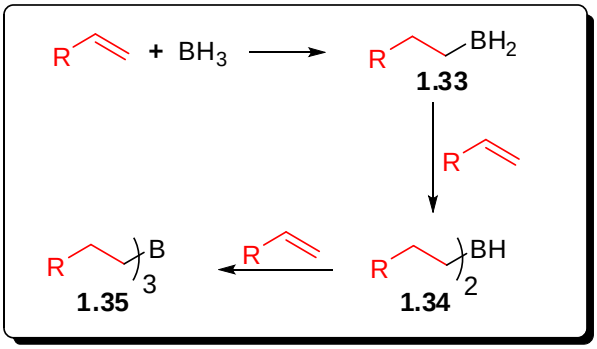


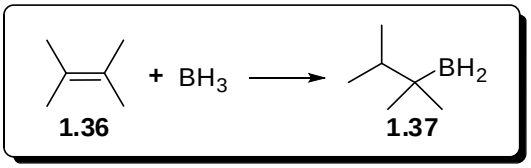
Figure 1.1: Regioselectivity in hydroboration with BH_3•THF

The result of the initial addition of borane (BH_3) to the alkene's double bond is the corresponding monoalkylborane (RBH_2; **1.33**), which is able to undergo addition with another molecule of the alkene to give a dialkylborane (R_2BH; **1.34**), which is also able to undergo another addition to produce a trialkylborane (R_3B; **1.35**), in which all the three hydrogen atoms of the borane have been replaced by alkyl groups (Scheme 1.13).[6,22]



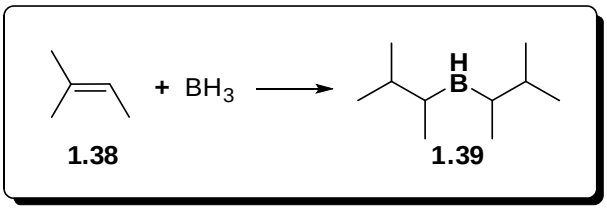
Scheme 1.13

In some cases, mixed trialkylboranes can be prepared by controlling the addition of the required molar equivalents of alkenes to the reaction mixture. Monoalkyl and dialkyl boranes can be produced under mild conditions (low temperature and short reaction time) when relatively hindered alkenes are involved. For example, thexylborane (**1.37**), which is a monoalkylborane, can be easily prepared by hydroboration of 2,3-dimethylbut-2-ene (**1.36**) with borane (BH_3; Scheme 1.14) since the second hydroboration with the bulky tetrasubstituted alkene is very slow.[6,24]



Scheme 1.14

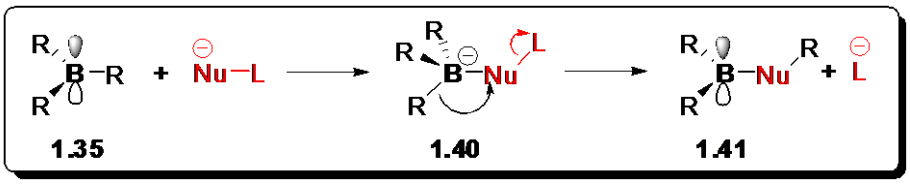
Disiamylborane (**1.39**) is a typical dialkylborane and can be made by hydroboration of 2-methyl-2-butene (**1.38**) with borane (Scheme 1.15). The first and the second hydroborations occur easily, but the third is very slow.[6,24] Totally "mixed" trialkylboranes, containing three different alkyl groups, can be obtained when a hindered alkene, an alkene of intermediate hindrance and an unhindered alkene are used sequentially.



Scheme 1.15

1.3.2 Reactions of Organoboranes

The structure of the organoboranes (monoalky–, dialkyl– and trialkylboranes) is trigonal planar with an empty *p* orbital on the boron atom perpendicular to the plane; this empty orbital makes them electrophilic and highly susceptible to nucleophilic attack, forming a tetrahedral species (organoborates; **1.40**) in which boron atom bears a negative charge. The presence of a leaving group (or an electron sink) in the attacking nucleophile stimulates the 1,2-migration of an alkyl group (with its electrons) that is anti-periplanar to the leaving group with retention of configuration at the carbon atom of the migrating group (Scheme 1.16). The migratory aptitudes depend on the structure of the leaving group and other factors such as steric and conformational effects.[6,20]

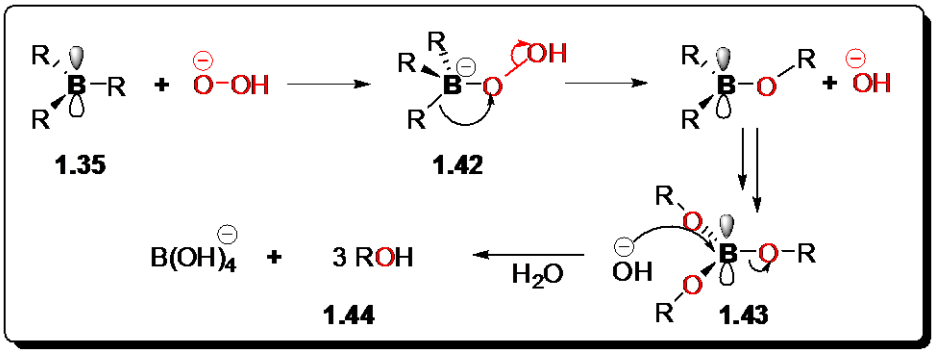


Scheme 1.16

1.3.2.1 Hydroboration–Oxidation Reactions

Hydroboration-oxidation is the simplest application of boranes in organic synthesis. By this means alkenes can be converted into the corresponding alcohols by the net *anti*-Markonikov addition of water across the double bond.

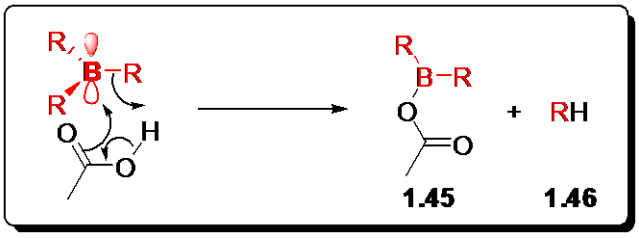
Treatment of trialkylboranes with alkaline hydrogen peroxide results the attack of the empty *p* orbital atom by the hydroperoxide anion followed by the migration of the alkyl groups from the boron to the oxygen atom accompanied with the leaving of the hydroxyl group (Scheme 1.17). The whole process is repeated twice giving the borate ester (trialkoxyborane) **1.43**. Then hydroxide attacks the electrophilic boron atom displacing the alkoxide, and finally an acid base reaction takes place giving the desired alcohol **1.44** and tetrahydroxyborate (Scheme 1.17).[20,25]



Scheme 1.17

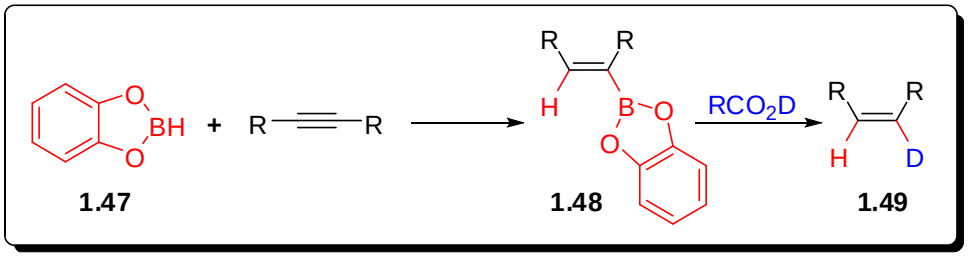
1.3.2.2 Hydroboration-Protonolysis

One of the interesting applications that organoboranes offer is the hydrogenation of C=C or C≡C bonds. This method is considered to be a convenient alternative to the catalytic hydrogenation of alkenes. Heating a mixture of a trialkylborane and excess ethanoic or propanoic acid in diglyme results in protonolysis of the B-alkyl bond with retention of configuration, which is determined by the concerted cyclic mechanism (Scheme 1.18).[20,26]



Scheme 1.18

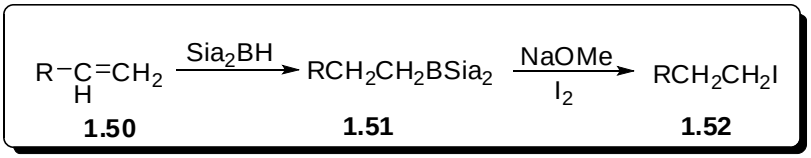
Hydroboration of alkynes using catechol-borane (**1.47**), prepared by the reaction of catechol with BH_3, leads to the formation of alkenylboranes (**1.48**, Scheme 1.19). Such organoboranes can also be protonolysed by the above method, giving the corresponding *cis*-alkenes, with potential for incorporation of deuterium (**1.49**; Scheme 1.19).[20]



Scheme 1.19

1.3.2.3 Hydroboration-Halogenolysis

In the presence of a base such as sodium methoxide, trialkylboranes react readily with iodine or bromine to give the corresponding alkyl halides. The overall reaction involves an *anti*–Markonikov addition of HX to the starting alkene, from which the alkylborane is made *via* hydroboration. Disiamylborane (Sia_2BH) is a suitable hydroborating reagent that can be used to convert terminal alkenes into alkyl iodides **1.52** in excellent yields (Scheme 1.20).[27]

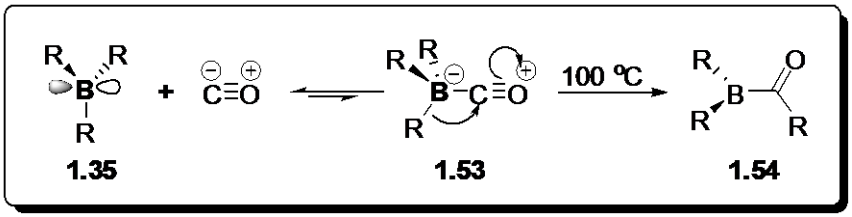


Scheme 1.20

The reaction proceeds with absolute inversion of configuration at the carbon atom of the alkyl group of the alkyborane in the cases of both bromination and iodination reactions. Chlorination reactions, by contrast, are achieved *via* a radical mechanism using NCl_3 as a chlorinating reagent. In this case the product from a single enantiomer of an alkylborane is a mixture of both enantiomers.[20]

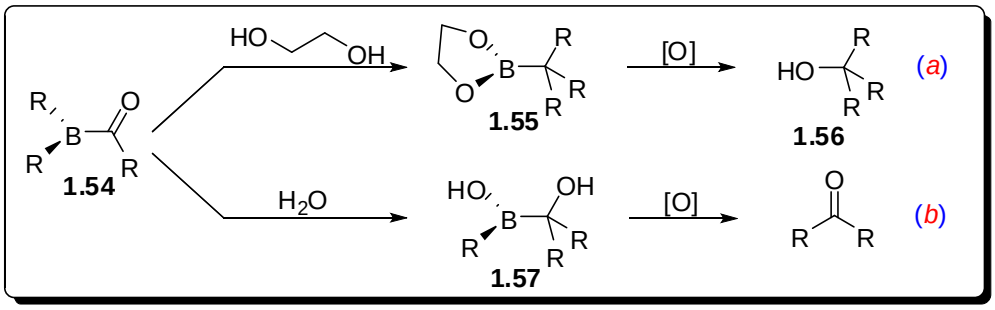
1.3.2.4 Hydroboration-Carbonylation

Aldehydes, ketones and tertiary alcohols can be produced *via* carbonylation of trialkylboranes.[20,24] The reaction of carbon monoxide with a trialkylborane at high temperature (100 °C) leads to the formation of the intermediate **1.54** as a result of a single alkyl migration (Scheme 1.21); this is a key step in the formation of ketones and tertiary alcohols *via* the carbonylation of organoboranes. [28,29]



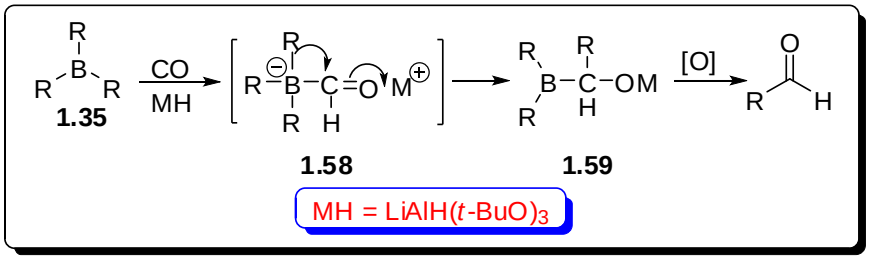
Scheme 1.21

Carbonylation of organoboranes in the presence of ethylene glycol at 150 °C results the migration of the other two alkyl groups to form **1.55**, which is then oxidized to give the corresponding tertiary alcohol (Scheme 1.22*a*),[28] it was found that conducting the carbonylation reaction at 100 °C and in the presence of water instead of ethylene glycol inhibits the migration of the third alkyl group leading to the formation of the corresponding ketone (Scheme 1.22*b*).[29]



Scheme 1.22

Carbonylation of trialkylboranes in the presence of a hydride source such as LiAlH(*t*-BuO)$_3$ results a single migration leading to the formation of **1.59** as an intermediate which can be converted to the corresponding aldehyde upon oxidation (Scheme 1.23).[30]

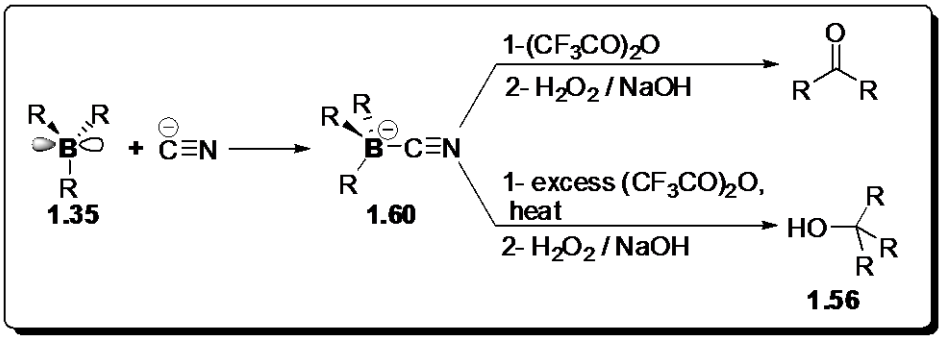


Scheme 1.23

1.3.2.5 Hydroboration-Cyanidation

Another route for the synthesis of ketones or tertiary alcohols *via* hydroboration is the cyanidation reaction. Cyanide anion reacts with trialkylboranes to give a stable

organoborate **1.60**, for which the migration of alkyl groups from the boron to the carbon atom can be induced in the presence of trifluoroacetic anhydride. Alkaline oxidation as a last step in this reaction gives the corresponding ketone[31a] or tertiary alcohol [31b] depending on reaction conditions (Scheme 1.24).



Scheme 1.24

The above examples represent some of the applications of borane reagents in organic synthesis. A key feature of organoborane chemistry is the 1,2-migration of alkyl groups in borate complexes, and such migrations can be conducted under the control of auxiliaries, leading to the production of chiral compounds, often with high enantiomeric excess.[32,33]

In many recent publications researchers have reported different applications in which hydroboration is the key step.[34]

Due to the enormous increase in the development of borane chemistry, this chapter could not accommodate a reasonably complete survey of the field with individual discussion. Some other reactions are used in the work reported in Chapter 2 and each one is introduced at that point. In the next section of this chapter we focus on the development in the production of borane reagents, which is the subject of the study in the first part of this thesis.

1.4 Borane Reagents

Borane complexes are highly versatile reagents with numerous applications in organic syntheses and industrial processes.[35-37] The most commonly used reagents are borane-tetrahydrofuran (BH_3•THF)[38] and borane-dimethyl sulfide (BH_3•SMe_2, BMS).[39] However, both of the reagents possess certain unfavourable characteristics.[39] BH_3•THF is commercially available only as a dilute solution, nominally 1.0 M in BH_3, and it undergoes

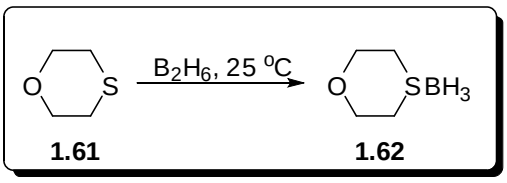
slow decomposition *via* cleavage of THF at room temperature. BMS is free from these disadvantages, as it is a neat complex, 10.0 M in BH_3, can be used in a variety of solvents and is highly stable. However, BMS liberates a stoichiometric amount of water-insoluble dimethyl sulfide, which has an obnoxious odour, high volatility and flammability, thereby creating environmental and safety problems, particularly for large scale use. Over the years researchers have therefore endeavoured to develop borane complexes that are free of these disadvantages.

1.4.1 Amine-Borane Reagents

Several amine-borane reagents have been reported. In 1998 Brown *et al.*[40] have demonstrated a series of *N*-alkyl-*N*-*iso*-propylaniline-boranes (*e.g.* *N*-ethyl-*N*-*iso*-propylaniline-borane) and *N*-alkyl-*N*-*iso*-butylaniline-boranes (*e.g.* *N*-ethyl-*N*-*iso*-butylaniline-borane) as convenient hydroborating agents. In later studies they introduced *N*-ethyl-*N*-*iso*-propylaniline-borane as a superior reagent for hydroboration and reduction reactions.[41,42] *tert*-Butyldialkylamine–borane complexes such as *tert*-butylisopropylmethylamine–borane and *tert*-butylisopropylethylamine–borane, have also been reported by Brown's research group as highly reactive borane complexes.[43] All of these reagents are liquids, the syntheses of the amines in all cases are multistep syntheses and purification processes are required. None of these complexes has been sufficiently advantageous to rival the two simple complexes of borane with THF and dimethyl sulfide. In the following section we will focus on sulfide and polymeric borane complexes, which are closely related to the objectives in this research project.

1.4.2 Sulfide-Borane Reagents

1,4-Thioxane (**1.61**) is a readily available reagent; it has lower vapour pressure and a less annoying odour than dimethyl sulfide. Furthermore, it is moderately soluble in water, and can be oxidized selectively in the presence of organoboranes by sodium hypochlorite to give a sulfoxide that is highly soluble in water. 1,4-Thioxane can be easily removed from the reaction mixture by washing with water; these advantages led Brown and co-workers to introduce borane-1,4-thioxane (**1.62**) as a new borane complex. Diborane gas (B_2H_6), which is generated by reaction of sodium borohydride ($NaBH_4$) with boron triflouride etherate (BF_3•OEt_2) was passed into neat 1,4-thioxane to give the borane-1,4-thioxane (Scheme 1.25). It was reported that the reagent is a convenient hydroborating and reducing reagent, and such work was patented in 1981. [44, 45]



Scheme 1.25

In 1992, Brown and Mandal introduced borane-1,4-thioxane as a new convenient hydroborating reagent for the synthesis of different borane reagents such as disiamylborane (**1.39**), dicyclohexylborane (**1.63**), 9-borabicyclo[3,3,1]nonane (**1.64**), and thexylborane (**1.37**) (Figure 1.2).[46]

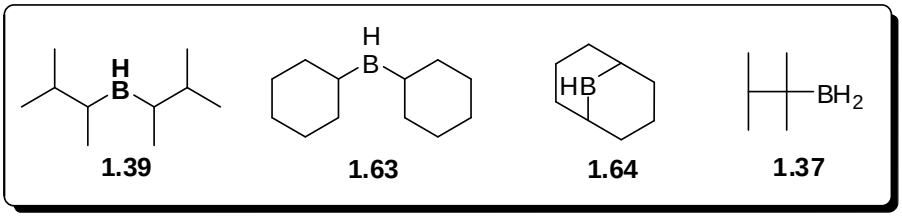
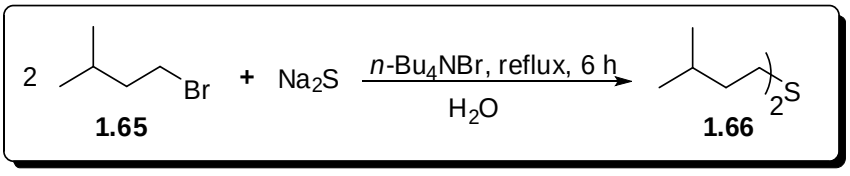


Figure 1.2: Borane reagents have been synthesized using 1.62

Borane-1,4-thioxane (**1.62**) is a liquid that is *ca.* 8.0 M in borane. It has low melting point (11–15 °C) and crystallizes on cooling to 0 °C.[44-46] It is stable over prolonged periods, but unfortunately, the commercially available reagent is relatively more expensive than BH_3•THF and BH_3•SMe_2.[47]

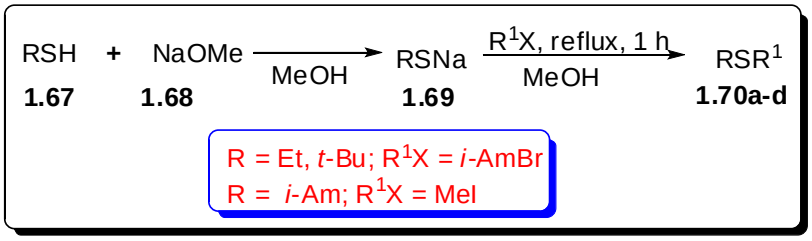
In 2000, Brown's research group reported a series of borane complexes with organic sulfides,[47] including a number of *iso*-amyl alkyl sulfides and some other sulfides.

Diisoamyl sulfide (**1.66**) was synthesized in 90% yield by the reaction of isoamyl bromide (**1.65**) and sodium sulfide in the presence of *n*-Bu_4NBr as a catalyst under reflux conditions (Scheme 1.26).[47] The product was purified by simple distillation.



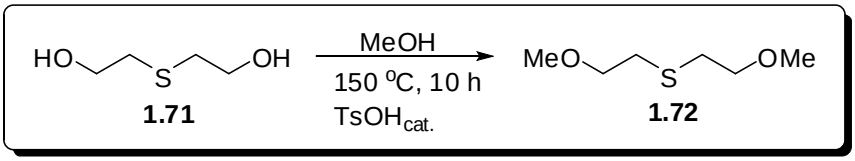
Scheme 1.26

The mixed isoamyl sulfides (**1.70a-d**) were synthesized in high yields according to Scheme 1.27.[47]



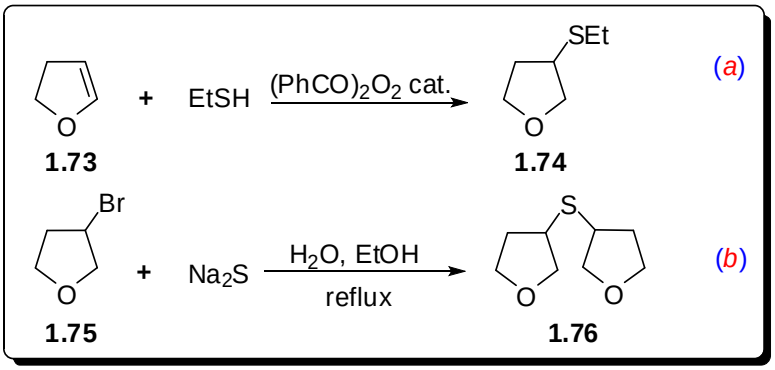
Scheme 1.27

Bis(2-methoxyethyl) sulfide (**1.72**), was synthesized in 66% yield by the reaction of thiodiethanol (**1.71**) with *p*-toluenesulfonic acid monohydrate in methanol (Scheme 1.28).[47] The product was isolated by simple distillation and the unreacted starting material was recovered and reused.



Scheme 1.28

Two tetrahydrofuranyl sulfides were also synthesised and were purified by distillation. 3-(Ethylthio)tetrahydrofuran (**1.74**) was synthesized in 94% yield by the free radical addition of ethanethiol to 2,3-dihydrofuran (**1.73**) in the presence of benzoyl peroxide as catalyst (Scheme 1.28*a*); *bis*(3-tetrahydrofuranyl) sulfide (**1.76**) was synthesized in 69% yield by the reaction of an alcoholic solution of 3-bromotetrahydrofuran (**1.75**) with aqueous sodium sulfide solution under reflux conditions, Scheme 1.29*b*.[47]



Scheme 1.29

For the prepared sulfides, Brown *et al.*[47] have compared their odour and borane complexing ability by borane exchange with BMS. Borane complexes were prepared

independently by passing diborane gas through the neat sulfides at 0 °C until saturation. All the complexes were liquids above 0 °C and their borane contents are shown in Table 1.1.

Table 1.1: Borane complexes with organic sulfides [47]

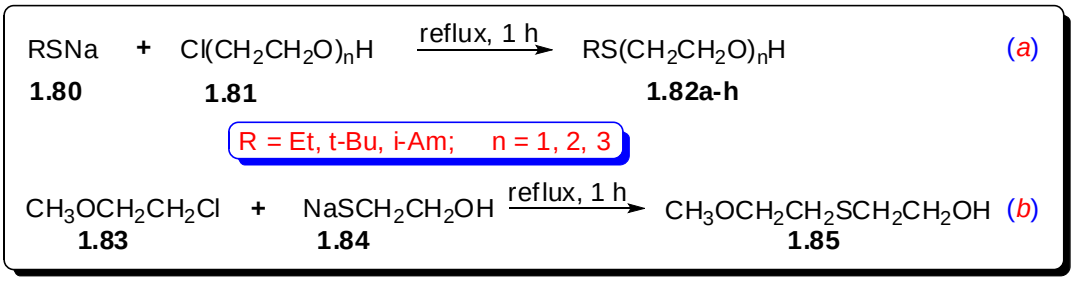
Sulfie		**Odour**	**Exchange with BMS[a] (%)**	**$[BH_3]^b$ (Complexes)**
isoamyl methyl sulfide	(**1.70a**)	Ethereal, very strong	46	5.8
tert-butyl methyl sulfide	(**1.70b**)	stench	39	6.6
ethyl isoamyl sulfide	(**1.70c**)	ethereal, strong	44	5.2
tert-butyl isoamyl sulfide	(**1.70d**)	ethereal, mild	32	4.3
diisoamyl sulfide	(**1.66**)	ethereal, mild, agreeable	40	4.2
3-ethylthiotetrahydrofuran	(**1.74**)	stench	21	5.8
bis(2-methoxyethyl) sulfide	(**1.72**)	stench	16	6.0
bis(3-tetrahydrofuryl) sulfide	(**1.76**)	stench	0	4.6
thioanisole	(**1.77**)	stench	0[c]	3.0
tetrahydrothiophene	(**1.78**)	stench	46	8.1
tetrahydrothiopyran	(**1.79**)	stench	45	7.5

[a] BMS and sulfide mixed at 1:1 molar ratio. [b] Estimated by hydrolysis in water-glycerol-methanol (1:1:1), [c] Calculated from the exchange with borane *tert*-butyl methyl sulfide.

It was found that the complexing ability of the sulfides toward borane decreases in the following order: dimethyl sulfide > dialkyl sulfides > ether-sulfides > thioanisole. The prepared complexes were tested as hydroborating reagents and the results showed that the reactivity of the corresponding borane complexes toward 1-octene increases in the reversed order. The conclusion of this study was that diisoamyl sulfide was a new promising borane carrier. It has a mild, ethereal agreeable aroma, its synthesis is simple and the borane adduct, 4.2 M in borane, is a liquid above 0 °C and stable over prolonged periods at room temperature . It was also found that *bis*(2-methoxyethyl) sulfide can be used for borane complexation as a less costly alternative to 1,4-oxathiane.[47]

In 2001, borane complexes with hydroxydialkyl sulfide borates were reported by Brown and co-workers as essentially odourless, water-soluble sulfide borane acceptors for

hydroboration.[48] A series of hydroxydialkyl sulfides (**1.82a–h**) and thiodiethanol monomethyl ether (**1.85**) have been synthesized according to Scheme 1.30 *a* and *b* respectively. The properties of **1.82a-h** and **1.85** are shown in Table 1.2.



Scheme 1.30

Table 1.2: Odour and miscibility with water of hydroxydialkyl sulfides 1.82a-h and 1.85[48]

Hydroxydialkyl sulfides		Odour	Miscibility with water[a]
t-BuSCH$_2$CH$_2$OH	(**1.82a**)	mild	50
i-AmSCH$_2$CH$_2$OH	(**1.82b**)	agreeable; strong	<100
EtS(CH$_2$CH$_2$O)$_2$H	(**1.82c**)	very mild	miscible
t-BuS(CH$_2$CH$_2$O)$_2$H	(**1.82d**)	mild	15
i-AmS(CH$_2$CH$_2$O)$_2$H	(**1.82e**)	agreeable; weak	<100
EtS(CH$_2$CH$_2$O)$_3$H	(**1.82f**)	very mild	miscible
t-BuS(CH$_2$CH$_2$O)$_3$H	(**1.82g**)	Mild	miscible
i-AmS(CH$_2$CH$_2$O)$_3$H	(**1.82h**)	agreeable; weak	100
CH$_3$OCH$_2$CH$_2$SCH$_2$CH$_2$OH	(**1.85**)	Mild	miscible

[a] Milliliters of water required to dissolve 1.0 g of hydroxydialkyl sulfide.

Borane complexes of the borates **1.82a-h** and **1.85** were synthesized by a one-pot reaction; diborane gas was passed through a neat hydroxydialkyl sulfides (**1.82a-h** and **1.85**) at 50 °C to form the corresponding borate ester (**1.86a-h** and **1.87**), and then it was absorbed by the ester till saturation giving **1.88a-i**. The obtained complexes were soluble in diethyl ether, tetrahydrofuran and dichloromethane. No borane loss was observed after 1 week at room temperature. The complexing ability of the synthesized borates was compared to borane-dimethyl sulfide by studying the borane exchange between them and BMS.

The borane exchange with 1.0 M borane-tetrahydrofuran solution was examined as well, but the values can be considered only as qualitative since the solution contains tetrahydrofuran in large excess (Table 1.3).[48]

Table 1.3: Borane complexes with borate esters of hydroxydialkyl sulfides (1.86a-h and 1.87) [48]

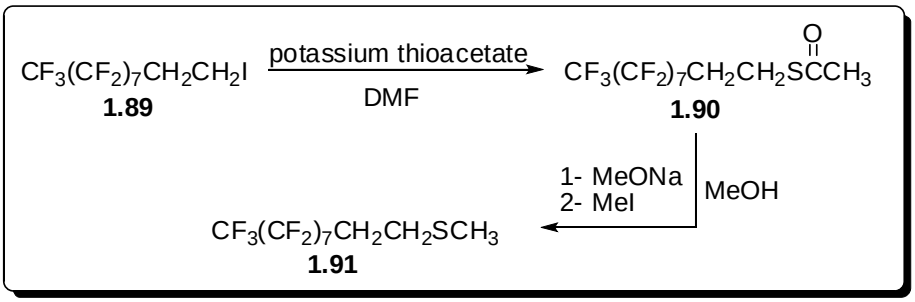
Borate ester		Exchange (%)[a] BMS	Exchange (%)[a] BH_3•THF	Complex[b]	State[c]	$[BH_3]$[d]
(*t*-$BuSCH_2CH_2O)_3B$	(**1.86a**)	8	68	**1.88a**	liquid	6.4
(*i*-$AmSCH_2CH_2O)_3B$	(**1.86b**)	0	67	**1.88b**	liquid	5.9
$[EtS(CH_2CH_2O)_2]_3B$	(**1.86c**)	28	83	**1.88c**	liquid	5.7
[*t*-$BuS(CH_2CH_2O)_2]_3B$	(**1.86d**)	11	70	**1.88d**	liquid	5.5
[*i*-$AmS(CH_2CH_2O)_2]_3B$	(**1.86e**)	0	75	**1.88e**	liquid	5.0
$[EtS(CH_2CH_2O)_3]_3B$	(**1.86f**)	23	81	**1.88f**	liquid	5.2
[*t*-$BuS(CH_2CH_2O)_3]_3B$	(**1.86g**)	9	68	**1.88g**	liquid	4.2
[*i*-$AmS(CH_2CH_2O)_3]_3B$	(**1.86h**)	0	66	**1.88h**	liquid	4.0
$[CH_3OCH_2CH_2SCH_2CH_2O]_3B$	(**1.87**)	0	62	**1.88i**	liquid	6.0

[a] BMS or BH_3•THF and borate ester mixed at 3:1 molar ratio. [b] Complexes contain three borane molecules per ester molecule, *e.g.* H_3B:S(*t*-Bu)$CH_2CH_2O]_3B$ (**1.88a**). [c] At 20 °C. [d] Estimated by hydrolysis in water/glycerol/THF, 1:1:1, and measurement of the hydrogen evolved.

It was found that complexes **1.88a-i** hydroborate terminal, di-, tri-, and tetrasubstituted olefins. The corresponding hydroxydialkyl sulfides **1.82d** and **1.85** can be washed out easily during the workup of hydroboration-oxidation reaction products. Therefore, **1.88d** and **1.88i** were considered as highly promising, efficient, new hydroborating agents of high potential for large scale applications in hydroborations and reductions.[48]

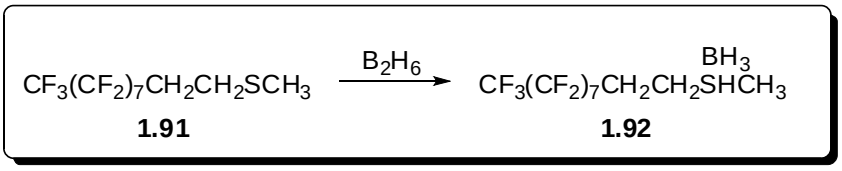
In 2002 Crich and Neelamkavil presented a new fluorous dialkyl sulfide as a convenient, odourless, recyclable borane carrier.[49] They chose 2-(perfluorooctyl)ethyl methyl sulfide (**1.89**) due to the following reasons: (i) it has 65.4% F by weight, which facilitates its recycling by fluorous extraction; (ii) the effect of the strong electron-withdrawing fluorous group is moderate due to the insulation by a spacer; and (iii) economic considerations.

2-(Perfluorooctyl)ethyl methyl sulfide (**1.91**), which is an oily material, was synthesized in 76% overall yield (81% and 94% yields for the first and the second steps, respectively), by the reaction of 2-(perfluorooctyl)ethyl iodide (**1.89**) with potassium thioacetate followed by saponification with concomitant alkylation of the thiolate with methyl iodide (Scheme 1.31). The reactions were done under argon atmosphere and the products were purified by column chromatography. [49]



Scheme 1.31

Passing diborane gas through the neat liquid sulfide (Scheme 1.32) resulted in the formation of a white solid that was estimated by ^{1}H NMR spectroscopy to be an approximately 1:1 mixture of **1.91** and **1.92** (1 mmol BH_3/g solid).[49]

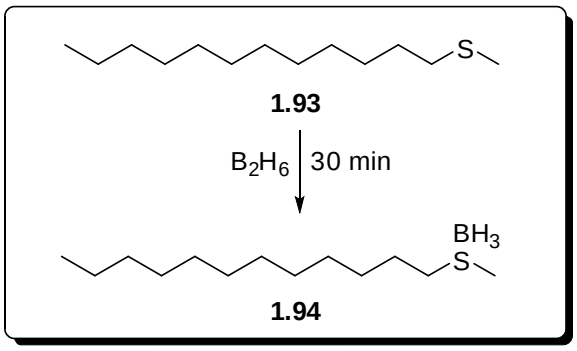


Scheme 1.32

It was found that the solid obtained (mixture of **1.91** and **1.92**) was stable and hydrolyzed only slowly on standing in air at room temperature, and it also showed no tendency to ignite under those conditions. Moreover it was indefinitely stable under an inert atmosphere in the refrigerator.[49] This complex was tested in hydroboration-oxidation and reduction reactions and was found to perform in a manner exactly similar to BMS. A method for hydroboration of alkenes and alkynes and reducing variable functional groups using such a fluorous borane-sulfide was patented in 2005.[50]

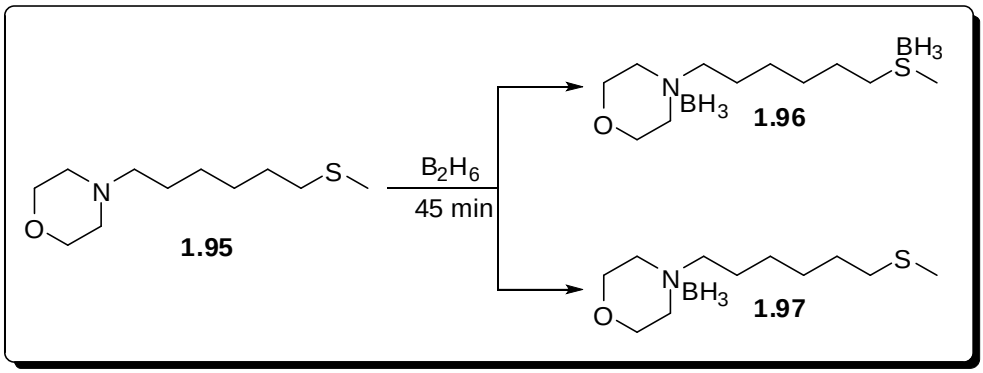
Patra *et al.*[51] have presented dodecyl methyl sulfide (Dod-S-Me; **1.93**) and methyl 6-morpholinohexyl sulfide (MMS; **1.95**) as efficient odourless borane carriers. By passing diborane gas through the neat Dod-S-Me for about 30 min, Dod-S-Me•BH_3 (**1.94**) was

synthesized (Scheme1.33) quantitatively as an oily material with 4.37 mmol BH_3 per gram of complex.



Scheme 1.33

Passing the diborane gas through neat MMS (**1.95**) for 45 min resulted in a viscous colourless liquid which was found to be a mixture of **1.96** and **1.97** (Scheme 1.34).[51] ^{1}H NMR analysis showed that ratio of **1.96**:**1.97** was 4:1. It was found that the amine-borane complex **1.97** was stable enough to be isolated and purified by silica gel column chromatography. The sulfide-borane was the active reagent and consequently the borane content was 3.35 mmol BH_3/g of mixture (4.1 mmol BH_3/g of **1.96**/**1.97**).[51]



Scheme 1.34

Both of Dod-S-Me•BH_3 and the mixture of MMS borane complexes were tested in hydroboration-oxidation and reduction reactions and were used in excess and found to be good hydroborating and reducing reagents.[51]

1.4.3 Polymer Supported Borane Reagents

Polymer-bound borane complexes offer the possibility of stable and easily handled materials of low volatility, with minimal odour and with easily recoverable polymeric carriers. Indeed, a number of polymer-bound complexes have been reported.[52-57]

In 1975 Crosby *et al.*[52] patented a number of polymeric sulfide-borane complexes. They reported the modification and synthesis of different solid, insoluble, cross-linked thiohydrocarbon polymers [*e.g.*; poly(vinyl)benzylmethylsulfide (**1.98**), polyphenylene sulfide (**1.99**) and poly(cyclohexene sulfide) (**1.200**)] (Figure 1.3). The syntheses or modification processes included more than one step in all cases.

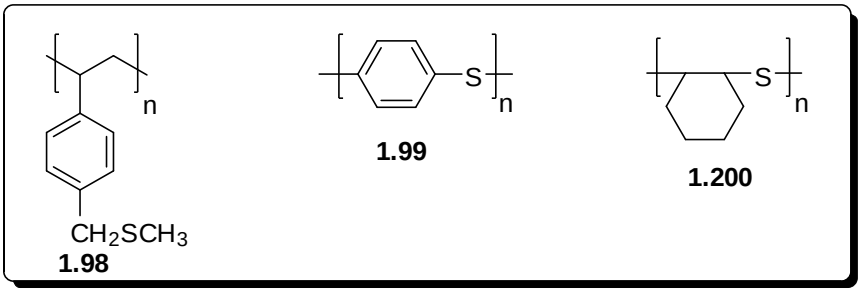


Figure 1.3: Examples of polymeric sulfides

The polymeric borane complexes were prepared by contacting the polymeric material with diborane gas at −196 ºC. It was found that at least 80% of the sulfur atoms in the polymers were in complex combination with BH_3. For the borane complex of **1.98**, the borane content was found to be 4.92 mmol BH_3/g. In general, these complexes are stable when stored under argon at ambient temperature. They were examined in hydroboration-oxidation and reduction reactions and the results revealed that these complexes were useful hydroborating and reducing reagents.[52]

In 1984 Domb and Avny[53] reported the graft polymerization of propylene sulfide on cross-linked polystyrene. The cross-linked polystyrene was lithiated by *n*-BuLi in the presence of tetramethylethylenediamine (TMEDA) and used to initiate graft polymerization of propylene sulfide to give polymer **1.201** with high sulfur content (10 mmol S/g). Chloromethylated polystyrene was grafted by the reaction of the chloromethylene groups with terminal sodium thiolate groups of living poly(propylene sulfide) and with sulfide groups of preformed poly(propylene sulfide) to give **1.202** (Figure 1.4).

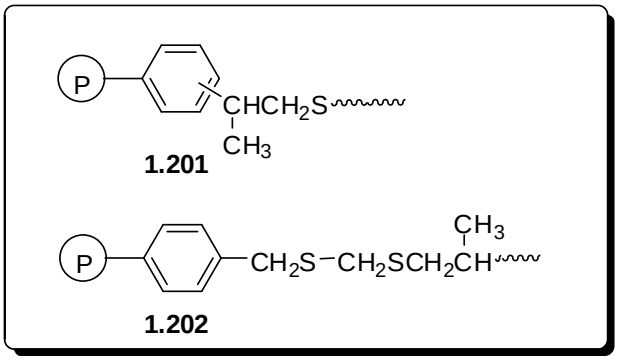


Figure 1.4: Cross-linked polystyrene grafted with poly(propylene sulfide)s

Synthesis of sulfide borane and haloborane complexes of poly(propylene sulfide) grafted onto cross-liked polystyrene has been reported by Domb and Avny.[54] These reagents have been used for hydroboration of alkenes and reduction of aldehydes and ketones to produce the corresponding alcohols. The reuse of the polymer was also studied and the results showed that 85% of the original BH_3 content could be generated at the end of the fourth cycle.

The borane content of the grafted poly(propylene sulfide) complex was low (around 2.44 mmol BH_3/g). A higher borane content (up to 7.05 mmol BH_3/g of polymer) was claimed for a homo poly(propylene sulfide) complex, but this material was prepared and used only as a dilute solution in dichloromethane and it was not clear whether removal of the solvent would have left a solid with such a high concentration of borane. There are no reports of the use of such complexes in synthesis, possibly because of the low borane content of the solid borane-polymer complex and the inconvenience of transporting a dilute solution of the homo poly(propylene sulfide)-borane complex. [54]

In 1985 Domb and Avny[55] reported the synthesis of borane complexes of cross-linked poly(4-vinylpyridine) (**1.203**, Figure 1.5). These complexes were prepared by two different methods: (i) the exchange reaction with BH_3•THF, (ii) the reaction of cross-linked poly(4-vinylpyridine) –boron trifluoride, –halogen and –hydrochloride with sodium borohydride. It was found that the cross-linked poly(4-vinylpyridine)-borane complex had a high degree of stability toward hydrolysis under acidic conditions and the borane content was up to 7.8 mmol/g.[55]

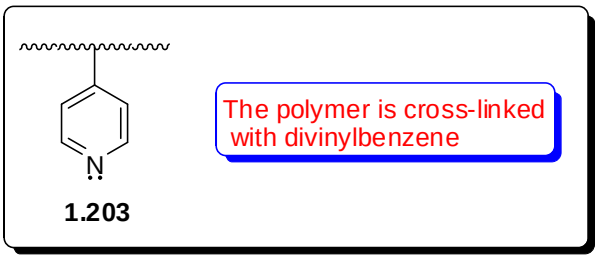
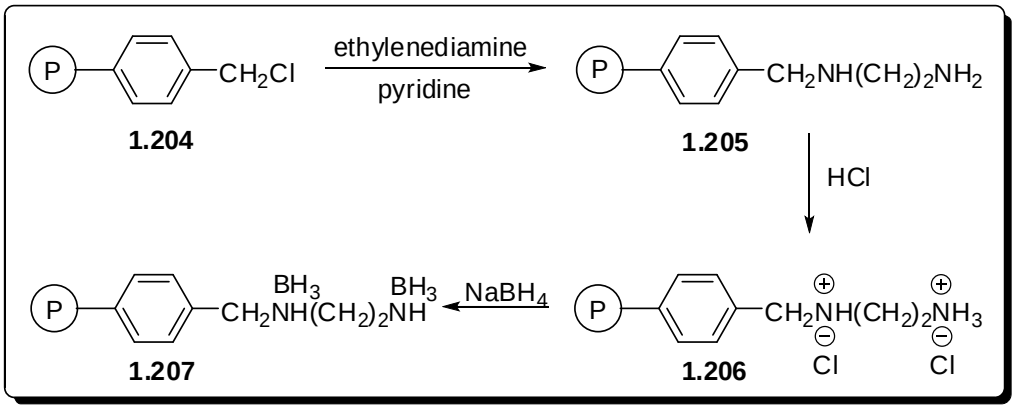


Figure 1.5: Cross-linked poly(4-vinylpyridine)

Later, Domb and Avny[56] studied the reduction of carbonyl compounds using the borane complex of **1.203** and found that only two of the of the boron hydrides are available for reduction; the third one is consumed by hydrolysis of the borane derivatives that formed during and after reaction. An acid catalyst (hydrochloric acid) was required; no product was formed in its absence even after several days. Thus, its reactivity profile is significantly different (and less useful) than that of BH_3•THF or BMS, so it cannot be viewed as a potential replacement.

In 2001 Rajasree and Devaky[57] introduced a polymer-supported ethylenediamine borane complex (**1.207**) as a new polymeric reducing agent. The polymeric reagent was prepared using a Merrifield resin (copolymer of styrene and chloromethylstyrene) or a 1,6-hexanediol diacrylate-cross-linked polystyrene resin (HDODA-PS). The latter was prepared by suspension polymerization of styrene and HDODA in toluene with benzoyl peroxide as the initiator. The polymer obtained was chloromethylated *via* a Friedel–Crafts reaction to give **1.204**. The polymer-bound ethylenediamine-borane reagent was prepared by a series of reactions including amination of the chloromethyl resins, conversion to amine hydrochloride, and, finally, with sodium borohydride to give the borane complex (Scheme 1.35).[57]



Scheme 1.35

The polymer could be regenerated easily and reused without loss in reactivity. These borane complexes have been used for reduction of aldehydes to the corresponding alcohols in high yields at room temperature, but the concentration of borane in the complexes was low (2.82 mmol BH_3/g for the Merrifield resin and 3.68 mmol BH_3/g for the HDODA-PS resin) and the use of a two molar excess of the polymeric reagent was required.[57]

1.5 Conclusions

It is clear that borane reagents are very important reagents for organic synthesis. Professor Keith Smiths's group has long-standing interests in the use of solids in green methodologies[58] and in boron chemistry,[59] which led us to consider the possibility of other polymeric sulfides as suitable borane carriers. In particular, we wished to develop complexes possessing high molarity in BH_3, based on solids that are easy to prepare, convenient to handle, have mild odour and low volatility and are environmentally benign. In the next chapter, we report the results of our efforts to develop such reagents.

1.6 References

1. Bruice, P. Y. *Organic Chemistry*, 4th ed., Pearson Education, New Jersey, USA, 2004.
2. Smith, J. G. *Organic Chemistry*, 3rd ed., McGraw-Hill, New York, USA, 2011.
3. Lane, C. F. *Aldrichim. Acta* **1975**, *8*, 20–23.
4. Lane, C. F. *Aldrichim. Acta* **1977**, *10*, 41–51.
5. Brown, H. C.; Heim, P.; Yoon, N. M. *J. Am. Chem. Soc.* **1970**, *92*, 1637–1646.
6. Clayden, J.; Greeves, N.; Warren, S.; Wothers, P. *Organic Chemistry*, Oxford University Press, New York, USA, 2008.
7. Brown, H. C.; Choi, Y. M. *Synthesis* **1981**, 439–440.
8. Brown, H. C.; Heim, P. *J. Org. Chem.* **1973**, *38*, 912–915.
9. Brown, H. C.; Narasimhan, S.; Choi, Y. M. *Synthesis* **1981**, 441–442.
10. Cho, B. T. *Aldrichim. Acta* **2002**, *35*, 3–16.
11. Saito, S.; Ishikawa, T.; Kuroda, A.; Koga, K.; Moriwake, T. *Tetrahedron* **1992**, *48*, 4067- 4086.
12. Corey, E. J.; Helal, C. J. *Angew. Chem. Int. Ed.* **1998**, *37*, 1986–2012.

13. Cai, D.; Desmond, R.; Shi, Y.–J.; Tschaen, D. M.; Verhoeven, T. R. *US Patent*, 5484923, **1996**.
14. Arase, A.; Hoshi, M.; Yamaki, T.; Nakanishi, H. *J. Chem. Soc., Chem. Commun*. **1994**, 855–856.
15. Amedia Jr., J. C.; Bernard, P. J.; Fountain, M.; Van Wagenen Jr., G. *Synth. Commun.* **1999**, *29*, 2377–2391.
16. Cha, J. S,; Moon, S. J.; Park, J. H. *J. Org. Chem.* **2001**, *66*, 7514–7515.
17. See for example: (a) Cho, B. T. *Chem. Soc. Rev.* **2009**, *38*, 443–452. (b) Hilborn, J. W.; Lu, Z.–H.; Jurgens, A. R.; Fang, Q. K.; Byers, P.; Wald, S. A.; Senanayake C. H. *Tetrahedron Letters* **2001**, *42*, 8919–8921. (c) Burgard, A.; Lang H.-J.; Gerlach, U. *Tetrahedron* **1999**, *55*, 7555–7562. (d) Boal, J. H.; Wilk, A.; Scremin, C. L.; Gray, G. N.; Phillips, L. R.; Beaucage, S. L. *J. Org. Chem.* 1996, *61*, 8617–8626. (e) Xu, J.; Wei, T.; Zhang, Q. *J. Org. Chem.* **2003**, *68*, 10146–10151. (f) Cha, J. S.; Nam, H. T.; Jang, S. H.; Kwon, S. Y.; Park, S. J.; Kwon, O. O. *Bull. Korean Chem. Soc*. **2004**, *25*, 1948–1950.
18. Shi, L.; Liu, Y.; Liu, Q.; Wei B.; Zhang, G. *Green Chem.* **2012**, *14*, 1372–1375.
19. Pelter, A.; Smith, K.; Brown, H.C. *Borane Reagents*, Academic Press, London, UK, 1988.
20. Thomas, S. E. *Organic Synthesis: The Role of Boron and Silicon*, Oxford University Press, New York, USA, 2004.
21. Sykes, P. *A Guide Book to Mechanism in Organic Chemistry*, 6th ed., Longman, UK, 2000.
22. Morrison, R. T.; Boyd, R. N. *Organic Chemistry*, 6th ed., Prentice Hall, New Jersey, USA, 1992.
23. Ramachandran, P. V.; Brown H. C. *Organoboranes for Syntheses*; ACS Symposium Series; American Chemical Society: Washington, DC, USA, 2001.
24. Brown H. C. *Organic Syntheses via Boranes*, John Wiely and Sons, New York, USA, 1975.
25. Smith, M. B.; March, J. *March's Advanced Organic Chemistry*, 6th ed., John Wiley and Sons, New Jersey, USA, 2007.
26. Brown H. C.; Murray, K. *J. Am. Chem. Soc.* **1959**, *81*, 4108–4109.
27. Brown H. C.; Rathke, M. W.; Rogic, M. M. *J. Am. Chem. Soc.* **1968**, *90*, 5038–5040.
28. Hillman, M. E. D. *J. Am. Chem. Soc.*, 1963, *85*, 982–984.

29. Brown, H. C.; Rathke, M. W. *J. Am. Chem. Soc.* 1967, *89*, 2738–2740.

30. Hubbard, J. L.; Smith, K. *J. Organomet. Chem.* **1984**, *276*, C41-C44.

31. (a) Pelter, A.; Hutchings, M. G.; Smith, K. *J. Chem. Soc., Chem. Commun.* **1970**, 1529–1530. (b) Pelter, A.; Hutchings, M. G.; Rowe, K.; Smith, K. ***J. Chem. Soc., Perkin Trans. 1***, **1975**, 138–142.

32. Aggarwal, V. K.; Fang, G. Y.; Ginesta, X.; Howells, D. M.; Zaja, M. *Pure Appl. Chem.* **2006**, *78*, 215–229.

33. Crudden, C. M.; Glasspoole, B. W.; Lata, C. J. *Chem. Commun*. **2009**, 6704–6716.

34. See foe example: (a) Kikuchi, T.; Nobuta, Y.; Umeda, J.; Yamamoto, Y.; Ishiyama, T.; Miyaura, N. *Tetrahedron* **2008**, *64*, 4967–4971. (b) Haraguchi, K.; Horii, C.; Yoshimura, Y.; Ariga, F.; Tadokoro, A.; Tanaka, H. *J. Org. Chem.* **2011**, *76*, 8658−8669. (c) Oshima, K.; Ohmura, T.; Suginome M. *J. Am. Chem. Soc.* **2012**, *134*, 3699−3702. (d) Harder, S.; Spielmann, J. *J. Organomet. Chem.* **2012**, *698*, 7−14. (e) Birch, P.; Parsons, A. F.; Cross, P. *Tetrahedron Letters* **2012**, *53*, 822−824. (f) Zhu, Y.; Jang, S. H. A.; Tham, Y. H.; Algin, O. B.; Maguire, J. A.; Hosmane N. S. *Organometallics* **2012**, *31*, 2589–2596. (g) Arrowsmith, M.; Hill, M. S.; Hadlington, T.; Kociok-Köhn, G.; Weetman C. *Organometallics* **2011**, *30*, 5556−5559.

35. (a) Pelter, A.; Smith, K.; Brown, H. C. *Borane Reagents*, Academic Press, London, 1988. (b) Ramachandran, P. V.; Brown, H. C. *Organoboranes for Syntheses*, American Chemical Society, Distributed by Oxford University Press, Washington DC, 2001.

36. (a) Follet, M. *Chem. Ind.* **1986**, 123–128. (b) Lane, C.F. *Aldrichim Acta* **1973**, *6*, 51–58. (c) Potyen, M.; Josyula, K.V.B.; Schuck, M.; Lu, S.; Gao, P.; Hewitt, C. *Org. Process Res. Dev*. **2007**, *11*, 210–214.

37. (a) Brown, H. C.; Heim, P.; Yoon, N. M. *J. Am. Chem. Soc.* **1970**, *92*, 1637–1646. (b) Zaidlewicz, M.; Brown, H. C. *Encyclopedia of Reagents for Organic Synthesis (EROS)*, Wiley, Chichester, UK, 1995, Vol 1.

38. (a) Adams, R. M.; Braun, L. M.; Braun, R. A.; Crissman, H. R.; Opprman, M. *J. Org. Chem.* **1971**, *36*, 2388–2389. (b) Lane, C. F. *J. Org. Chem.* **1974**, *39*, 1437–1438. (c) Brown, H. C.; Mandal, A.K.; Kulkarni, S. U. *J. Org. Chem.* **1977**, *42*, 1392–1398.

39. Brown, H. C.; Rao, B. C. S. *J. Am. Chem. Soc*. **1959**, *81*, 6423–6428.

40. Brown, H. C.; Zaidlewicz, M.; Dalvi, P. V. *Organometallics* **1998**, *17*, 4202–4205.

41. Brown, H. C.; Kanth, J. V. B.; Zaidlewicz, M. *J. Org. Chem.* **1998**, *63*, 5154–5163.
42. Brown, H. C.; Kanth, J. V. B.; Zaidlewicz, M. *Tetrahedron* **1999**, *55*, 5991–6000.
43. Brown, H. C.; Kanth, J. V. B.; Dalvi, P. V.; Zaidlewicz, M. *J. Org. Chem.* **1999**, *64*, 6263–6274.
44. Brown, H. C.; Mandal, A. K. *Synthesis* **1980**, 153–155.
45. Brown, H. C. *US Patent*, 4298750, **1981**.
46. Brown, H.C.; Mandal, A. K. *J. Org. Chem.* **1992**, *57*, 4970–4976.
47. Zaidlewicz, M.; Kanth, J. V. B.; Brown, H. C. *J. Org. Chem.* **2000**, *65*, 6697–6702.
48. Brown, H. C.; Zaidlewicz, M.; Dalvi, P. V.; Biswas, G. K. *J. Org. Chem.* **2001**, *66*, 4795–4798.
49. Crich, D.; Neelamkavil, S. *Org. Lett.* **2002**, *4*, 4175-4177.
50. Crich, D.; Neelamkavil, S. *US Patent*, 849767 B2, **1981**.
51. Patra, P. K.; Nishide, K.; Fuji, K.; Node, M. *Synthesis* **2004**, 1003–1006.
52. Crosby, G. A. *US Patent*, 3928293, **1975**.
53. Domb, A.; Avny, Y. *J. Appl. Polym. Sci.* **1984**, *29*, 2517–2528.
54. Domb, A.; Avny, Y. *J. Appl. Polym. Sci.* **1985**, *30*, 3589–3604.
55. Domb, A.; Avny, Y. *J. Macromol. Sci. Part A pure Appl. Chem*. **1985**, *22*, 167–181
56. Domb, A.; Avny, Y. *J. Macromol. Sci. Part A pure Appl. Chem*. **1985**, *22*, 183–201.
57. Rajasree K.; Devaky, K. S. *J. Appl. Polym. Sci.* **2001**, *82*, 593–600.
58. See for example: (a) Smith, K. *Solid Supports and Catalysts in Organic Synthesis*, Ellis Harwood, Chichester, UK, 1992. (b) Smith, K. *Selectivity through the use of Heterogeneous Catalysts*, In *Supported Catalysts and Their Applications*, Sherrington, D. C.; Kybett, A. P. Eds., The Royal Society of Chemistry, Cambridge, **2001**, pp. 233–241. (c) Delaude, L.; Laszlo, P.; Smith, K. ***Acc. Chem. Res.* 1993**, ***26***, **607–613.** (d) Smith, K. Ajarim, M. D.; El-Hiti, G. A. *Catal. Lett*. **2010**, *134*, 270–278. (e) Smith, K.; Ajarim, M. D.; El-Hiti, G. A. *Top. Catal*. **2009**, *52*, 1696–1700. (f) Smith, K.; El-Hiti, G. A. *Curr. Org. Chem.*, **2006**, *10*, 1603–1625. (g) Smith, K.; El-Hiti, G. A. *Curr. Org. Synth.* **2004**, *1*, 253–274. (h) Smith, K.; Ewart, G. M.; El-Hiti, G. A.; Randles, K. R. *Org. Biomol. Chem.* **2004**, *2*, 3150–3154. (i) Smith, K.; Roberts, S. D.; El-Hiti, G. A. *Org. Biomol. Chem*. **2003**, *1*, 1552–1559. (j) Smith, K.; El-Hiti, G. A.; Jayne, A. J.; Butters, M. *Org. Biomol. Chem*. **2003**, *1*, 2321–2325. (k) Smith, K.; El-Hiti, G. A.; Jayne, A. J.; Butters, M. *Org. Biomol. Chem*. **2003**, *1*, 1560–1564. (l) Smith, K.; Liu, C. –H. ***Chem.***

***Commun.* 2002, 886–887**. (m) Smith, K.; Almeer, S.; Peters, C. *Chem. Commun*. **2001**, 2748–2749. (n) Smith, K.; El-Hiti, G. A.; Hammond, M. E. W.; Bahzad, D.; Li, Z.; Siquet, C. *J. Chem. Soc., Perkin Trans. 1* **2000**, 2745–2752. (o) Smith, K.; Jones, D. ***J. Chem. Soc., Perkin Trans. 1* 1992, 407–408**.

59. See for example: (a) Smith, K. *Organoboron Chemistry*, In *Organometallics in Syntheses: A Manual*, 2nd ed., Schlosser, M. Ed., Wiley, Chichester, UK, **2004**, Chapter III, pp. 465–533. (b) Smith, K.; El-Hiti, G. A.; Hou D.; DeBoos, G.A. *J. Chem. Soc., Perkin Trans. 1* **1999**, 2807–2812. (c) Pelter, A.; Smith, K.; Hutchings, M. G.; Rowe, K. *J. Chem. Soc., Perkin Trans. 1* **1975**, 129–138. (d) Pelter, A.; Hutchings, M. G.; Rowe, K.; Smith, K. *J. Chem. Soc., Perkin Trans. 1* **1975**, 138–142. (e) Pelter, A.; Hutchings, M. G.; Smith, K. *J. Chem. Soc., Perkin Trans. 1* **1975**, 142–145. (f) Pelter, A.; Hutchings, M. G.; Smith, K.; Williams, D. J. *J. Chem. Soc., Perkin Trans. 1* **1975**, 145-150.

Chapter Two

Synthesis and Applications of New Polymeric Sulfide–Borane Complexes

Synthesis and Applications of New Polymeric Sulfide–Borane Complexes

2.1 Introduction

We have shown earlier in Chapter 1, that borane is a highly versatile reagent with numerous applications in organic syntheses and industrial processes and it is usually employed as a Lewis acid–base complex. However, it is clear that all borane–complexes beside their advantages also have several disadvantages. In this chapter we shall report the synthesis and the applications of new polymeric sulfide–borane complexes that overcome most of the disadvantages associated with borane reagents.

2.2 Synthesis of Poly(alkylene sulfide)s

Poly(alkylene sulfide)s are useful polymers because they have weatherability, excellent thermal stability, solvent resistance and oil resistance.[1-3] Therefore, such polymers have been used in coatings, adhesives, sealants, insulators and different other applications.[4-8] The wide range of properties of poly(alkylne sulfides)s makes the syntheses of such polymers always of interest.

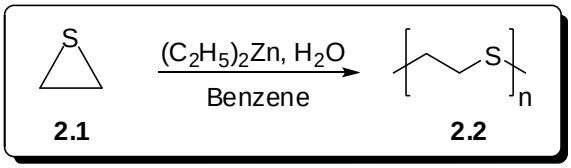
It is revealed from the literature that there are four major processes for the synthesis of poly(alkylene sulfide)s.[9] These processes involve: polymerization of episulfides; reactions of dithiols with carbonyl compounds; addition of dithiols to diolefins; and reactions of dithiols with dihalides.

2.2.1 Synthesis of Poly(alkylene sulfides) by Polymerization of Episulfides

Poly(ethylene sulfide) (**2.2**) can be produced by the ring opening polymerization of ethylene sulfide (**2.1**) in the presence of basic catalyst such as sodium hydroxide, sodium alkoxide, ammonia, amines and alkali metals.[13] The polymerisation was also found to be effective in the presence of acidic catalysts such as mineral acids, boron trifloride,[11] triethylaluminium,[12] phosphorus pentafloride.[13]

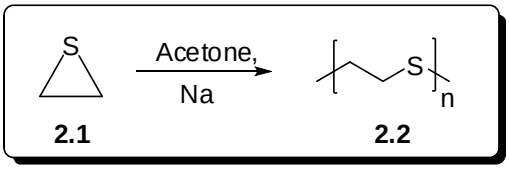
Various co-catalysts can be used, including water, glycols, alcohols, oxygen, hydrogen sulfide, mercaptans and sulfur.[14,15] Polymerization of ethylene sulfide (**2.1**) using a diethylzinc–water catalyst (Scheme 2.1) is a representative process for this kind of polymerization. The procedure involves mixing dry ethylene sulfide, water and the

catalyst in a stainless steel polymerization cylinder under an inert atmosphere in dry benzene as a solvent. The vessel is then sealed and the temperature is raised to 80 °C for 2 h with stirring. Following work up and drying a white powdery polymeric solid is obtained.



Scheme 2.1

Poly(ethylene sulfide) (**2.2**) can also be synthesised by polymerization of **2.1** using acetone-sodium as a catalyst (Scheme 2.2). In this procedure **2.1** is added to a mixture of acetone and sodium dispersion (10% by weight) in toluene. The exothermic reaction starts immediately and the polymer is precipitated as a powder while the temperature rises to bring the acetone to reflux. The polymerization is complete within 10 min and the polymer is obtained in 99% yield.[16]

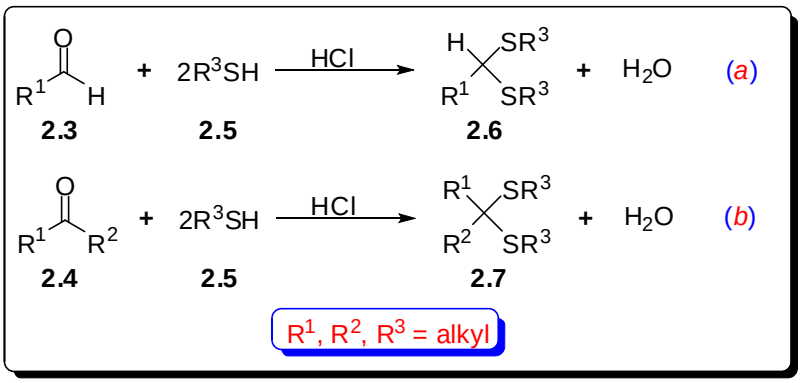


Scheme 2.2

Synthesis of poly(alkylene sulfide)s by ring-opening polymerization of other cyclic sulfides was also reported by Stille and Empen.[17] They found, however, that tetrahydrothiophene and 7-thiabicyclo[2.2.1]heptane do not polymerize in the presence of various initiators such as PF_5, BF_3•$(C_2H_5)_2O$, $(C_2H_5)_3Al$-H_2O and $(CH_3)_3OBF_4$.[17]

2.2.2 Synthesis of Poly(alkylene sulfide)s by the Reactions of Dithiols with Carbonyl Compounds

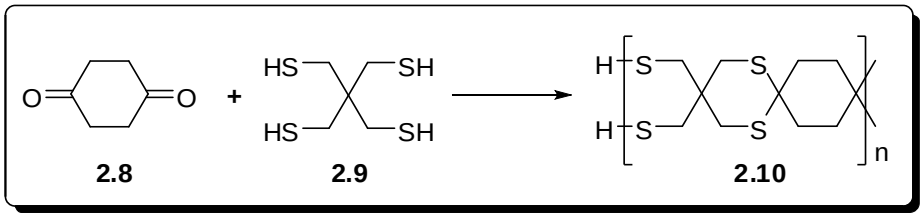
Baumann reported that in acidic medium, aldehydes **2.3** or ketones **2.4** react with thiols **2.5** to give the corresponding dithioacetals **2.6** and **2.7**, respectively, in high yields (Scheme 2.3 *a* and *b*).[18]



Scheme 2.3

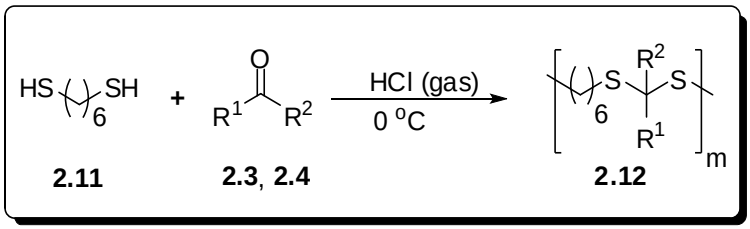
Later on Autenrieth and Geyer[19] reported that crystalline cyclic dithioacetals can be formed from reaction of 1,5-pentanedithiol with a ketone such as acetone or diethyl ketone. They also reported the production of non-crystalline products from the use of different carbonyl compounds such as benzophenone, acetaldehyde and benzaldehyde. However these materials were probably polymeric but not fully characterized.

Synthesis of spirocyclic poly(dithioacetal) **2.10** from the reaction of 1,4-cyclohexanedione (**2.8**) and tetrathiol **2.9**, derived from pentaerythritol, was reported by Fisher and Wiley (Scheme 2.4).[20]



Scheme 2.4

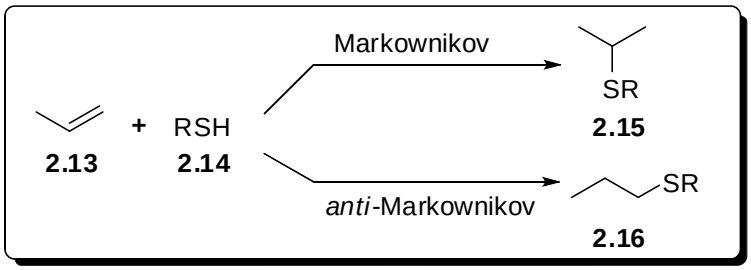
Synthesis of linear poly(dithioacetal)s was reported by Marvel *et al.*[21] For example, the polymeric materials **2.12** were produced from reactions of dithiols [*e.g.* 1,6-hexanedithiol (**2.11**)] with aldehydes **2.3** or ketones **2.4** in the presence of dry hydrogen chloride with or without the use of solvent (*e.g.* dioxane) (Scheme 2.5).



Scheme 2.5

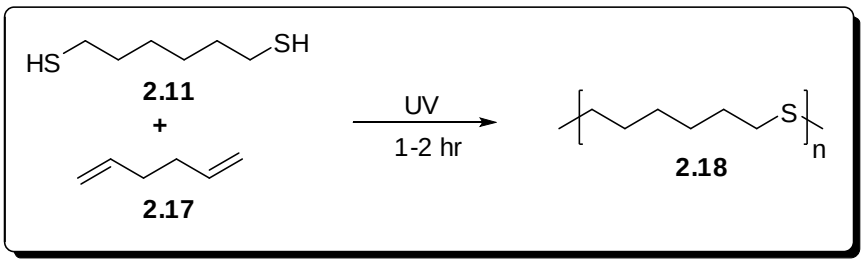
2.2.3 Synthesis of Poly(alkylene sulfide)s by the Addition of Dithiols to Dienes

Production of monosulfides by the reaction of thiols with alkenes was described by Posner in 1905.[22] Later on Mayo and Walling established that the production of sulfides **2.15** and **2.16** by the addition of thiols **2.14** to alkenes (*e.g.* **2.13**), this process could happen in two modes, Markownikov and *anti*-Markownikov additions (Scheme 2.6). In the presence of acid as catalyst the reaction follows Markownikov addition and yields branched sulfides **2.15**, while in the presence of a free radical catalyst it follows *anti*-Markownikov addition and yields linear sulfides **2.16**.[23]



Scheme 2.6

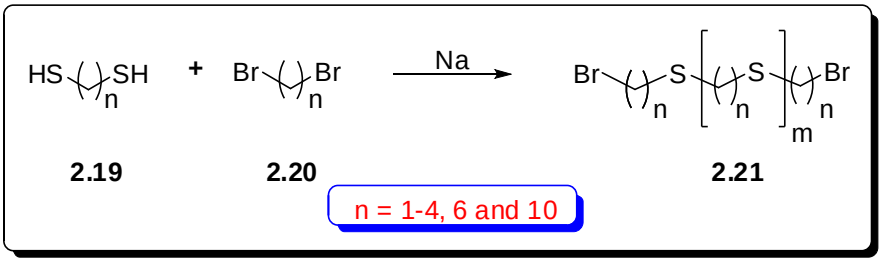
Synthesis of poly(alkylene sulfide)s from reactions of biallyl or diallyl ethers with hydrogen sulfide was reported by Vaughan and Ruts[24], but the polymers obtained were found to be of low molecular weights (less than 300). Coffman[25] has reported the synthesis of poly(alkylene sulfide)s of larger molecular weights (*ca*. 1300) from reaction of dithiols with dienes. Poly(alkylene sulfide)s (*e.g.* **2.18**) with molecular weights up to 14,000 were prepared by Marvel *et al.*,[30,26] using UV irradiation of a mixture of 1,6-hexanedithiol (**2.11**) and 1,5-hexadiene (**2.17**) in cyclohexane in a closed quartz test tube for 1–2 h (Scheme 2.7).



Scheme 2.7

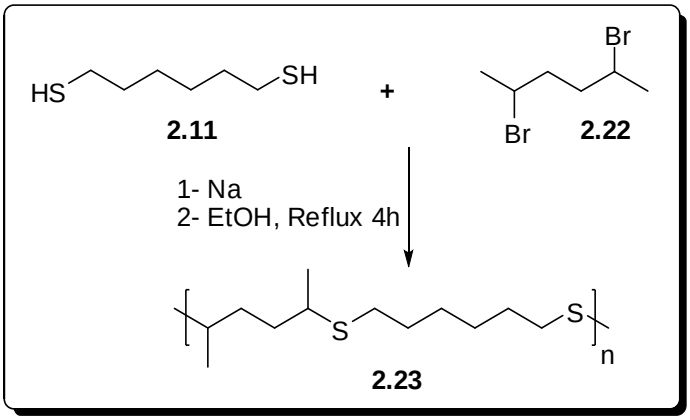
2.2.4 Synthesis of Poly(alkylene sulfides) by the Reaction of Dithiols and Dihalides

Tucker and Reid[27] have studied the reactions of the sodium salt of 1,2-ethanedithiol with various α,ω-dibromides. They found that cyclic products as well as amorphous polymers were produced. Syntheses of additional cyclic products and polymers were also reported by Meadow and Reid in 1934.[28] Later, synthesis of poly(hexamethylene sulfide) from reaction of 1,6-hexanedithiol and 1,6-dibromohexane was also reported.[29] Following the same method Marvel and Chambers produced poly(hexamethylene sulfide), but they found that the polymeric materials were of low molecular weight.[30] Production of different poly(alkylene sulfide)s **2.21** by the reaction of dithiols **2.19** with the corresponding dihalides **2.20** under the influence of sodium as catalyst (Scheme 2.8) has also been reported.[31]



Scheme 2.8

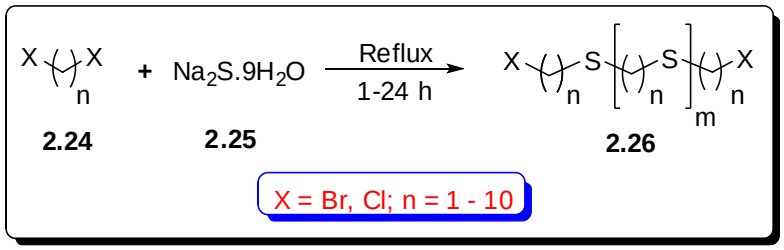
The process represented in Scheme 2.8 was found to be applicable for the synthesise of branched poly(alkylene sulfide)s. For example, reaction of the disodium salt of 1,6-hexanedithiol **2.11** and 2,5-dibromohexane (**2.22**) in refluxing ethanol for 4 h produced the polymeric material **2.23** (Scheme 2.9).[30]



Scheme 2.9

2.2.5 The synthesis of Poly(alkylene sulfide)s by Reaction of Dihaloalkanes with Sodium Sulfide

A simple, general, convenient, catalyst free and solvent free procedure for the production of poly(alkylene sulfide)s of the general formula **2.26** has been developed by Keith Smith`s research group.[32a] According to this method poly(alkylene sulfide)s can be synthesized in excellent yields by the reactions of α,ω-dibromo- and/or α,ω-dichloroalkanes **2.24** with sodium sulfide nonahydrate (**2.25**) under reflux conditions (Scheme 2.10). The process was found to be applicable for the production in commercial scale and has been produced successfully in the laboratory in kilograms scale.[32b]

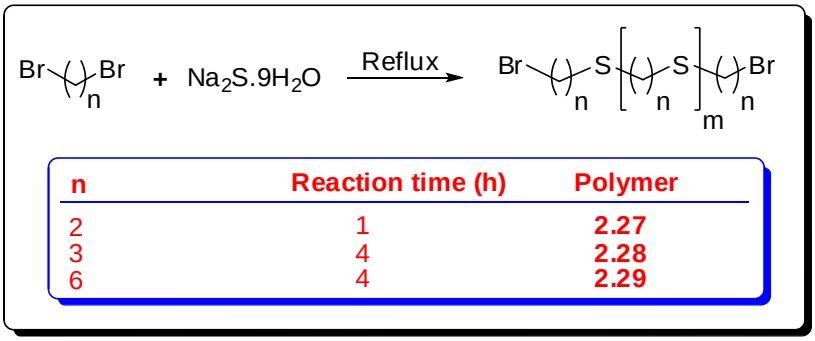


Scheme 2.10

Having such a method developed within our research group prompted us to try to find application for such polymeric materials in organic synthesis. Therefore, we have decided to produce a range of such polymers and try to produce the corresponding borane complexes and use them as reducing and hydroborating reagents, which if successful could replace the traditional borane complexes such as borane–dimethyl sulfide.

2.3 Synthesis Poly(alkylene sulfide)s as Polymeric Borane Carriers

The first task in this project was to synthesize a number of poly(alkylene sulfide)s to be used as borane carriers. We have prepared poly(alkylene sulfide)s **2.27** (n = 2), **2.28** (n = 3) and **2.29** (n = 6) using the corresponding α,ω-dibromoalkanes and sodium sulfide nonahydrate according to the method developed within the group (Scheme 2.11). The mixture was refluxed for 1–4 h and left to cool to room temperature. Following workup, the white solid obtained was filtered and washed with water and dried under reduced pressure to give the corresponding polymeric materials **2.27–2.29** in quantitative yields.



n	Reaction time (h)	Polymer
2	1	**2.27**
3	4	**2.28**
6	4	**2.29**

Scheme 2.11

Polymer **2.27** was found to behave differently than **2.28** and **2.29**. Polymeric material **2.27** had a relatively high melting point (185–186 °C) compared to the others (55–77 °C). Also, **2.27** was highly insoluble in most organic solvents. Therefore, no ^{1}H NMR, ^{13}C NMR or gel permeation chromatography (GPC) analysis were recorded for **2.27**. In contrast **2.28** and **2.29** were very soluble in chlorinated solvents. The ^{1}H NMR, and ^{13}C NMR spectra of **2.28** and **2.29** showed signals that are well correlated to the structures of the repeating units (detailed characterization data are explained in the experimental section). Table 2.1 represents the melting points and relative molecular weights (determined by GPC analysis) for polymeric materials **2.27–2.29**.

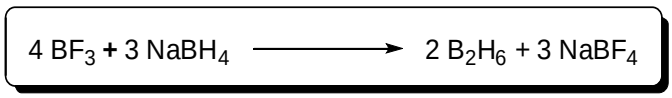
Table 2.1: Synthesis of poly(alkylene sulfide)s 2.27–2.29 according to Scheme 2.11.

Polymer	Mp (°C)	Mn[a] (Daltons)	Mw[b](Daltons)	PDI[c]
2.27	185-186	—	—	—
2.28	55-57	4100	9000	2.2
2.29	70-77	4600	10000	2.2

[a] Number average molecular weight. [b] Weight average molecular weight. [c] Polydispersity index.

2.4 Synthesis Poly(alkylene sulfide)–Borane Complexes

Having successfully prepared poly(ethylene sulfide) **2.27**, poly(propylene sulfide) **2.28** and poly(hexylene sulfide) **2.29** the next task was to attempt the preparation of their complexes with borane. Borane gas, which can be produced by the reaction of trifluoroborane etherate (BF_3•OEt_2) and sodium borohydride ($NaBH_4$) (Scheme 2.12), exists as a mixture of the monomer (BH_3) and the dimer (B_2H_6).[33]

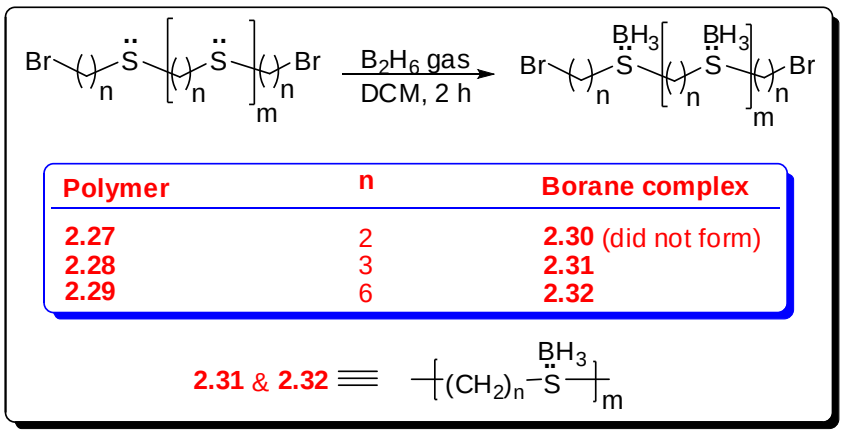


Scheme 2.12

Based on the fact the boron atom has three electrons in *2p* orbitals, it is able to form three two-centre two-electron bonds with other atoms in a planar monomeric structure, leaving a vacant *2p* orbital which is able to accept a lone pair of electrons from a Lewis base. The vacant orbital of the borane molecule should be able, therefore, to accept a lone pair of electrons from a sulfur atom of a poly(alkylene sulfide) to form a complex.

The ability of these polymers to form borane complexes was studied by bringing them in contact with *ex-situ* generated diborane gas or BH_3•THF. Some experiments were conducted by one of our group members to find the best way of making the desired complexes using four different procedures: (i) reaction of neat solid polymeric sulfide with diborane gas; (ii) reaction of neat polymer with BH_3•THF; (iii) reaction of a solution of the polymeric material (suspension in the case of **2.27**) with BH_3•THF; and (iv) reaction of a solution of the polymeric material (suspension in the case of **2.27**) with *ex-situ* generated diborane gas. It was found that procedure (iv) was the most convenient one and the effects of several solvents in this process of the preparation of borane complexes were also tested. The hydride content of the resulting complexes from reaction in chloroform ($CHCl_3$) or diglyme was lower by about 10% than for complexes formed in dichloromethane (DCM).

Accordingly, following the most convenient procedure, *ex-situ* generated diborane gas was passed into a solution (suspension in the case of **2.27**) of the polymeric materials **2.28** and **2.29** (3.0 g) in dichloromethane (20 mL) at room temperature for 2 h (Scheme 2.13). The solvent was removed under inert atmosphere by blowing with nitrogen and the solid left was kept under nitrogen in each case. Removal of solvent in the case of **2.31** was much easier than in the case of **2.32** which required use of reduced pressure to remove the solvent. Polymers **2.28** and **2.29** absorbed significant quantities of borane, while no borane complex was obtained in the case of polymeric material **2.27** which could be attributed to its poor solubility in the solvent used.

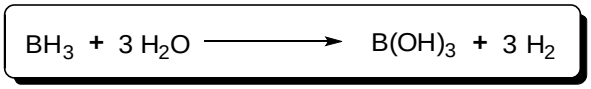


Polymer	n	Borane complex
2.27	2	2.30 (did not form)
2.28	3	2.31
2.29	6	2.32

Scheme 2.13

2.5 Estimation of the Borane Content in the New Poly(alkylene sulfide)-Borane Complexes 2.31 and 2.32

A method of quantitative analysis of hydride solutions using a gas burette[34] was used to determine the borane content (mmols of BH_3 in 1 g of the borane complex). This method is based on measurement of the volume of the hydrogen gas that evolves from hydrolysis of the borane with water, which liberates 1 mole of hydrogen per hydride (Scheme 2.14). The hydrolysis of borane with water happens in two stages. Two of the hydrides in borane hydrolyse rapidly, but the third one hydrolyses relatively slowly. Therefore, a mixture of water: glycerol: 3 M HCl (1:1:1 by volume) was used as a hydrolysing reagent because in the presence of glycerol, all three hydrides are easily displaced, perhaps due to a chelating effect.[35]



Scheme 2.14

The hydrolysing reagent (5.0 mL) was added to a flask containing the solid complex (0.1 g) and dry diglyme (3.0 mL) with efficient stirring and the hydrogen evolution was observed and measured accurately. From the volume of the evolved hydrogen gas the number of moles of the hydride, which represents three times the amount of the borane in the sample, was worked out. The measurement was repeated until coherent outputs were collected. It is reported that this method gives an accuracy of ±5% when applied for the analysis of BH_3•THF.[34] Table 2.2 shows the results that were obtained from

four measurements for a single batch of the polymeric complex **2.31**. The average of these results was 8.5 mmol BH_3/g which was then used as the value for this batch.

Table 2.2: Data obtained from four measurements for a single batch of the polymeric complex 2.31

Mesurment	mmol BH_3/g
1st	8.3
2^{nd}	8.7
3^{rd}	8.5
4th	8.5

To determine the amount the of coordinated sulfur in the poly(alkylene sulfide)-borane complexes, microanalyses for polymers **2.28** and **2.29** were carried out, then, the complexes **2.31** and **2.32** were prepared and their borane contents were estimated. Table 2.3 shows the percentage sulfur in the complex, the borane content per gram of complex and the calculated B/S ratio.

Table 2.3: The ratio of B/S in the prepared borane complexes 2.31 and 2.32

Polymer	Complex	n	mmol S/g	mmol BH_3/g	B/S ratio[a]
2.28	**2.31**	3	11.33	8.5	0.75
2.29	**2.32**	6	7.25	5.0	0.69

[a] Ratio of BH_3 molecules (estimated by measurement of hydrogen evolved on hydrolysis in THF:glycerol:3 M HCl (1:1:1) to S atoms present (measured by microanalysis for the polymer).

2.6 Stability of Poly(propylene sulfide)–Borane Complex (2.31)

The borane–complexes **2.31** and **2.32** could both potentially be used as reducing and hydroborating reagents. However, complex **2.31** has two advantages over **2.32**, which are its easy isolation as a solid by just blowing with nitrogen and its higher borane content. Therefore, we decided to test the stability of **2.31** over a period of time. The stability of **2.31** was studied by three different methods: (i) the use of infrared (IR) spectroscopy to check its stability in air; (ii) the use of thermogravimetric analysis (TGA) to study its thermal stability; and (iii) the estimation of the BH_3 content at regular time intervals using the gas analysis technique.

2.6.1 Stability Study of Poly(propylene sulfide)–Borane Complexe 2.31 in Air by IR Spectroscopy

The stability of **2.31** in air was tested to see whether it is possible to weigh it on a simple balance without protection from air or not. An experiment was conducted by one of our group members that involved measurement of the IR spectra of the borane complex **2.31** at regular intervals (from 5 min to 4 h). The IR spectrum of the freshly prepared sample of **2.31** showed two distinct peaks at 2398 and 1095 cm^{-1}, which may be attributed to B-H and B-S stretching vibrations, respectively.[36] No peak around 3200 cm^{-1} corresponding to boric acid was observed initially. After the sample had stood for 4 hours in air the peaks at 2398 and 1095 cm^{-1} began to diminish noticeably and a strong peak around 3200 cm^{-1} began to appear, thereby indicating hydrolysis of the borane complex. Only on prolonged standing did the solid begin to darken. This significant stability in air enabled the solid borane complexes to be weighed on a simple balance without need of any protective technique. Furthermore complex **2.31** was non-ignitable and has a very mild odour which indicates that it does not release borane readily.

2.6.2 Thermal Stability Study of Poly(propylene sulfide)-Borane Complexe 2.31 by Thermogravimetric Analysis (TGA)

The second method for investigating the stability of **2.31** involved thermogravimetric analysis for the polymer **2.28** and the borane complex **2.31.** The TGA of **2.28** indicated that there was no weight loss until above 200 ºC, while the TGA of **2.31** (which was conducted under nitrogen) indicated that there was no weight loss below 120 ºC, which suggests that the loss of borane just started at that high temperature. Figure 2.1 shows the weight loss against temperature for **2.28** and **2.31**.

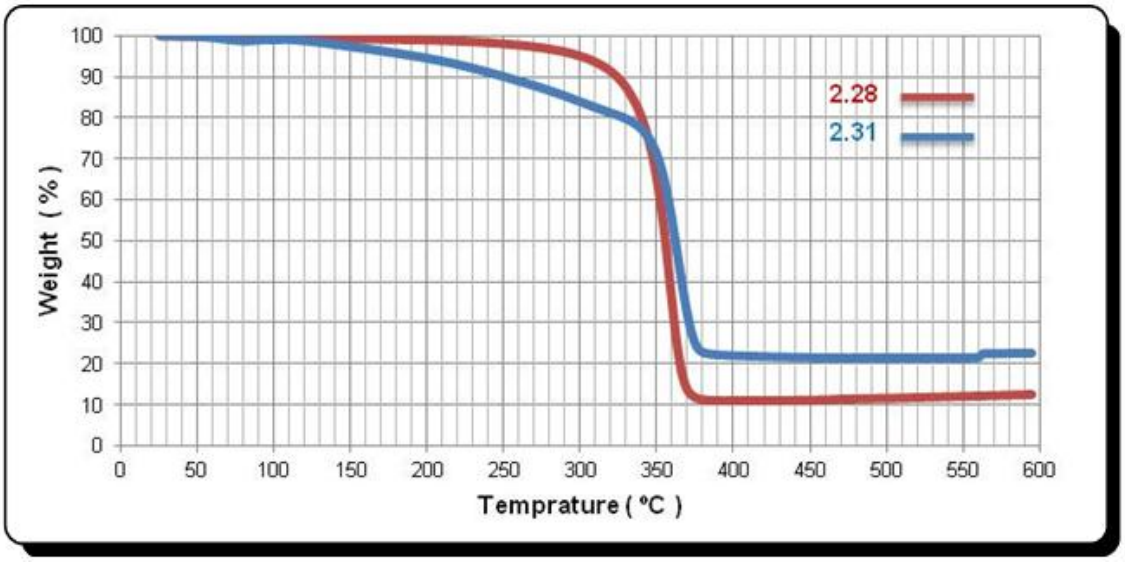


Figure 2.1: Thermogravimetric analysis of 2.28 and 2.31

2.6.3 Stability Study of Poly(propylene sulfide)–Borane Complex 2.31 by Gas Analysis

For this study a fresh sample of **2.31** was prepared and its borane content was estimated by gas analysis on the day of preparation. The sample was then kept in a flask sealed with a rubber septum and flushed with nitrogen. At the time intervals shown in Figure 2.2, the flask was opened, samples were taken and the flask was then re-sealed. The samples were weighed on a simple balance in the open atmosphere and subjected to gas analysis to estimate the BH_3 content. The results are shown in Figure 2.2. It was clear that complex **2.31** was fairly stable even under such conditions. For a sample kept in such a way for 3 years without sampling, the loss of BH_3 was only 30%. Another sample was prepared, its BH_3 content was estimated and it was stored in a flask flushed with nitrogen and sealed well by a glass stopper, it was found that its BH_3 content was 100% even after 3 months, indicating that deterioration in the other case was primarily through contact with air during sampling or by diffusion through the rubber septum.

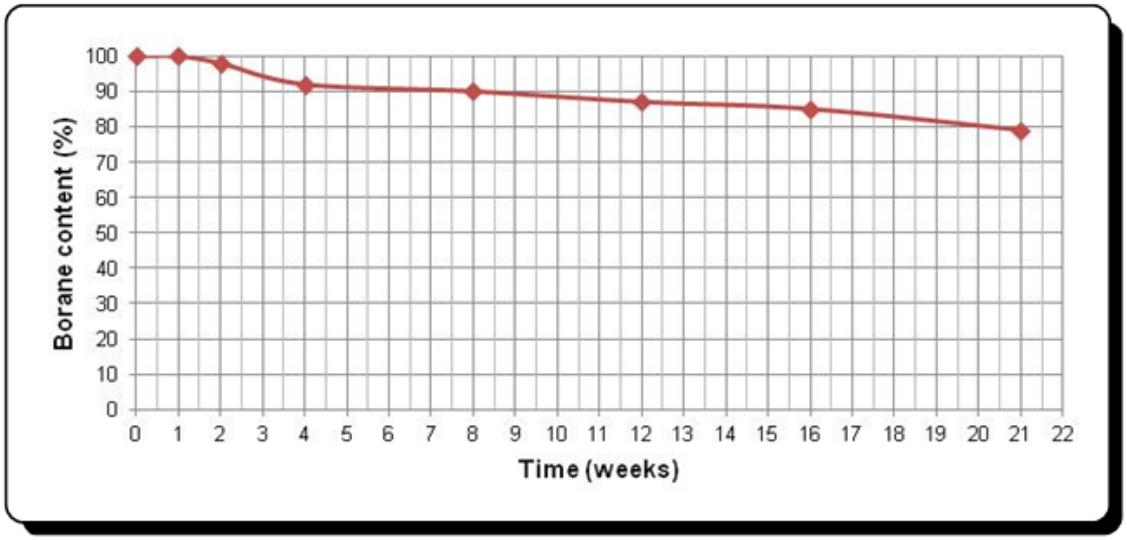
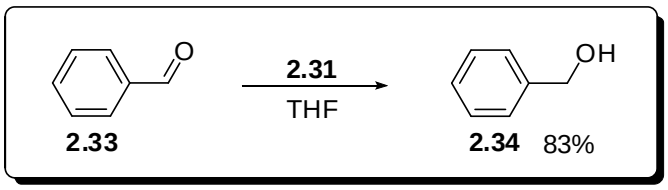


Figure 2.2: Loss of borane content of 2.31 over time when stored under a septum

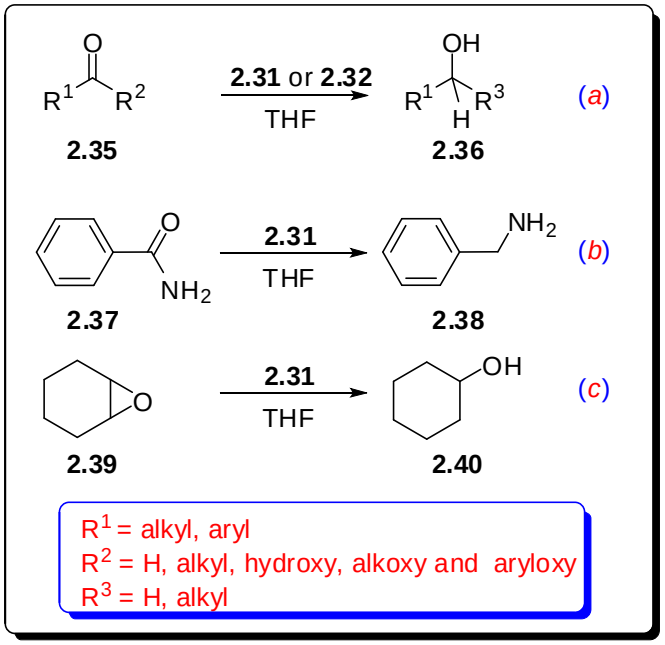
2.7 The Use of the New Polymeric Sulfide-Borane Complexes 2.31 and 2.32 as Reducing Agents

As we showed earlier in Chapter One, borane reagents are widely used in reduction reactions. To investigate the appropriateness of the new polymeric borane complexes for such uses, we decided to use benzaldehyde **2.33** as a substrate in a test reduction reaction using **2.31** as the reducing agent (Scheme 2.15). The reaction was carried out by dissolving **2.31** (*ca.* 2 mmol) in dry THF followed by the addition of benzaldehyde (5 mmol) and the mixture was stirred at 0 °C for 30 min then at room temperature for 2 h. The reaction was worked-up by the addition of methanol, followed by diethyl ether to precipitate the polymeric material **2.28** which was removed by filtration. Solvent was then removed under reduced pressure to give a crude liquid material for which GC analysis showed that the starting material (**2.33**) had disappeared and had been replaced by a single component that had a retention time identical to an authentic sample of benzyl alcohol (**2.34**) obtained from Sigma – Aldrich. ^{1}H NMR analysis confirmed that the product was benzyl alcohol. It showed that the signal of the aldehyde proton had disappeared and an exchangeable signal at δ = 2.26 corresponding to the hydroxyl proton, had appeared. It also showed a singlet signal at δ = 4.45 corresponding to the methylene group of benzyl alcohol. All of the spectroscopic data of the crude product were identical with the authentic sample. It was clear that benzyl alcohol (**2.34)** was obtained (Scheme 2.15). The yield of the isolated product was 83%, with no purification process being required.



Scheme 2.15

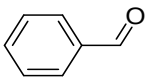
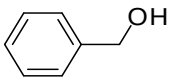
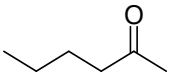
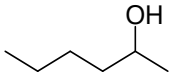
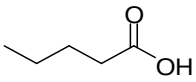
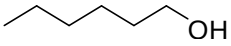
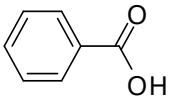
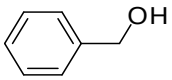
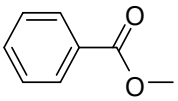
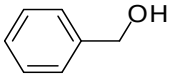
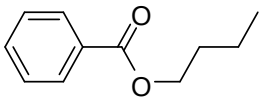
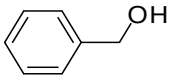
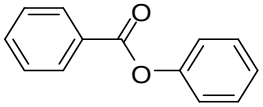
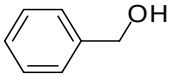
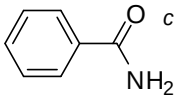
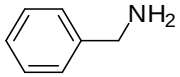
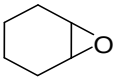
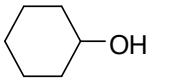
According to the result obtained from the above test reaction we then decided to study the reduction of other carbonyl compounds (*e.g.* Scheme 2.16*a* for reduction of aldehydes, ketones, esters, and carboxylic acids) using **2.31** and **2.32**. Benzamide (**2.37**) and cyclohexene oxide (**2.39**) were also used as substrates (Scheme 2.16*a* and *b* respectively).



Scheme 2.16

According to the mechanisms of reduction of each particular type of compounds the expected stoichiometries (substrate to borane) are: 1:0.33 for aldehydes, ketones and epoxides; 1:0.67 for esters; 1:1 for acids and finally 1:1.33 for primaryamides. However we used an excess (*ca.* 20%) of borane in all cases except for the reduction benzamide where *ca*. 40% excess borane was used. The results obtained are recorded in Table 2.4.

Table 2.4: Reduction of functional groups with borane–complex 2.31 in anhydrous THF under reflux for 4 ha

Starting material	2.31 (mol. eq.)	Product	Yield (%)[b]
	0.4		100
	0.4		94
	1.2		92
	1.2		90
	0.8		99
	0.8		97
	0.7		88
	1.9		51 (66)[d]
	0.4		85

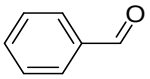
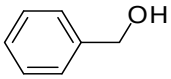
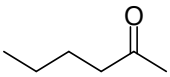
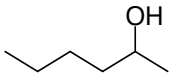
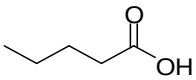
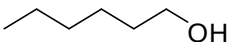
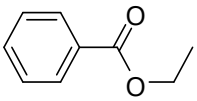
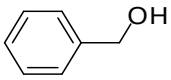
[a] Organic compound (5 mmol) was added to a solution of **2.31** in THF and the mixture was stirred at 0 °C for 30 min and then refluxed for 4 h. Methanol (3 mL) was added and the mixture was stirred for 15 min, then the product was extracted into diethyl ether (20 mL). [b] By GC analysis using hexadecane as internal standard. [c] After reaction HCl (1.0 M, 3 mL) was added and the mixture was refluxed for 2 h, cooled to 0 °C, then diethyl ether (20 mL) and NaOH (pellets) were added to neutralize the solution followed by the separation of the organic layer. [d] The reaction time was 16 h.

The optimized procedure for the reduction process involved addition of a standard solution of the organic compound in THF to an appropriate quantity of borane–complex **2.31** in anhydrous THF at 0 °C and then the mixture was refluxed for 4 h. The excess borane was then quenched with methanol, the polymeric material was precipitated by diethyl ether and the product was analyzed by GC. Reduction of most substrates was straightforward and gave high yields (85-100%) of the corresponding alcohols, similar to the yields obtained with borane dimethyl sulfide (BMS).[37,38] Although the reactions were carried out under standard conditions under reflux for 4 h, such forcing conditions were

often not necessary. However, the reduction of benzamide was slow and a yield of only 66% of benzylamine was obtained even after a longer reaction time (16 h).

Having successfully reduced a range of compounds with the borane–complex **2.31** our attention was next turned to see if the complex **2.32** could be used as a reducing reagent. Therefore, reductions of various carbonyl compounds were attempted by the use of **2.32** under conditions similar to those used with **2.31**. The results reported in Table 4.5 clearly indicated that the complex **2.32** can be used as a successful reducing agent and produce the corresponding alcohols in high yields (84-100%). Again, the reactions were carried out under standard conditions at reflux for 4 h, although not all examples needed such forcing conditions.

Table 2.5: Reduction of carbonyl compounds with borane complex 2.32 in THF

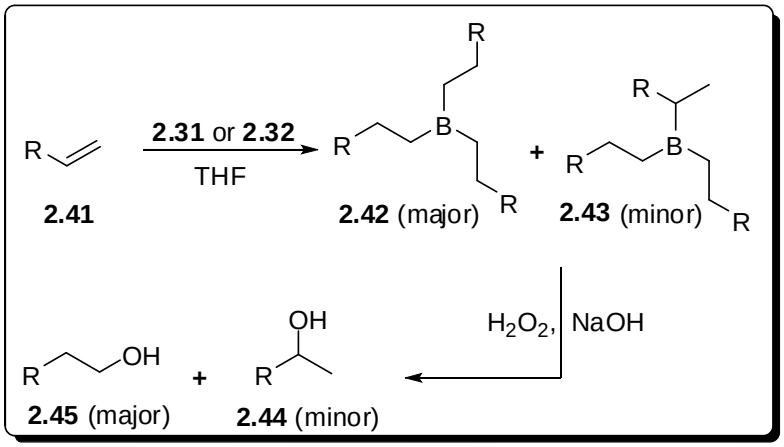
Starting material	2.32 (mol. eq.)	Product	Yield (%)[b]
	0.4		100
	0.4		84
	1.1		93
	0.8		94

[a] Carbonyl compound (5.0 mmol) was added to a solution of **2.32** in THF and stirred at 0 °C for 30 min then refluxed for 4 h. Methanol (3 mL) was added and the mixture was stirred for 15 min then extracted with diethyl ether (20 mL). [b] By GC analysis using hexadecane as internal standard.

Both borane–complexes **2.31** and **2.32** were found to be excellent reducing reagents for various carbonyl compounds, and the yields obtained in all cases were high. It was of interest to explore another application of such complexes and therefore we decided to test them in hydroboration–oxidation reactions.

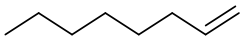
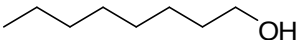
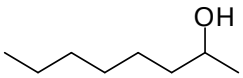
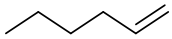
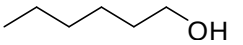
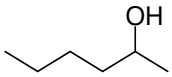
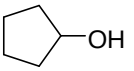
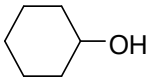
2.8 The Use of the New Polymeric Sulfide–Borane Complexes (2.31 and 2.32) in the Hydroboration–Oxidation of Alkenes

Hydroboration of alkenes is the key step in different synthetic pathways; hydroboration-oxidation is the simplest mode of these reactions. Therefore we decided to use the new polymeric borane complexes in such reactions. Initially hydroboration-oxidation of 1-octene (Scheme 2.17; R = *n*-C_6H_{13}) in anhydrous THF at room temperature was conducted with the borane complex **2.31** for 4 h. The reaction provided 61% overall yield (by GC) of a mixture of 1-octanol (59%) and 2-octanol (2%). Similar yields of 1- and 2-octanol were obtained when borane-complex **2.32** was used instead of **2.31**. Clearly, such borane-complexes are reactive and give comparable yields to those obtained with BMS[39] and BH_3•THF.[40] Thus, hydroboration of other representative alkenes was conducted initially with **2.31** as the borane complex (Scheme 2.17). The results are recorded in Table 2.6.



Scheme 2.17

Table 2.6: Hydroboration-oxidation of alkenes with the borane complex 2.31 in THF at room temperature for 4 h[a]

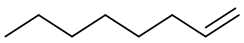
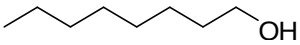
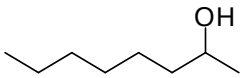
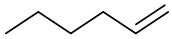
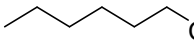
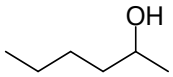
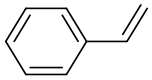
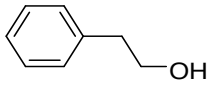
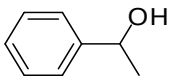
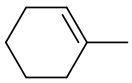
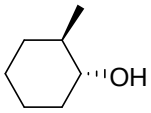
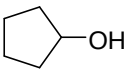
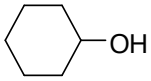
Alkene	Product	Yield (%)[b]
		59
		2
		71
		2
		80
		86

[a] Alkene (9.0 mmol) was added to a solution of **2.31** (*ca.* 3.6 mmol BH_3) in THF (14 mL) at 0-5 °C and stirred for 4 h at room temperature. The mixture was oxidized at 0-5 °C using NaOH (3.0 M, 3.0 mL) and H_2O_2 (30%, 3.5 mL) followed by warming to room temperature for 1 h to ensure complete oxidation. [b] By GC analysis using hexadecane as internal standard.

The procedure involved addition of an alkene (9.0 mmol) to a solution of borane complex **2.31** (3.6 mmol of BH_3) in THF at 0-5 °C followed by stirring for 4 h at room temperature and then oxidative work up with alkaline hydrogen peroxide. The alcohols produced were analyzed by quantitative GC and the yields obtained were in the range of 61-86% (Table 2.6).

A series of experiments was conducted in order to find conditions under which higher yields of 1- and 2-octanols could be obtained from hydroboration of 1-octene. It was found that use of a longer reaction time (16 h) gave higher overall yield (85%) and a mixture of 1-octanol (81%) and 2-octanol (4%). Therefore, a longer reaction time (16 h) was applied to a range of alkenes to provide the corresponding alcohols in better yields. The results obtained are recorded in Table 2.7.

Table 2.7: Hydroboration-oxidation of alkenes with the borane complex 2.31 in THF at room temperature for 16 ha

Alkene	Product	Yield (%)[b]
		81
		4
		80
		4
		79
		12
		99
		84
		86

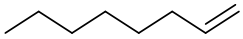
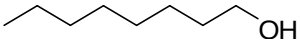
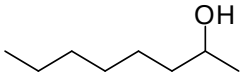
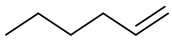
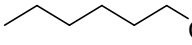
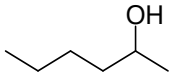
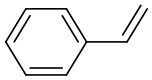
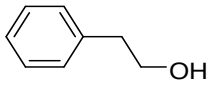
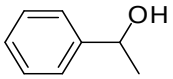
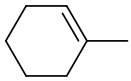
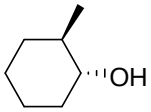
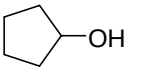
[a] Alkene (9.0 mmol) was added to a solution of **2.31** (*ca.* 3.6 mmol of borane) in THF (14 mL) at 0-5 °C and stirred for 30 min at 0 °C and 16 h at room temperature. The mixture was oxidized at 0-5 °C using NaOH (3.0 M, 3.0 mL) and H_2O_2 (30%, 3.5 mL) followed by warming to room temperature for 1 h to ensure complete oxidation. [b] By GC analysis using hexadecane as internal standard.

Reactions conducted over the longer reaction period (16 h) gave good yields (84-99%) of the alcohols. The regioselectivities of hydroboration of 1-hexene and styrene were similar to those reported for BMS[41] and BH_3•THF.[37] Thus, hydroboration of 1-hexene formed 1- and 2-hexanols in the ratio of 84:4, while styrene gave 1- and 2-phenylethanols in the ratio 79:12. Hydroboration of 1-methylcyclohexene produced *trans*-2-methylcyclohexanol in essentially quantitative yield. The complex **2.31** therefore functioned very similarly to BMS in hydroboration reactions, but with the significant advantage that the reactions are odour free and do not liberate dimethyl sulfide.

Our attention was next turned to use of borane complex **2.32**, to test whether it showed any significant differences in activity compared to **2.31**. Complex **2.32** was tested

in hydroboration of representative alkenes under conditions similar to those used with complex **2.31** (Scheme 2.17). The results obtained are recorded in Table 2.8.

Table 2.8: Hydroboration-oxidation of alkenes with the borane complex 2.32 in THF at room temperature for 16 h

Alkene	Product	Yield (%)[b]
		77
		4
		73
		5
		84
		13
		83
		88

[a] Alkene (9.0 mmol) was added to a solution of **2.32** (*ca.* 3.6 mmol BH_3) in THF (15 mL) at 0-5 °C and was stirred for 30 min at 0 °C and for 16 h at room temperature. The reaction mixture was oxidized at 0-5 °C using NaOH (3.0 M, 3.0 mL) and H_2O_2 (30%, 3.5 mL) followed by warming to room temperature for 1 h to ensure complete oxidation. [b] By GC analysis with hexadecane as an internal standard.

The results recorded in Table 2.8 clearly indicated that complex **2.32** can be used as a hydroborating agent. The small variations in yields obtained compared with those obtained from similar reactions involving use of complex **2.31** may be due to losses during work-up. However, the selectivities observed were entirely comparable. For example, hydroboration of 1-octene produced a mixture of 1- and 2-octanols in 77 and 4% yields, respectively, compared to 81 and 4%, respectively, with complex **2.31**. Similarly with styrene, 1- and 2-phenylethanols were formed in the ratio of 84:13, similar to the 79:12 ratio obtained with complex **2.32**.

2.9 The Use of Poly(propylene sulfide)–Borane Complex 2.31 in More Sophisticated Reactions

In the previous sections we showed that both borane-complexes **2.31** and **2.32** are good reducing and hydroborating reagents. At this stage we started to think about the ability of using **2.31** in more advanced reactions to see whether this reagent would allow extension of the utility of the polymer-supported borane for the first time to a range of more sophisticated applications. Therefore, we decided to use **2.31** in various synthetic pathways leading to various types of compound with specific functionality such as tertiary alcohol, alkyne, primary amine, ketone and (*Z*)-alkene (Figure 2.3). The following section will show the successful use of **2.31** in such reactions.

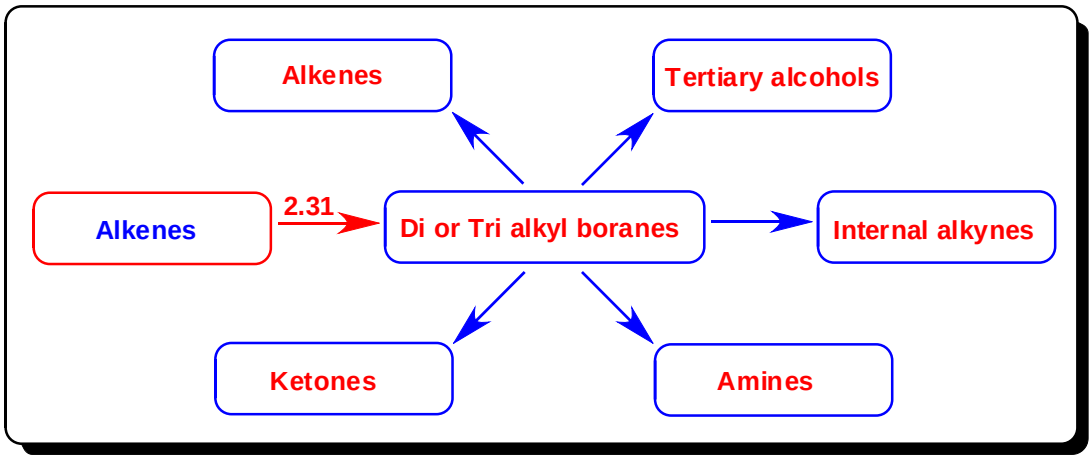


Figure 2.3: The use of 2.31 in some sophisticated transformations

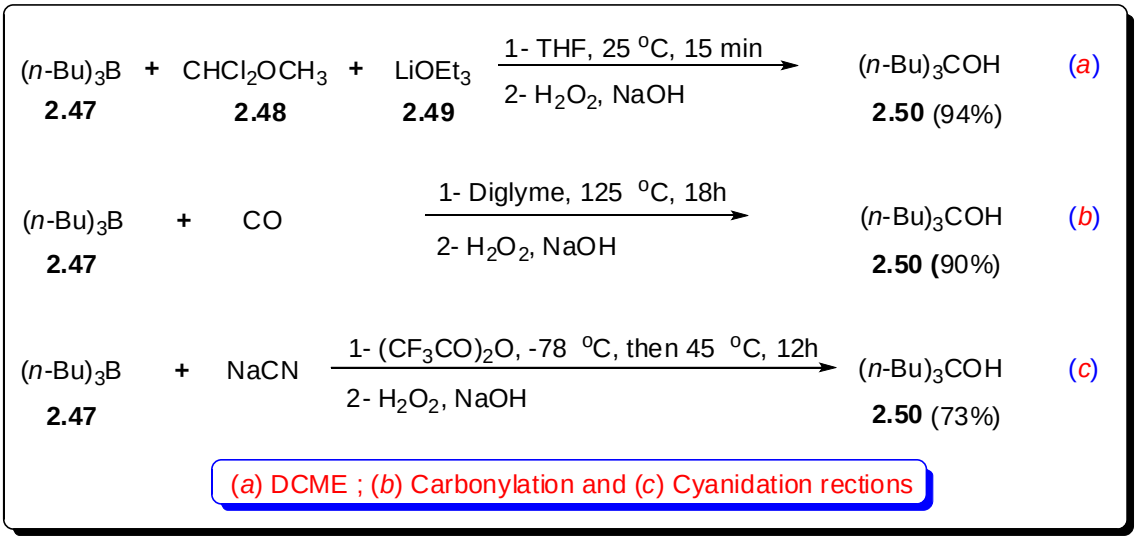
2.9.1 The Use of Poly(propylene sulfide)–Borane Complex 2.31 in the Synthesis of Tertiary Alcohols *via* the Haloform (DCME) Reaction

Synthesis of Tricyclopentylmethanol (2.46)

There are several methods for the synthesis of tertiary alcohols using borane reagents. Such methods include the migration of alkyl groups of the trialkyboranes from the boron atom to a single carbon atom, which happens in several reactions, including carbonylation,[42a] cyanidation[43a] and reaction with the anion of α,α-dichloromethyl methyl ether (DCME; **2.48**).[44]

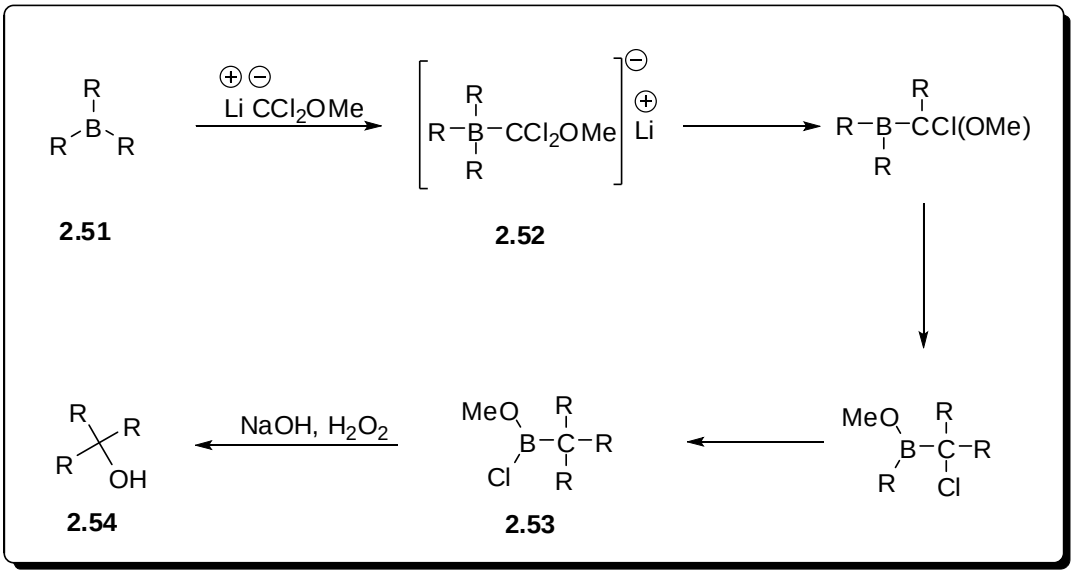
The DCME reaction is one of the most convenient ways for the synthesis of tertiary alcohols (*e.g.* compound **2.50**, Scheme 2.19*a*) in high yields. It is a base-induced reaction

of α,α-dichloromethyl ether (DCME; **2.48**) with trialkylboranes (*e.g.* tri-*n*-butylborane **2.47**; Scheme 2.19*a*) under relatively mild conditions. (0 ^{o}C for 15 min), followed by alkaline oxidation. This method was reported by Brown and Carlson[44] as a good alternative to the reaction of trialkylboranes with carbon monoxide, which takes place at high temperature (120 ^{o}C) for 8 h (Scheme 2.19*b*).[42b] The method can also replace the reaction of organoboranes with sodium cyanide and trifluoroacetic anhydride, which takes place at low temperature at the start of the reaction then at 45 ^{o}C for 12 h (Scheme 2.19*c*).[43b]



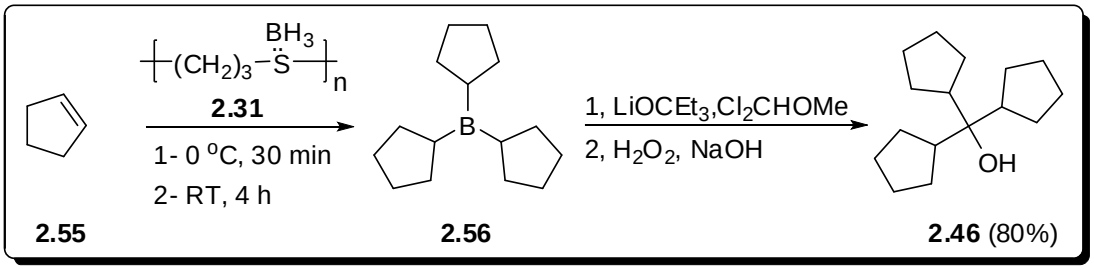
Scheme 2.19

In the first step of this reaction, the nucleophile (Li^{+} $^{-}CCl_2OMe$) is formed by the reaction of the base with DCME (**2.48**); the anion attacks the trialkylborane **2.51** to form the intermediate **2.52**, then subsequent migrations of the three alkyl groups from the boron atom to the carbon atom occur to give boronic ester **2.53**, which is then subjected to alkaline oxidation to give the desired tertiary alcohol **2.54** (Scheme 2.20).



Scheme 2.20

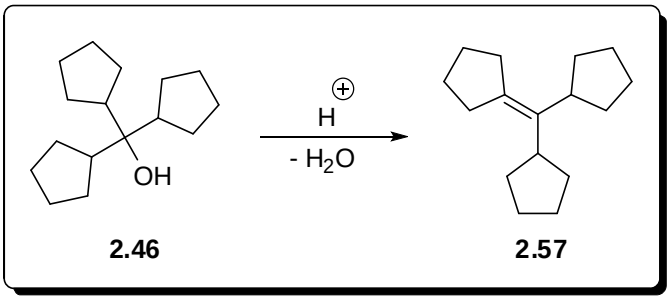
Accordingly we decided to carry out this reaction to try to prepare tricyclopentymethanol **2.46** using our polymeric borane complex **2.31** (Scheme 2.21). For this to be possible it would be necessary to prepare tricyclopentylborane **2.56** using the new hydroborating reagent. For the hydroboration-oxidation reactions reported earlier in this chapter, any cyclopentylboron species would have given similar results. The success of production of a tertiary alcohol starting with the hydroboration of the corresponding alkene using **2.31** would therefore verify the production of a trialkylborane as intermediate, and this was what we looked for from this reaction.



Scheme 2.21

We conducted an *in situ* preparation of tricyclopentylborane **2.56** from cyclopentene (28.0 mmol) and complex **2.31** (*ca.* 9.4 mmol). DCME was then added, followed by slow transfer of freshly prepared lithium triethylcarboxide to the mixture of the trialkylborane and the DCME [in the first experiment, we did a fast transfer of the lithium triethylcarboxide, consequently a low yield (50% isolated yield of **2.46**) was obtained, which could be attributed to the reaction of the lithium triethylcarboxide with the

trialkylborane rather than with the DCME]. After alkaline oxidation a crude yellow oily material was obtained. Since the expected product is tricyclopentylmethanol **2.46** we decided to use neutral alumina as a stationary phase for the purification by column chromatography and avoid the use of acidic silica which might stimulate the dehydration of the product to give the corresponding alkene **2.57** (Scheme 2.22) rather than the desired product **2.46**.



Scheme 2.22

A pure colourless oil was collected from the column. The ^{1}H NMR spectrum of the product showed an apparent pentet signal at δ = 2.06, a multiplet signal at δ = 1.36–1.51 and an exchangeable singlet at δ = 1.16 ppm which represent the three protons attached to C-1 of the cyclopentyl groups, the 24 protons of methylene groups and the hydroxyl proton, respectively. The ^{13}C NMR showed the expected four signals for the four different carbons of **2.46**. It showed a singlet (quaternary carbon) signal at 77.6 ppm which can be attributed to the quaternary carbon. Such carbons appear in the relatively down field region due to the effect of the hydroxyl group as an electron withdrawing group. Also, the ^{13}C NMR spectrum showed a doublet signal (CH) at 47.8 ppm for the tertiaty carbon and showed two triplets (CH_2) with higher intensities at 27.9 and 25.2 ppm corresponding to C-2/C-5 and C-3/C-4 of the cyclopentyl rings. The DEPT experiment verified the types of the carbons. The high resolution spectrometry (HRMS) for the isolated product confirmed the structure of **2.46**, it showed a peak at *m/z* = 218.2035 that correlates well to the calculated mass of $C_{16}H_{26}$ ($[M - H_2O]^+$), which is 218.2034 (see the experimental section for more detailed characterization data). The R_f value and all of the spectroscopic data of the isolated product were identical in all respects with those of an authentic sample (**2.46**) prepared according to the literature procedure.[44] Clearly, alcohol **2.46** was the product, and it was obtained in high yield (80%) after purification by column chromatography.

Isolation of **2.46** verified that tricyclopentylborane had indeed been formed in substantial yield. However, Brown and Carlson[44] had reported the synthesis of **2.46** in 91% yield starting with a standard solution of tricyclopentylborane (1 *M*) in THF on a 50 mmol scale. It was not clear whether the lower yield obtained in the reaction represented in Scheme 2.21 using polymer-borane complex **2.31** was an inherent issue associated with the reagent or whether it was merely a problem with the experimental procedure, caused by the use of a smaller scale or preparation of the organoborane *in situ* or some other differences. In order understand the situation better, we repeated the reaction represented in Scheme 2.21 but with BH_3•Me_2S instead of the polymer-borane complex **2.31**. Compound **2.46** was obtained in 80% yield, which was the same as that produced using **2.31**. Clearly, the differences in yields between the reported one and that obtained using **2.31** do not result from any inherent problems associated with the reagent. Our attention was next turned to the use of **2.31** for the synthesis of 1-cyclopentylhexyne.

2.9.2 The Use of Poly(propylene sulfide)–Borane Complex 2.31 in the Synthesis of Acetylenes

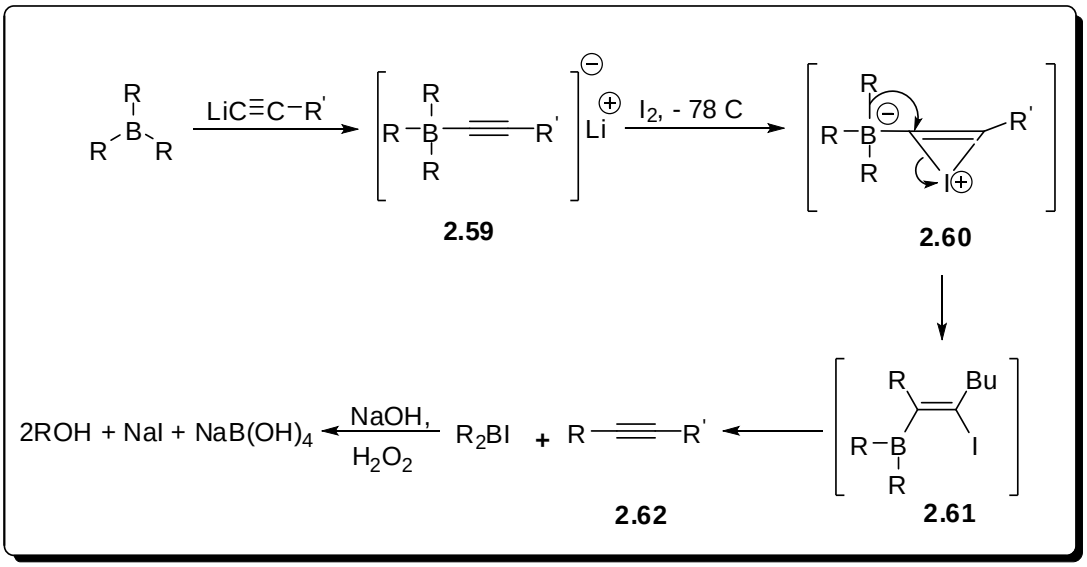
Synthesis of Hex-1-ynylcyclopentane (2.58)

At this stage we had proved in the previous example that we could use the new polymeric borane complex to produce a trialkyborane, which had then reacted with a nucleophile followed by a triple migration. In the next example the idea was to show another reaction of the trialkylborane, by reacting it with another type of nucleophiles, followed by a single migration (only one of the alkyl groups migrating to a carbon atom) to form a new carbon−carbon bond.

The reaction chosen was the synthesis of internal acetylene by use of an alkynyltrialkylborate. Suzuki *et al.*[45] have reported a convenient method for the synthesis of internal acetylenes *via* the reaction of lithium (1-alkynyl)trialkylborates with iodine. They developed this method to overcome the problems associated with syntheses of acetylenes *via* nucleophilic displacement of halide or sulfonate anions from their alkyl derivatives by acetylide anions. Such reactions are limited to primary derivatives, which undergo S_N2 reactions, while secondary or tertiary derivatives might undergo elimination rather than substitution leading to the undesired alkenes. Furthermore, due to reactivity of

the acetylide anion, compounds with reactive functional groups cannot be used in such preparations.

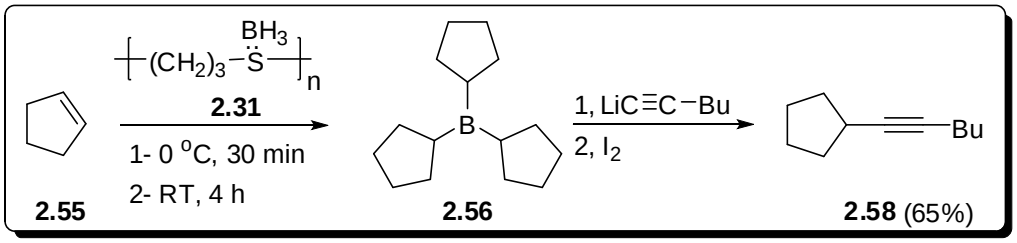
In this reaction a trialkylborane reacts with alk-1-ynyllithium to form the corresponding lithium (1-alkynyl)trialkylborate **2.59**, which reacts with iodine at low temperature to give **2.60**, then one of the alkyl groups migrates to the carbon atom to give **2.61** which gives the corresponding internal acetylene **2.62** by elimination of R_2BI. The reaction involves a single alkyl migration from boron to carbon atom to form a new carbon-carbon bond. It is convenient to work up the reaction by oxidation with alkaline hydrogen peroxide to destroy the dialkylboron iodode, to make separation of the product easier.



Scheme 2.22

We prepared tricyclopentylborane **2.56** (*ca.* 3.7 mmol) *in situ* from cyclopentene and complex **2.31** as described in the reaction represented in Scheme 2.21. In another flask hex-1-ynyllithium, prepared by addition of *n*-butyllithium to a solution of hex-1-yne in THF at 0 ^{o}C followed by stirring for 30 min at 0 ^{o}C, then it was transferred to the tricyclopentylborane solution and the mixture was cooled to –78 ^{o}C followed by the slow addition of the iodine as a solution in THF. The reaction was worked up after completion and the polymeric material was precipitated and removed by filtration. TLC analysis of the crude product showed a spot at R_f value identical to an authentic sample of **2.58** prepared according to the literature procedure.[45] The crude oily product was purified by column chromatography (silica gel; hexane). ^{1}H NMR analysis showed signals that correlated well

(in terms of chemical shift values, patterns and integration values) to the structure of **2.58**. The ^{13}C NMR spectrum showed two characteristic signals at δ = 84.4 and 79.6 ppm which correspond to the C≡C; it also showed the other seven signals that correspond to the other different types of carbon atoms of **2.58**. HRMS confirmed the elemental composition of **2.50**; it showed a peak at *m/z* = 150.1409, which correlates well with the calculated value for $C_{11}H_{18}$ (M^+ of **2.58**), which is 150.1407. More information about the characterization data is given in the experimental section. We found that all the spectroscopic data of isolated product **2.58** were identical in all respects with those of the authentic sample. It was obvious that 1-cyclopentylhexyne (**2.58)** had been synthesized using the new polymeric borane complex (**2.31**), as shown in Scheme 2.23. the product was obtained in 65% yield.



Scheme 2.23

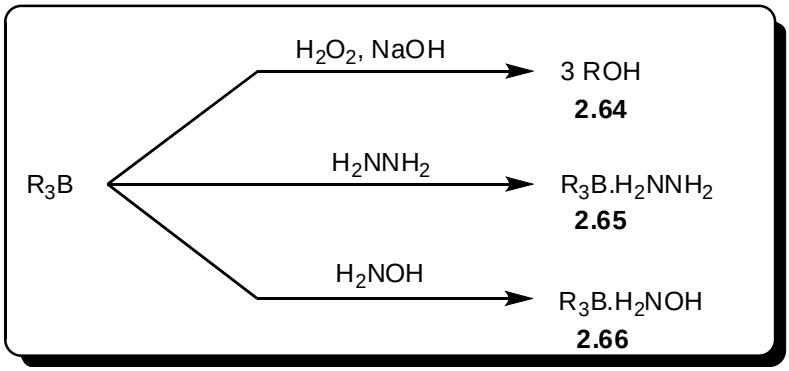
This is a clear indication that the presence of the polymeric sulfide in the reaction mixture causes no significant problems. Suzuki *et al.*[45] reported the synthesis of **2.58** in 100% yield, but for a reaction conducted on a larger scale (30.8 mmol of tricyclopentylborane compared with *ca.* 3.7 mmol in our case), using a standard solution of preformed organoborane rather than organoborane prepared *in situ*, and the yield was calculated by GC rather than being for isolated material. It is clear, therefore, that there is no significant disadvantage of using the complex **2.31** for the *in situ* preparation of the trialkylborane instead of preparing the organoborane using the traditional reagents for this type of reaction.

The polymeric sulfide **2.27** was recovered (75%) by precipitation with diethyl ether and was investigated by NMR spectroscopy. The ^1H and ^{13}C NMR spectra of the recovered polymer were almost identical with those obtained for the original polymer used to produce the borane complex **2.31**.

2.9.3 The Use of Poly(propylene sulfide)–Borane Complex 2.31 in Replacement of Boron by a Nitrogen Substituent

Synthesis of Cyclohexylamine (2.63)

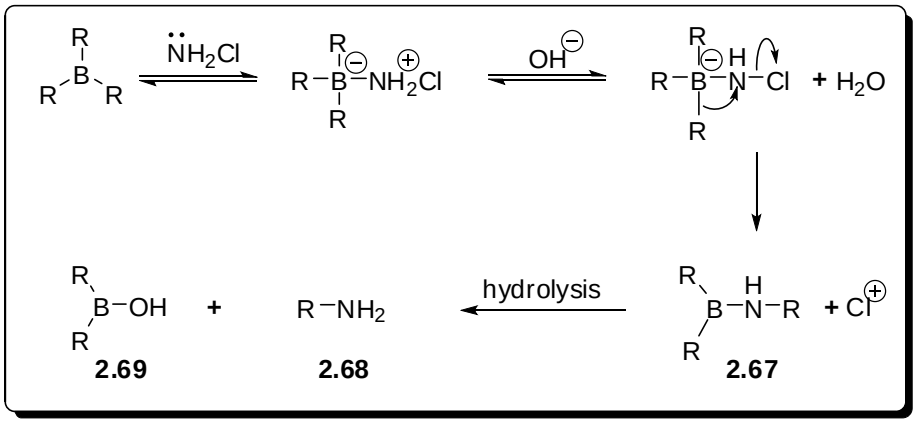
A general method for the preparation of primary amines from alkenes *via* hydroboration-organoborane reactions was introduced by Brown *et. al* in 1986.[46] By analogy with reactions of trialkylboranes with alkaline hydrogen peroxide (H_2O_2/NaOH) to produce the corresponding alcohols **2.64**, they tried to use hydrazine (H_2NNH_2) and hydroxylamine (H_2NOH) to produce the corresponding primary amine, but instead simple addition of these reagents to the trialkylborane took place to produce the corresponding derivatives **2.65** and **2.66**, respectively (Scheme 2.24).



Scheme 2.24

They concluded that a better leaving group than –OH and $–NH_2$ is required to stimulate the migration of the alkyl group to the nitrogen atom; therefore, they used freshly prepared chloramine (NH_2Cl) which reacts with trialkylboranes in the presence of sodium hydroxide to give the corresponding primary amine.

It is reported that this reaction involves coordination of chloramine to the boron atom of the trialkylborane; then, one of the alkyl groups migrates to the nitrogen atom to displace the chlorine giving **2.67** which on hydrolysis gives the corresponding amine **2.68** along with dialkylborinic acid **2.69** (Scheme 2.25). Compound **2.69** reacts with chloramine in the same way producing another equivalent of amine **2.68** and monoalkylboronic acid, $RB(OH)_2$.



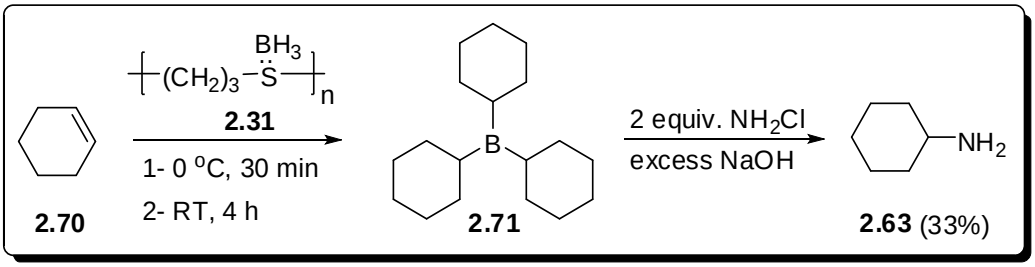
Scheme 2.25

The higher electron density on the boron atom of the monoalkyl boronic acid makes it less reactive, so it does not react further with the hydroxylamine, leading overall to a maximum of two of the three alkyl groups migrating from boron to nitrogen, thereby limiting the yield based on alkyl groups to 67%.[46] The reactions have usually been conducted with organoboranes prepared *in situ* using BH_3•THF.

We decided to test this interesting reaction as another possible application for the new polymeric borane complex. The use of chloramine could provide a possible complication for the use of the polymeric sulfide complex, since the reagent might oxidize the sulfide groups in the polymer. We also decided to use tricyclohexylborane, generated *in-situ* from cyclohexene and **2.31** (Scheme 2.26), because this would introduce a further potential complication to use of the polymeric complex, which produces a turbid reaction mixture. Hydroboration of cyclohexene with a simple borane complex such as BH_3•THF results in initial precipitation of dicyclohexylborane dimer, which then slowly dissolves on reaction with further cyclohexene to give tricyclohexylborane.[47] The reaction is normally self-indicating, therefore, and can be considered complete when no solid remains. By use of **2.31**, however, it would not be possible to monitor the dissolution of the dicyclohexylborane dimer very clearly and the hydroboration reaction time would have to be based on literature precedent for a simple complex. A reaction time of 4 h at room temperature was chosen by analogy with the standard procedure reported for the *in situ* preparation of trialkylboranes used in the original report of the generalized chloramine reaction.[47] Cyclohexene (36.5 mmol) and **2.31** (*ca.* 12.7 mmol BH_3) were stirred in anhydrous THF for 4 hours and then freshly prepared chloramine (from two mole equivalents of NaOCl) and sodium hydroxide solution were added. An oily crude product

was obtained, from which cyclohexylamine (**2.63**) was isolated in 33% yield (based on cyclohexene) by solvent extraction followed by distillation. The structure of the cyclohexylamine was confirmed by ^{1}H NMR, ^{13}CNMR, IR, MS and HRMS. The pattern and the integration values in the ^{1}H NMR spectrum correlated well with the structure of **2.63**. In the ^{13}CNMR spectrum a signal was observed at δ = 50.3 ppm, which corresponds to the C-1 of cyclohexyl and three other signals were also seen, which corresponded to the other carbon atoms in the structure of **2.63**. HRMS showed a peak at *m/z* = 99.1048 which correlates well with the calculated value for $C_6H_{14}N$ (M^+ of **2.63**), which is 99.1045. The boiling point and spectroscopic data of **2.63** were identical with those of an authentic sample obtained from Sigma–Aldrich tested under identical conditions.

Again, 75% of the polymeric sulfide was recovered by simple precipitation. The chloramine was prepared by the reaction of aqueous ammonium hydroxide and commercial bleach (aqueous sodium hypochlorite) at 0 ^{o}C for 1h. The sodium hypochlorite concentration in commercial beach was determined by a well-known redox titration method.[48]



Scheme 2.26

The published yield for the production of cyclohexylamine from tricyclohexylborane prepared using BH_3•THF was 49%.[47] However, the process involved use of chloramine of known concentration (whereas in the present reaction its concentration was assumed based on an estimation of the bleach concentration used in its preparation) and the reaction had been applied on a significantly larger scale (100 mmol of alkene). It is also likely that the hydroboration reaction to produce the organoborane had been left for a longer period in view of the author's experience with such processes. In the present case, everything was carried out in one pot without isolation of any intermediates, but synthesis of the intermediate, tricyclohexylborane, was achieved successfully, even if in somewhat lower yield as a result of the short period for the hydroboration step. The

lower yield of **2.63** than that reported by using BH_3•THF was not a major concern since there were many separate steps involved and none of them were individually optimized for the specific case. It is clear, however that the complex **2.31** can be used as a borane source even for a reaction involving chloramine as a reagent and producing a primary amine as product.

2.9.4 The Use of Poly(propylene sulfide)–Borane Complex 2.31 in the Synthesis of Ketones

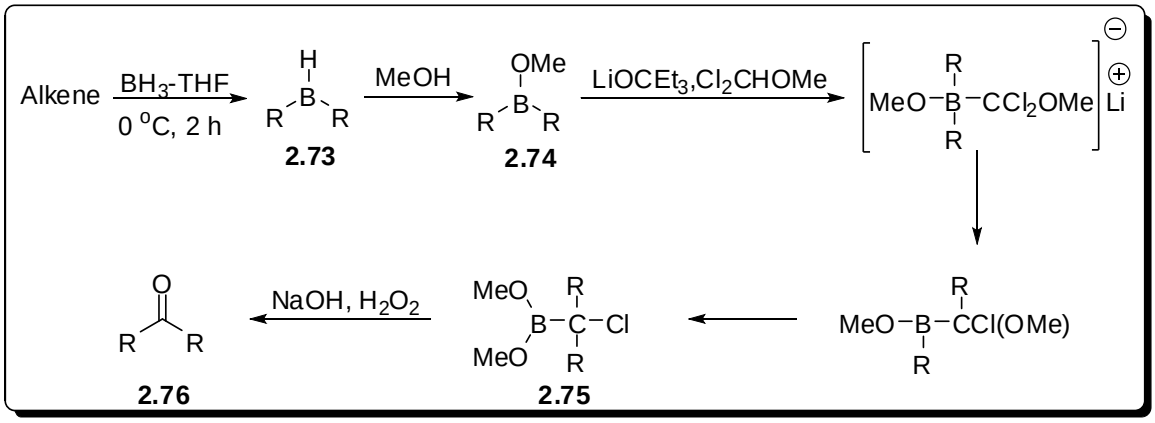
Synthesis of Dicyclohexyl Ketone (2.72)

The previous examples showed the successful production of symmetrical trialkylboranes as intermediates by the use of borane complex **2.31**. However, many reactions require either unsymmetrical trialkylboranes or organoboranes that contain a mixture of alkyl groups and other types of substituents. This involves an initial hydroboration that must stop cleanly at the monoalkylborane or dialkylborane stage prior to the addition of a different alkene or an alternative type of reagent. Although conditions have been worked out for achieving this in many cases in homogeneous solution, it was by no means obvious that the same conditions would be appropriate for a polymeric borane complex, where the relative rates of reactions might be different and intermediates produced might have different solubilities from the starting complex, potentially resulting in heterogeneous reaction mixtures and leading to mixtures of alkylboron compounds. The final two examples were therefore designed to explore the possibility of production of unsymmetrical organoboron compounds as well as testing out other further reactions. In each case dicyclohexylborane was selected as the initial target. As stated above, when prepared with BH_3•THF this normally precipitates out as a dimer, which assists in gaining selectivity, but it was not known whether the same would apply with the use of complex **2.31**.

After their success in the production of tertiary alcohols by the DCME reaction (Section 2.9.1) Carlson and Brown [49] developed a route for the synthesis of ketones *via* a base induced reaction of DCME with dialkylmethoxyboranes. By this method they overcame the limitations associated with the methods that involve reactions of trialkylboranes with sodium cyanide and trifluoroacetic anhydride or with carbon

monoxide in the presence of water. Such methods were considered as valuable routes to ketones.

The method represents a smooth process for the synthesis of ketones from the corresponding alkenes under mild conditions with no wastage of any alkyl groups. Furthermore, it is applicable for bulky alkyl groups. The first step in this process involves the formation of dialkylborane **2.73** from alkene followed by reaction with methanol to give dialkylmethoxyborane **2.74**, which reacts with the anion of DCME followed by subsequent migration of alkyl groups from boron to carbon to give **2.75**, which is then converted to the desired ketone **2.76** by alkaline oxidation (Scheme 2.27).

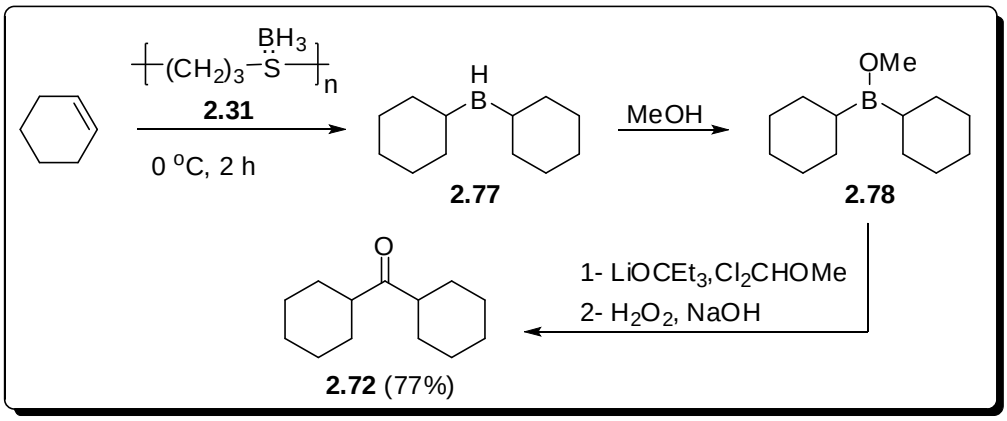


Scheme 2.27

We decided that the fourth reaction would be the attempted synthesis of dicyclohexylmethanone (**2.72**) from cyclohexene using **2.31** as hydroborating agent. Complex **2.31** (*ca.* 8.0 mmol BH_3) in THF was stirred with cyclohexene (15.8 mmol) at 0 ^oC for 2 hours and then methanol (7.80 mmol) was added. The mixture was treated with DCME in the presence of lithium triethylcarboxide (prepared *in situ*) followed by oxidation with alkaline hydrogen peroxide, (Scheme 2.28). A crude oily material was obtained and after distillation dicyclohexyl ketone (dicyclohexylmethanone; **2.72**) was isolated in 77% yield. The structure of the product was confirmed by ^1H NMR, ^{13}C NMR, IR, MS and HRMS. The pattern and the integration values in the ^1H NMR spectrum correlated well to the structure of **2.72**. The ^{13}C NMR spectrum showed a characteristic signal at δ = 217.6 ppm, which corresponds to a carbonyl carbon atom; it also showed a signal at δ = 49.2 ppm, which corresponded to C-1 of the cyclohexyl group, along with signals corresponding to the other carbon atoms. HRMS showed a peak at *m/z* = 194.1671 which correlates well with the calculated value for $C_{13}H_{22}O$ (M^+ of **2.72**) which is

194.1670. More detailed characterization data are given in the experimental section. We found that the boiling point and spectroscopic data of the isolated product were identical with those of an authentic sample (**2.72**) obtained from Sigma–Aldrich.

The published procedure for the synthesis of **2.72** gave 85% isolated yield from a 50 mmol scale reaction of dicyclohexylmethoxyborane.[49] The modest diminution in yield for the present reaction is entirely understandable given the much smaller scale used and our limited practical experience with this particular type of reaction. It may be concluded that the complex **2.31** can be used without problem to produce **2.72**, as shown in Scheme 2.28. This is evidence that **2.31** is a suitable reagent for the formation of dialkylboranes (*e.g.* **2.77**) from which alkoxydialkylboranes (*e.g.* **2.78**) can be produced as intermediates.



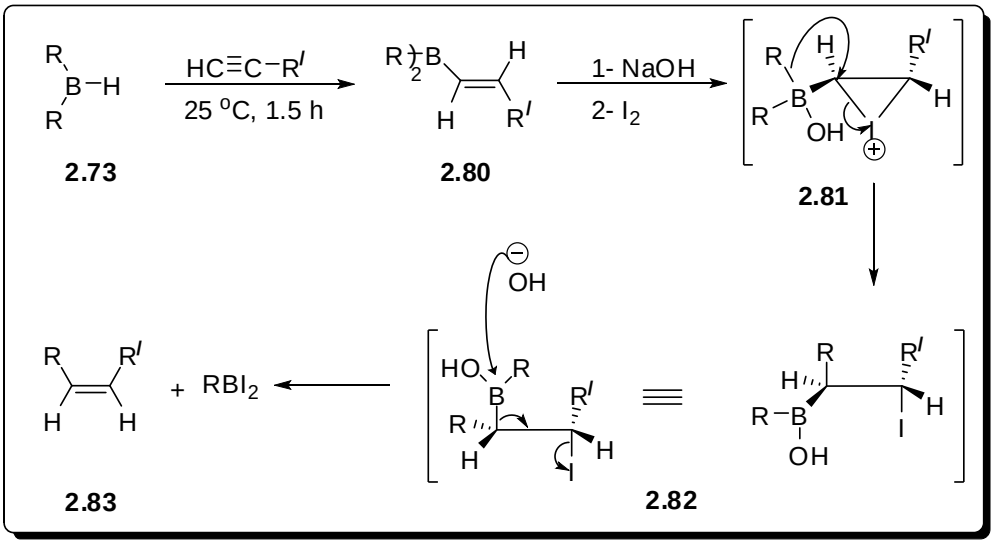
Scheme 2.28

2.9.5 The Use of Poly(propylene sulfide)–Borane Complex 2.31 in the Stereospecific Synthesis of Alkenes

Synthesis of (Z)-1-Cyclohexylhex-1-ene(2.79)

Zweifel *et. al*,[50] have reported a handy stereoselective synthesis of substituted alkenes *via* hydroboration–iodination of alkynes; by which they managed to produce substituted alkenes in high yields with *cis*–isomeric purity of 99%. This reaction involves the formation of a dialkylborane (**2.73**) which then behaves as a hydroborating agent for an added alkyne to form a vinylborane (**2.80**). Treatment of **2.80** with a mixture of sodium hydroxide (converts the borane into a hydroxyborate) and iodine (attacks the alkenyl group and induces rearrangement) gives an unstable (2-iodoalkyl)boron compound (**2.82**), which eliminates an iodoboron species to give the final product, a (*Z*)-alkene (**2.83**). The

particular geometrical isomer results from the stereospecific nature of all of the intermediate steps. The hydroboration step adds B and H in the *cis*-manner across the triple bond, to give the intermediate **2.80**; formation of the iodonium ion **2.81** does not allow change of the geometry, so that **2.81** has the stereochemistry shown; the migrating R group displaces the iodine with inversion of configuration at the carbon atom originally bearing the iodine to give **2.82**, and this must adopt an appropriate orientation for *anti*–elimination of the iodoborane unit, leading overall to the (*Z*)-alkene (Scheme 2.29).

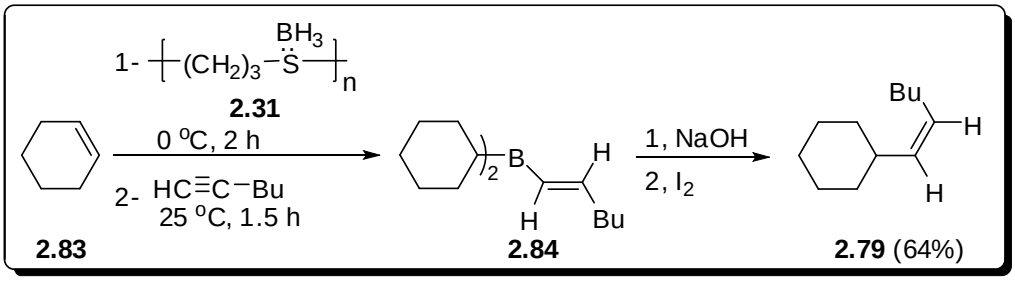


Scheme 2.29

Therefore, the final reaction we decided to undertake was the synthesis of a (*Z*)-alkene by the Zweifel reaction. The use of **2.31** in such a reaction would test its ability to hydroborate alkynes as well as alkenes and its ability to form an all-carbon unsymmetrical organoborane cleanly, as well as testing its performance under the conditions of the Zweifel reaction. Complex **2.31** (*ca.* 8.0 mmol BH_3) was therefore treated successively with cyclohexene (15.8 mmol) and 1-hexyne (7.8 mmol) in the hope of producing dicyclohexyl-1-hexenylborane, which was then subjected to alkaline iodination in the hope of producing **2.79**, (Scheme 2.30). A crude oily material was obtained. TLC analysis against an authentic sample prepared according to the literature procedure[50] showed a spot corresponding to the desired product (**2.79**). The product was isolated by column chromatography. ^{1}H NMR analysis of the purified material showed a multiplet signal at δ = 5.31-5.19 ppm corresponding to the CH=CH unit. It also showed signals with coupling patterns and integration values that correlated well to the cyclohexyl and butyl groups of **2.79**. In the ^{13}C NMR spectrum, signals at δ = 136.0 and 128.0 ppm,

corresponding to CH=CH, were observed, along with other signals corresponding to all of the other carbon atoms. HRMS confirmed the elemental composition of $C_{12}H_{22}$**.** It showed a peak at *m/z* = 166.1722 which correlates well with the calculated value for $C_{12}H_{22}$ (M^+ of **2.69**) which is 166.1721. More detailed characterization data are given in the experimental section. The boiling point and spectroscopic data of **2.79** were identical with those of the authentic sample. Accordingly, using our new polymeric borane complex (**2.31**), we had managed to produce compound **2.79**. It was obtained in 64% yield based on hex-1-yne (7.8 mmol).

The reported synthesis of (*Z*)-1-cyclohexylhex-1-ene (**2.79**) using BH_3•THF was accomplished in 75% yield for a reaction on a three times larger scale (25.0 mmol of 1-hexyne).[50] The modest diminution in yield achieved with **2.31** on a smaller scale and without individual optimization of reaction conditions is not of significance and it was concluded that the use of **2.31** is entirely appropriate for such reactions.



Scheme 2.30

2.10 Recycling of Poly(propylene sulfide) 2.28 and Regeneration and Reuse of Poly(propylene sulfide)–Borane Complex 2.31

At this point we had shown that complex **2.31** could be used to produce various types of organoboranes and a variety of further reactions could be conducted with such a complex. In two cases we had also recovered samples of the polymeric material **2.28** by precipitation following addition of diethyl ether and methanol, and their ^{1}H NMR spectra showed that both recovered samples were very similar to the original polymer. This suggested that it should be easy to reuse the polymer to prepare a fresh batch of complex **2.31** from the recovered polymer or to precipitate the polymer from a reaction mixture prior to subsequent reaction of the organoborane, which might in some cases be advantageous if the presence of the polymer is problematical. Therefore, we decided to investigate the recovery and reuse of the polymer in more detail. In order to do so we used

reduction of benzaldehyde with complex **2.31** as a simple reaction to study. To a sample of complex **2.31** (2.40 g, *ca.* 20.0 mmol borane) in THF (57 mL) was added benzaldehyde (5.30 g, 50.0 mmol) and the mixture was stirred for 30 min at 0 ^{o}C, then for 4 hours under reflux conditions, followed by the addition of methanol (15 mL) to quench the reaction. The polymeric material was precipitated as a white solid by the addition of diethyl ether (100 mL) during the work up process and was removed by filtration. The polymeric sulfide was washed with aqueous sodium hydroxide (3 *M*) to remove any boronic acid, then washed with water, dried under vacuum and weighed. A sample was withdrawn for analysis and the rest was treated with diborane gas to reform complex **4.31**. The new complex was then analysed for its borane content and used in a further reaction with benzaldehyde in a manner that was identical except for being on a slightly smaller scale. The whole process of recovery and reuse was then repeated once more. The benzyl alcohol was produced quantitatively each time. The amount of polymer recovered and the properties of the recovered polymer are recorded in Table 2.9.

Table 2.9: The Borane Content and GPC Results for the Recovered Polymeric Sulfide

Polymer	Rec. [a] (%)	Mn (Daltons)[b]	Mw (Daltons)	PDI [d]	BH_3 in complex 2.31 (mmol/g)
Original	—	4200	9400	2.2	8.5
1st Rec.[a]	70	6700	12000	1.8	8.3
2nd Rec. [a]	90	7700	13000	1.7	7.7

[a] Rec. = Recovery. [b] Number average molecular weight. [c] Weight average molecular weight. [d] Polydispersity index of the free poly(propylene sulfide).

The results showed that recovery of the polymer from the first run was around 70%, but the second recovery was significantly better (*ca*. 90%). The ^{1}H NMR spectrum of the polymer recovered from the first run was broadly similar to that of the initial polymer, but the average molecular weight of the polymer had increased, suggesting that the process of recovery of the polymer resulted in loss primarily of short chain polymeric material, which was probably more soluble in the ether used to precipitate the polymer. The polymeric sample recovered from the third use was quite similar to that recovered from the second use, in terms of both NMR spectrum and molecular weight, although the molecular weight was higher again and the polydispersity index was lower. It therefore seems that the initial polymer contains a small amount of relatively short chain oligomers that are lost during recovery, particularly during the first recovery. Thereafter, the recovered polymer is less polydisperse and has a somewhat higher average molecular weight. The polymer still forms a borane complex, but the amount of borane taken up is somewhat smaller,

suggesting that it is harder to complex every sulfur atom in longer chains. The yield of benzyl alcohol produced when borane complexes of the recovered polymer were used was always quantitative, showing that the recovered polymer borane complex could be used as a useful reagent comparable with the original complex **2.31**.

The ability to recover the polymer increases the attractiveness of the complex **2.31** as a reagent. Its recycling would reduce the cost of the reagent, while precipitation of the polymer after organoborane formation but before further reaction would allow such reactions to be conducted in the absence of the polymeric sulfide where this was appropriate.

2.11 Conclusions

In conclusion, borane complexes derived from polymeric sulfides are solids of high hydride content that can be readily weighed in air. Their mild smell, good solubility in THF, and reactivity comparable to that of BMS, make them attractive borane sources. Consequently, complex **2.31**, in particular, is a highly promising, new hydroborating reagent, which might well be suitable for large scale industrial application.

Poly(propylene sulfide)–borane complex **2.31** has proved to be a versatile, efficient and convenient reagent for *in situ* generation of a range of organoboron types (trialkylboranes, alkenyldialkylboranes, dialkylalkoxyboranes) and their subsequent conversion into a range of organic compound classes, tertiary alcohol, alkyne, (*Z*)-alkene, primary amine or ketone, by the use of several potentially problematical reagents (hydrogen peroxide, chloramine, iodine, strong bases). All of the reactions proceeded without problem and yields of isolated products were only marginally lower than those reported in the literature for reactions involving organoboranes prepared using BH_3•THF or borane–dimethyl sulfide (BMS), even though the current reactions were generally conducted on a much smaller scale and were not individually optimized. The new polymeric-borane complex contains around 8-8.5 mmol of borane per gram of reagent, which is much greater than that of BH_3•THF solutions and around two thirds of that of BMS. However, compared to BMS it is much more stable in air and the liberated sulfide is much less volatile, does not have an obnoxious odour and is much less flammable. The polymeric sulfide, which is not very expensive to produce at the outset, can be easily recovered after reactions of the borane complex, and by recycling the material it could

further mitigate any differences in cost compared to BMS. Complex **2.31** could replace BH_3•THF and BH_3•SMe_2 complexes in all cases tried and might well be suitable for large scale industrial application.

2.12 Experimental

2.12.1 General

All reactions were performed under a nitrogen atmosphere. Glassware was oven dried, assembled hot and allowed to cool under a stream of nitrogen gas. All chemicals and reagents were purchased from commercial sources and used without further purification. THF was distilled from sodium benzophenone ketyl and other solvents were purified by standard procedures.[51] Alkyllithiums were obtained from Aldrich Chemical Company and were estimated prior to use by the method of Watson and Eastham.[52]

2.12.2 Instruments

^{1}H and ^{13}C NMR spectra were recorded on a Bruker AV400 spectrometer operating at 400 MHz for ^{1}H and 100 MHz for ^{13}C measurements. Chemical shifts δ are reported in parts per million (ppm) relative to tetramethylsilane (TMS) and coupling constants *J* are in Hz. ^{13}C multiplicities were revealed by DEPT signals. Assignments of signals are based on integration values, coupling patterns and expected chemical shift values and have not been rigorously confirmed. Signals with similar characteristics might be interchanged. Low-resolution mass spectra were recorded on a Waters GCT Premier spectrometer and high-resolution mass spectra were recorded on a Waters LCT Premier XE instrument. IR spectra were recorded on a Jasco FT/IR-660 plus instrument on a NaCl plate. Column chromatography was carried out using Fischer Scientific silica 60A (35-70 micron). Thermo-Gravimetric Analysis (TGA) was performed using the device Thermal Analysis SDT Q600 at a heating rate of 20 °C/min from room temperature to 1000 °C. Gel permeation chromatography was carried out using a GPC MAX variable loop equipped with two KF-805L SHODEX columns in THF, with a RI(VE3580) detector using a GPC MAX pump operating at flow rate of 1 mL/min. Calibration was achieved using a series of Viscotek polystyrene standards up to Mw = 9.4×10^5. GC analyses were carried out on a Shimadzu Gas Chromatograph fitted with a ZEBRON ZB-5 (5% phenyl polysiloxane) 30 m length column. The GC conditions used for analysis were: 40 °C for 2 min, ramped

to 300 °C at 20 °C/min and held for 2 min. The injection temperature was 250 °C and the detection temperature 250 °C.

2.12.3 GC Analytical Procedure

The standard materials of all the products to be measured by GC were available (purchased from commercial sources with purity of 98–99%). To know the retention time of each compound, they were injected individually into the GC (See Table 2.10).

Table 2.10: Retention time of the standards

Compounds	Retention time (min)
1-octanol	4.00
2-octanol	3.27
1-hexanol	1.73
2-hexanol	1.06
cyclopentanol	0.97
cyclohexenol	1.80
2-phenylethanol	4.37
1-phenylethanol	3.88
trans-2-methylcyclohexanol	2.47
benzylamine	3.33
benzyl alcohol	3.62
hexadecane	7.88

To calculate the response factor (RF) of each compound, accurately weighed quantities of the compound and hexadecane were mixed and dissolved in 25 mL DCM. A 0.5 μL aliquot of the mixture was injected into the GC. The RF was calculated using equation 2.1.

$$RF = \frac{\text{Wt.of the compound}}{\text{Wt.of hexadecane}} \times \frac{\text{peak area of hexadecane}}{\text{peak area of the compound}}$$

Equation 2.1

The injection was repeated 4 times and the average RF was taken. The weight of the product from each reaction was determined by adding a known weight of hexadecane to the dried organic extract of the reaction mixture after work-up, injecting 0.5 μl of the solution into the GC and using equation 2.2 to calculate the weight of the product.

$$\text{Wt.of the product} = \frac{(\text{RF})\ (\text{Wt.of hexadecane})\ (\text{peak area of the compound})}{\text{peak area of hexadecane}}$$

Equation 2.2

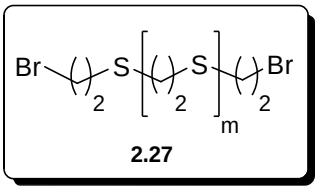
The injection was repeated 4 times and the average weight was taken. The yield of each product was calculated using equation 2.3.

$$\text{Yield of product} = \frac{\text{no. of mmol of the product}}{\text{no. of mmol of the starting matrial}} \times 100$$

Equation 2.3

2.12.4 Synthesis of Pol(alkylene sulfide)s 2.27–29

In a 250 mL round bottom flask charged with a magnetic bar and fitted with a water condenser, a mixture of dibromoalkane (40.9 mmol) and $Na_2S.9H_2O$ (14.8 g, 61.5 mmol) was placed and refluxed with vigorous stirring at 140–160^{o}C for the indicated reaction time. Water (*ca.* 25 mL) was added to the hot reaction mixture with efficient stirring and stirring was maintained until the mixture had cooled to room temperature. The white precipitate was removed by filtration and washed thoroughly with water. The white powder was then dried under reduced pressure for 48 h.



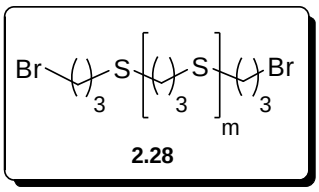
2.27

Poly(ethylene sulfide) (**2.27**)

Reaction time: 4 h

Yield: 2.5 g [100%, based on an assumed empirical formula for the product of $(CH_2)_2S$]

Mp: 185–186 °C.



2.28

Poly(propylene sulfide) (**2.28**)

Reaction time: 4 h

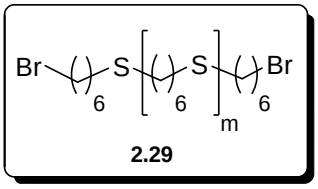
Yield: 3.0 g [100%, based on an assumed empirical formula for the product of $(CH_2)_3S$]

Mp: 55–57 °C.

GPC: Mn = 4100 Daltons, Mw = 9000 Daltons, PDI = 2.2.

^{1}H NMR (400 MHz, $CDCl_3$), δ (ppm): 2.6 (t, J = 7.1 Hz, 4 H, CH_2CH_2S), 1.9 (p, J = 7.1 Hz, 2 H, CH_2CH_2S).

^{13}C NMR (100 MHz, $CDCl_3$), δ (ppm): 31.3 (t, CH_2S), 29.7 (CH_2CH_2S).



2.29

Poly(hexamethylene sulfide) (**2.29**)

Reaction time: 4 h

Yield: 4.8 g [100%, based on an assumed empirical formula for the product of $(CH_2)_6S$]

Mp: 70–77 °C.

GPC: Mn = 4600 Daltons, Mw = 10000 Daltons, PDI = 2.2.

^{1}H NMR (400 MHz, $CDCl_3$), δ (ppm): 2.7 (t, J = 7.2 Hz, 0.4 H, CH_2Br) 2.5 (t, J = 7.2 Hz, 4 H, CH_2S), 1.6 (m, 4 H, CH_2CH_2S), 1.4 (m, 4 H, $CH_2CH_2CH_2S$).

^{13}C NMR (100 MHz, $CDCl_3$), δ (ppm): 32.1 (t, CH_2S), 29.6 (t, CH_2CH_2S), 28.6 (t, $CH_2CH_2CH_2S$).

2.12.5 Synthesis of Poly(alkylene sulfide)–Borane Complexes **2.31** and **2.32**

Diborane gas generated by reaction of sodium borohydride (5.67 g, 0.150 mol) in diglyme (50 mL) with BF_3•Et_2O (24.5 mL, 0.200 mol) was passed slowly through a dichloromethane (25 mL) solution of polymeric sulfide **2.28** or **2.29** (3.00 g) at room

temperature over a period of 2 h. Excess diborane was allowed to be absorbed in THF (15 mL) in a second bubbler. A white solid precipitated out when passage of the borane gas was nearing completion. The solvent was removed from the mixture by blowing with nitrogen (evaporation under reduced pressure was required in the case of **2.32**). The resulting borane-sulfide complex was analyzed for active hydride by a standard procedure using THF:glycerol:3 M HCl (1:1:1) as the hydrolyzing mixture (Section 2.12.6). The borane content in the obtained adduct was 8.5 mmol BH_3/g of complex.

2.12.6 Gas Analysis

A simple gas titration system (Figure 2.4) was used in this experiment to estimate hydrogen liberated from the complexed borane. An oven dried 50 mL round bottomed flask was charged with the solid borane complex (0.10 g) and a magnetic bar and then sealed with a rubber septum and flushed with nitrogen. The system was flushed with nitrogen twice by filling the burette with nitrogen while lowering the levelling bulb, then by raising the bulb, nitrogen was expelled through the needle. After expelling most of the nitrogen for the second time, the needle was inserted into the flask. By turning the double oblique tap to the fume hood and raising the bulb, the water level in the burette was brought to zero and levelled with the bulb, and at this point the three war tap was turned to connect the burette to the flask. Diglyme (5.0 mL) was injected into the flask followed by 5.0 mL hydrolysing reagent (water : glycerol : 3 M HCl, 1:1:1) with efficient stirring. The volume of hydrogen evolved (V_h) was measured by lowering the bulb to get the levels of the water inside the burette and the bulb equal. The borane content (mmol BH_3 / g of complex) was calculated using equation 2.4. [where P_a = atmospheric pressure (mmHg), P_s = vapour pressure of water at temperature T, V_h = volume of hydrogen evolved (mL) and T = temperature (K)].

$$\text{Borane Content (mmol borane / g complex)} = \frac{(P_a - P_s)\,(273)\,(V_h - 10)}{(760)\,(T)\,(22.4)\,(0.1)\,(3)}$$

Equation 2.4

The measurement was repeated until reproducible results were obtained.

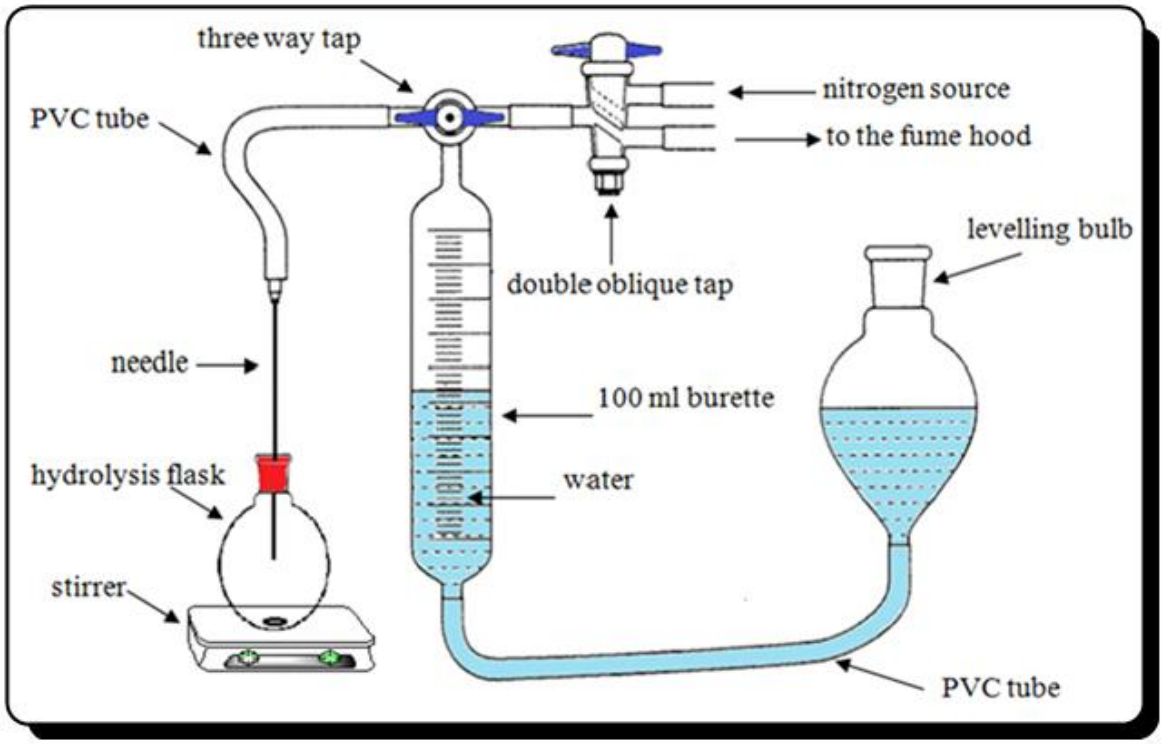
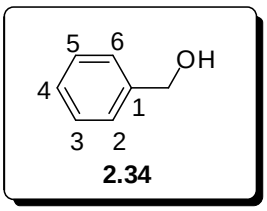


Figure 2.4: Gas analysis system

2.12.7 Reduction of Functional Groups: Typical Procedure for Reduction of Benzaldehyde with 2.31

A 50 mL two neck flask equipped with a reflux condenser and a magnetic bar was flushed with nitrogen and charged with **2.31** (0.240 g, 2.00 mmol BH_3) and cooled to 0 ^{o}C. THF (10 mL) was added and the resulting colourless solution was cooled to 0 °C. Benzaldehyde (0.530 g; 5.00 mmol) was then added dropwise. The reaction mixture was stirred at 0 °C for 30 min and a further 4 h under reflux. The flask was then cooled to 0 °C and methanol (3 mL) was added to quench any excess borane. Subsequently, diethyl ether (10 mL) was added to precipitate the released polymeric sulfide. GC analysis of the organic layer showed the formation of benzyl alcohol (100%). The organic layer from the reaction mixture was washed with brine (3 × 20 mL), and most of the solvent was removed under vacuum. Hexane (10 mL) and ether (10 mL) were added to the residue, which precipitated further polymeric material. The polymer was filtered off and the filtrate was dried ($MgSO_4$). The solvent was removed under reduced pressure to give benzyl alcohol (0.45 g, 4.17 mmol; 83%) as a colourless oil identical to an authentic sample.



2.34

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28-7.20 (m, 5 H, Ph), 4.54 (s, 2 H, CH_2), 2.27 (s, exch., 1 H, OH);

^{13}C NMR (100 MHz, $CDCl_3$): δ 140.9 (s, C-1 of Ph), 128.6 (d, C-3/C-5 of Ph), 127.6 (d, C-4 of Ph), (d, C-2/C-6 of Ph), 65.2 (t, CH_2).

MS (EI) *m/z* = 108 (M^+, 71%), 107(68), 91 (37), 79(100), 77(50).

HRMS (EI): calcd for C_7H_8O (M^+) 108.0575, found 108.0577.

Other substrates (excluding benzamide) were treated identically, except that the appropriate molar equivalent quantities were used. Molar equivalents, yields and the exceptional conditions for the reduction of benzamide are shown in Table 2.4. The above conditions were applicable for the reduction of different substrates with **2.32**, see Table 2.5.

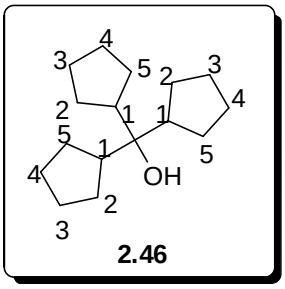
2.12.8 Hydroboration–oxidation of Alkenes with 2.31 and 2.32

In an oven dried 50 mL flask protected by a rubber septum was placed **2.31** (0.44 g, 3.6 mmol BH_3) or **2.32** (0.72 g, 3.6 mmol BH_3). The flask was cooled to 0 ^{o}C under a stream of nitrogen and freshly distilled THF (14 mL) was added. Alkene (9.0 mmol) was added and the mixture was stirred at 0 ^{o}C for 30 min and then at room temperature for 16 h. The reaction mixture was cooled to 0 ^{o}C and NaOH (3.0 M, 3.0 mL) was added, followed by slow addition of hydrogen peroxide (30%, 3.5 mL). The contents were further stirred at room temperature for 1 h. Hexadecane (0.75 g) was added followed by addition of diethyl ether (10 mL) to precipitate the liberated polymeric sulfide. Yields were calculated by the GC analysis of the organic layer. Results are shown in Tables 2.7 and 2.8.

2.11.9 Synthesis of Tricyclopentylmethanol (2.46)

Cyclopentene (1.90 g; 28.0 mmol) was added to a stirred, cooled (0 °C) mixture of **2.31** (1.10 g, *ca.* 9.4 mmol BH_3) and anhydrous THF (20 mL) under nitrogen and the mixture was stirred at 0 ^{o}C for 30 min and then at room temperature for 4 h. In another

dried 50 mL flask 3-ethyl-3-pentanol (1.05 g, 9.04 mmol) was added to a stirred, cooled solution of *n*-BuLi in hexane (6.00 mL of 1.50 M, 9.00 mmol) and the mixture was stirred for 30 min at 0 °C. The tricyclopentylborane solution was cooled to 0 °C and DCME (1.20 g, 10.4 mmol) was added followed by the transfer of the lithium triethylcarboxide solution by a double ended needle over a period of 10 min. The cooling bath was removed and the reaction mixture was stirred for 1 h. Then the flask was cooled to 0 °C and ethanol (10 mL, 95%) was added, followed by sodium hydroxide (2.40 g, *ca*. 60 mmol) and slow addition of hydrogen peroxide (9 mL, 35%, *ca*. 90 mmol). The mixture was stirred for 1 h at 70 °C and then allowed to cool. Diethyl ether (20 mL) was added to precipitate the polymeric material, which was filtered, and anhydrous potassium carbonate was added to the filtrate to salt out the aqueous phase. The mixture was filtered and the solid was washed with further ether (2 × 10 mL), the filtrate and washings were combined and the organic layer was separated, washed with brine (3 × 20 mL) and dried over anhydrous magnesium sulfate. The solvent was evaporated under reduced pressure and the crude product was purified by column chromatography (alumina; hexane-ether; 1:1) to give **2.46** (1.70 g, 7.20 mmol, 80%) as colourless oil.



2.46

^{1}H NMR (400 MHz, $CDCl_3$), δ (ppm): 2.06 (appt. pentet, J = 9.5 Hz, 3 H, H-1 of 3 cyclopentyl), 1.36–1.51 (m, 24 H, H-2/H-3/H-4/H-5 of 3 cyclopentyl), 1.16 (s, exch., 1 H, OH).

^{13}C NMR (100 MHz, $CDCl_3$), δ (ppm): 77.6 (s, C-OH), 47.8 (d, C-1 of 3 cyclopentyl), 27.9 (t, C-2/C-5 of 3 cyclopentyl), 25.2 (t, C-3/C-4 of 3 cyclopentyl).

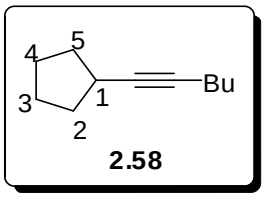
MS (EI), *m/z* (%): 218 ([M - H_2O]$^+$, 6), 167 (90), 149 (96), 125 (19), 97 (100), 81 (52), 69 (99).

HRMS (EI): calcd for $C_{16}H_{26}$ ([M - H_2O]$^+$): 218.2034; found: 218.2035.

IR (FT), ν_{max}: 3623, 3521, 2941, 1451 cm^{-1}.

2.12.10 Synthesis of Hex-1-ynylcyclopentane (2.58)

Tricyclopentylborane (*ca.* 3.70 mmol) was prepared as described in the synthesis of **2.46** from cyclopentene (0.750 g; 11.0 mmol) and complex **2.31** (0.450 g, *ca.* 3.80 mmol BH_3). A freshly prepared solution of hex-1-ynyllithium (*ca*. 3.50 mmol), prepared by addition of a solution of *n*-butyllithium in hexane (1.5 M, 2.4 mL) to a solution of hex-1-yne (0.290 g, 3.50 mmol) in THF (10 mL) at 0 ^{o}C, was added slowly by syringe and the mixture was stirred for 30 min at 0 ^{o}C. The reaction mixture was stirred efficiently, cooled to – 78 ^{o}C, a solution of iodine (1.00 g, 3.94 mmol) in dry ether (15 mL) was added by syringe over 30 min and the mixture was stirred for a further 45 min at -78 ^{o}C. The reaction mixture was left to warm up to room temperature and few drops of saturated aqueous sodium thiosulfate solution were added to decompose the excess iodine. Diethyl ether (20 mL) was added to precipitate the polymer, followed by filtration. The solid was washed with further ether (2 × 10 mL) and the combined filtrate and washings were washed with aqueous sodium hydroxide solution (2 × 20 mL, 3 *M*). The aqueous layer was extracted with diethyl ether (2 × 20 mL) and sodium hydroxide (4 mL, 3M, 12 mmol) was added to the combined organic layers, followed by dropwise addition of hydrogen peroxide (1.5 mL, 30%, *ca*. 13 mmol). The aqueous layer was saturated with K_2CO_3 and the organic layer was separated and then dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure to give a yellow oily material, which was purified by column chromatography (silica gel, hexane) to give hex-1-ynylcyclopentane **2.58** (0.340 g, 2.27 mmol, 65%) as colourless oil.



2.58

^{1}H NMR (400 MHz, $CDCl_3$), δ (ppm): 2.57 (m, 1 H, H-1 of cyclopentyl), 2.16 (dt, J = 2 and 7 Hz, 2 H, $CH_2CH_2CH_2CH_3$), 1.92-1.35 (m, 12 H, $CH_2CH_2CH_3$ and H-2/H-3/H-4/H-5 of cyclopentyl), 0.91 (t, J = 7 Hz, 3 H, CH_3);

^{13}C NMR (100 MHz, $CDCl_3$), δ (ppm): 84.4 (s, C≡*C*-cyclopentyl), 79.6 (s, C≡*C*-CH_2), 34.1 (t, C-2/C-5 of cyclopentyl), 31.3 (t, $CH_2CH_2CH_2CH_3$), 30.4 (d, C-1 of cyclopentyl), 24.9 (t, C-3/C-4 of cyclopentyl), 21.9 (t, $CH_2CH_2CH_3$), 18.5 (t, CH_2CH_3), 13.6 (q, CH_3).

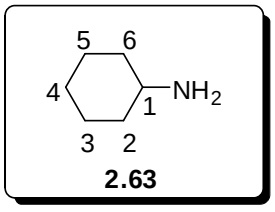
MS (EI), *m/z* (%): 150 (M^+, 53), 137 (55), 121 (57), 137 (87), 108 (85), 93 (100), 91 (97), 67 (98).

HRMS (EI): calcd for $C_{11}H_{18}$ (M^+): 150.1407; found: 150.1409.

IR (FT), ν_{max}: 2957, 2933, 2871, 2236 cm^{-1}.

2.12.11 Synthesis of Cyclohexylamine (2.63)

Cyclohexene (3.00 g; 36.5 mmol) was added to a stirred cooled (0 °C) solution of **2.31** (1.50 g, *ca.* 12.7 mmol BH_3) in anhydrous THF (20 mL) under nitrogen and the mixture was stirred at room temperature for 4 h. An aqueous NaOH solution (3 *M*, 18 mL) was added to the mixture followed by addition of a freshly prepared solution of chloroamine [*ca.* 25.0 mmol; prepared as follows: in a 100 mL flask were placed water (25 mL) and aqueous ammonium hydroxide (5.0 mL, 5 *M*); the mixture was cooled to 0 ^oC after which commercial bleach (aqueous sodium hypochlorite, 50.0 mL, 0.50 *M*) was added and the mixture was stirred at 0 ^oC for 1 h to produce chloramine]. The mixture was stirred at room temperature for a further 2 h and then acidified (checked by pH paper) with hydrochloric acid (2 *M*). Diethyl ether (25 mL) was added to precipitate the polymeric material, which was removed by filtration. Solid sodium hydroxide was used to make the solution strongly alkaline. The organic layer was separated and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure and the product was purified by distillation under reduced pressure using an oil pump to give pure **2.63** (1.20 g, 12.0 mmol, 33% based on cyclohexene) as colourless oil.



2.63

^1H NMR (500 MHz, $CDCl_3$), δ (ppm): 2.55 (m, 1 H, H-1 of cyclohexyl), 1.76-1.50 (m, 6 H, H-2/H-6 of cyclohexyl and NH_2), 1.24-0.94 (m, 6 H, H-3/H-4/H-5 of cyclohexyl).

^{13}C NMR (125 MHz, $CDCl_3$), δ (ppm): 50.3 (d, C-1 of cyclohexyl), 36.7 (t, C-2/C-6 of cyclohexyl), 25.6 (t, C-4 of cyclohexyl), 25.0 (t, C-3/C-5 of cyclohexyl).

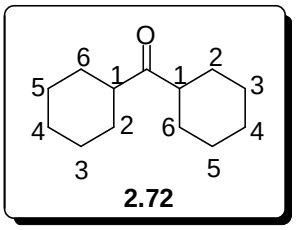
MS (EI), *m/z* (%): 99 (M^+, 15), 82 (4), 70 (12), 67 (6), 56 (100).

HRMS (EI): calcd for $C_6H_{14}N$ (M^+): 99.1045; found: 99.1048.

IR (FT), ν_{max}: 3348, 3276, 2927, 2853 cm^{-1}.

2.12.12 Synthesis of Dicyclohexylmethanone (2.72)

Cyclohexene (1.30 g; 15.8 mmol) was added to a stirred, cooled (0 °C) solution of **2.31** (0.940 g, *ca.* 8.0 mmol BH_3) in anhydrous THF (14 mL) under nitrogen and the mixture was stirred at 0 °C for 2 h. Methanol (0.250 g, 7.80 mmol) was then added to form dicyclohexylmethoxyborane. In another 50 mL flask, 3-ethyl-3-pentanol (0.930 g, 9.00 mmol) was added to a cooled (0 °C) solution of *n*-BuLi in hexane (5.00 mL of 1.60 *M*; 8.00 mmol) and the mixture was stirred for 30 min at 0 °C to form lithium triethylcarboxide. DCME (1.06 g, 9.20 mmol) was added to the dicyclohexylmethoxyborane solution, followed by transfer of lithium triethylcarboxide solution by a double ended needle over a period of 10 min, then the reaction mixture was allowed to warm up to room temperature and stirred for 1 h. Ethanol (3.5 mL) was added followed by NaOH (0.60 g, 15 mmol) then careful addition of hydrogen peroxide (2.4 mL, 30%, *ca*. 21 mmol). The reaction mixture was stirred for 1 h at 50 °C then left to cool down to room temperature. The reaction mixture was worked up by addition of brine (20 mL). Diethyl ether (50 mL) was added followed by filtration. The aqueous layer was separated and re-extracted with diethyl ether (50 mL). The combined organic layers were dried over $MgSO_4$ and solvent was removed under reduced pressure. The crude product was purified by distillation under reduced pressure using an oil pump to give **2.72** as colourless oil (1.20 g, 6.18 mmol, 77%).



2.72

^{1}H NMR (400 MHz, $CDCl_3$), δ (ppm): 2.41 (m, 2 H, H-1 of 2 cyclohexyl), 1.78–1.56 (m, 10 H of 2 cyclohexyl), 1.39–1.01 (m, 10 H of 2 cyclohexyl).

^{13}C NMR (100 MHz, $CDCl_3$), δ (ppm): 217.6 (s, C=O), 49.2 (d, C-1 of 2 cyclohexyl), 28.6 (t, C-2/C-6 of 2 cyclohexyl), 25.9 (t, C-3/C-5 of 2 cyclohexyl), 25.7 (t, C-4 of 2 cyclohexyl).

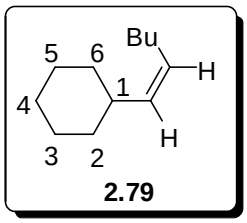
MS (EI), *m/z* (%): 194 (M^+, 30), 127 (12), 111 (85), 95 (38), 84 (100), 67 (35).

HRMS (EI): calcd for $C_{13}H_{22}O$ (M^+): 194.1670; found: 194.1671.

IR (FT), ν_{max}: 2928, 2853, 1704 cm^{-1}.

2.12.13 Synthesis of (*Z*)-1-Cyclohexylhex-1-ene (2.79)

Dicyclohexylborane (*ca.* 7.90 mmol) was prepared as described for the synthesis of **2.72** from cyclohexene (1.30 g; 15.8 mmol) and complex **2.31** (0.940 g, *ca.* 8.00 mmol BH_3). 1-Hexyne (0.640 g, 7.80 mmol) was added while the temperature was maintained at room temperature. The mixture was stirred for 1.5 h at room temperature and then cooled to -10 ^oC and aqueous sodium hydroxide solution (6 *M*, 10 mL, 60 mmol) and iodine solution (2.50 g, 9.80 mmol) in THF (15 mL) were added by syringe dropwise over 15 min. The reaction mixture was allowed to warm up to room temperature and a small amount of saturated aqueous sodium thiosulfate solution was added to decompose the excess iodine. Diethyl ether (20 mL) was added, followed by filtration to remove the polymeric sulfide. The solid was washed with further ether (2 × 10 mL) and the filtrate and washings were combined. Pentane (30 mL) was added and the organic layer was separated from the aqueous layer, washed with brine (2 × 20 mL) and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure and the crude product was purified by column chromatography (silica; hexane) to give pure **2.79** (0.830 g, 5.00 mmol, 64%) as a colourless oil.



2.79

^1H NMR (400 MHz, $CDCl_3$), δ (ppm): 5.31-5.19 (m, 2 H, CH=CH), 2.28 (m, 1 H, H-1 of cyclohexyl), 2.06 (m, 2 H, $CH_2CH_2CH_2CH_3$), 1.76-1.61 (m, 4 H of cyclohexyl), 1.36-1.05 (m, 10 H, 6 H of cyclohexyl and $CH_2CH_2CH_3$), 0.93 (t, J = 7 Hz, 3 H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$), δ (ppm): 136.0 (d, CH=*C*H-cyclohexyl), 128.0 (d, CH=*C*HCH_2), 36.3 (d, C-1 of cyclohexyl), 33.4 (t, C-2/C6 of cyclohexyl), 32.2 (t, $CH_2CH_2CH_2CH_3$), 27.2 (t, $CH_2CH_2CH_2CH_3$), 26.1 (t, C-4 of cyclohexyl), 26.0 (t, C-3/C-5 of cyclohexyl), 22.4 (t, CH_2CH_3), 14.0 (q, CH_3).

MS (EI), *m/z* (%): 166 (M^+, 56), 154 (5), 137 (5), 124 (10), 109 (84), 96 (90), 81 (96), 67 (100).

HRMS (EI): calcd for $C_{12}H_{22}$ (M^+): 166.1721; found: 166.1722.

IR (FT), ν_{max}: 2999, 2956, 2925, 2851, 1654, 1607 cm^{-1}.

2.13 References

1. Ellerstein, S. *Handbook of Polymers*, 3rd ed., Wiley-Interscience, New York, USA, 1985.
2. Lee, T. C. P. In *Properties and Applications of Elastomeric Polysulfides*, Dolbey, R. Ed., Rapra Technology Ltd., Shrewsbury, 1999, Vol. 9.
3. Mahon, A.; Kemp, T. J.; Coates, R. J. *Polym. Degrad. Stab*. **1998**, *62*, 15–24.
4. Vo, C. D;. Kilcher, G.; Tirelli, N. *Macromol. Rapid Commun*. **2009**, *30*, 299–315.
5. Lee, C; Chang, T. C.; Huang, Y. H. *US Patent*, 5432257, **1995**.
6. Tobolsky, A. V. *The Chemistry of Sulfides*, Wiley-Interscience, New York, USA, 1968.
7. Bahh, C. A.; Baah, J. I.; Gianadda, P.; Fisher, C. *Mater. Des*. **2000**, *21*, 211–215.
8. Lucke, H. *ALIPS–Aliphatic Polysulfides*, Hüthig and Wepf: Basel, 1994.
9. Sandler, S. R; Karo, W. *Polymer Synthesis*, volume 3, 2nd ed., Academic Press, California, USA, 1996.
10. Marvel, C. S.; Weil, E. D. *J. Am. Chem. Soc*., **1954**, *76*, 61–69.
11. Lal, J.; Pesch, P. H. *The Chemistry of Cationic Polymerization*, Macmillan, New York, USA, 1963.
12. Bacskai, R. *J. Polym. Sci. Part A* **1963**, *1*, 2777–2790.
13. Stille, J. K.; Empen, J. A. 150th *Meet. Am. Chem. Soc*., (Atlantic City, N. J.) *Polym. Prepr*. **1965**, *6*, 619–625.
14. Gobran, R. H.; Osborn, S. W. *US Patent*, 3365429, **1968**.
15. Gobran, R. H.; Osborn, S. W. *US Patent*, 3365431, **1968**.
16. Sander, M. *US Patent*, 3317489, **1967**.
17. Stille, J. K.; Empen, J. A. *J. Polym. Sci. Part A* **1967**, *5*, 273–285.
18. Baumann, E. *Ber. Dtsch. Chem. Ges*. **1885**, *18*, 258–267.
19. Autenrieth, W.; Geyer, A. *Ber. Dtsch. Chem. Ges*. **1908**, *41*, 4249–4256.
20. Fisher, N. G.; Wiley, R. H. *US Patent*, 2389662, **1945**.
21. Marvel, C. S.; Shen, E. H. H.; Chambers, R. R. *J. Am. Chem. Soc*., **1950**, *72*, 2106–2109.
22. Posner, T. *Ber. Dtsch. Chem. Ges*. **1905**, *38*, 646–657.
23. Mays, F. R.; Walling, C. *Chem. Rev*. **1940**, *27*, 351–412.
24. Vaughan, W. E.; Rust, F. F. *J. Org. Chem*. **1942**, *7*, 472–476; *US Patent*, 2392294, 2392295, 2398479 and 2398480, **1946**.

25. Coffman, D. D. *US Patent*, 2347182 **1944**.
26. Marvel, C. S.; Aldrich, P. H. *J. Am. Chem. Soc*. **1950**, *72*, 1978–1981. (b) Marvel, C. S.; Olson, L. E. *J. Polym. Sci*. *Part A* **1957**, *26*, 23–28.
27. Tucker, N. B.; Reid, E. E. *J. Am. Chem. Soc*. **1933**, *55*, 775–781.
28. Meadow, J. R.; Reid, E. E. *J. Am. Chem. Soc*. **1934**, *56*, 2177–2180.
29. Carothers, W. H. *US Patent*, 2201884, **1940**.
30. Marvel, C. S.; Chambers, R. R. *J. Am. Chem. Soc*. **1948**, *70*, 993–998.
31. Lal, J.; Trick, G. S. *J. Polym. Sci. Part A* **1961**, *50*, 13–19.
32. (a) Smith, K.; El-Hiti, G. A.; Al-Zuhairi, A. J. *J. Sulfur Chem*. **2011**, *32*, 521–531. (b) Smith, K.; El-Hiti, G. A. Personal communication, **2012**.
33. Clayden, J.; Greeves, N.; Warren, S.; Wothers, P. In *Organic Chemistry*, Oxford University Press, Oxford, UK, 2001.
34. Leonard, J.; Lygo, B.; Procter, G. *Advanced Practical Organic Chemistry*, 2nd ed., Nelson Thornes, Cheltenham, UK, 2001.
35. Brown H. C. *Organic Syntheses via Boranes*, John Wiley and Sons, USA, 1975.
36. Heal, H. G. *J. Inorg. Nucl. Chem.* **1960**, *12*, 255–258.
37. Mincione, E. *J. Org. Chem.* **1978**, *43*, 1829–1830.
38. (a) Lane, C. F.; Myatt, H. L.; Daniels, J.; Hopps, H. B. *J. Org. Chem.* **1974**, *39*, 3052–3054. (b) Lane, C. F. *Aldrichimica Acta.* **1975**, *8*, 20–23. (c) Brown, H. C.; Choi, Y. M.; Narasimham, S. *J. Org. Chem.* **1982**, *47*, 3153–3163.
39. (a) Adams, R. M.; Braun, L. M.; Braun, R. A.; Crissman, H. R.; Opprman, M. *J. Org. Chem.* **1971**, *36*, 2388–2389. (b) Lane, C. F. *J. Org. Chem*. **1974**, *39*, 1437–1438. (c) Brown, H.C.; Mandal, A.K.; Kulkarni, S. U. *J. Org. Chem.* **1977**, *42*, 1392–1398.
40. Brown, H. C. *Hydroboration*, Benjamin, W. A. Inc., New York, USA, 1962.
41. Brown, H. C.; Rao, B. C. S. *J. Am. Chem. Soc*. **1959**, *81*, 6423–6428.
42. (a) Brown, H. C.; Rathke *M. W. J. Am. Chem. Soc.* **1967**, *89*, 2737–2738, (b) Hillman, M. E. D. *J. Am. Chem. Soc.*, **1962**, 84, 4715–4720
43. (a) Pelter, A.; Hutchings, M. G.; Rowe, K.; Smith, K. *J. Chem. Soc., Perkin Trans. 1* **1975**, 138–142, (b) Pelter, A.; Hutchings, M. G.; Smith, K. *J. Chem. Soc., Chem. Commun.*, **1971**, 1048–1050.
44. Brown, H. C.; Carlson, B. A. *J. Org. Chem.* **1973**, *38*, 2422–2424.
45. Suzuki, A.; Miyaura, N.; Abiko, S.; Itoh, M.; Midland, M. M.; Sinclair, J. A.; Brown, H. C. *J. Org. Chem.* **1986**, *51*, 4507–4511.

46. Brown, H. C.; Kim, K.; Srebnik, M.; Singaram, B. *Tetrahedron* **1987**, *43*, 4071–4078.
47. Brown, H. C.; Moerikofer, A. W. *J. Am. Chem. Soc.* **1962**, *84*, 1478–1484.
48. Beran, J. A. *Laboratory Manual for Principles of General Chemistry*, 9th ed., John Wiley and Sons, USA, 2011.
49. Brown, H. C.; Carlson, B. A. *J. Am. Chem. Soc.* **1973**, *95*, 6876–6877.
50. Zweifel, G.; Arzoumanian, H.; Whitney, C. C. *J. Am. Chem. Soc.* **1967**, *89*, 3652–3653.
51. (a) Furniss, B. S.; Hannaford, A. J.; Smith, P. W. G.; Tatchell, A. R. *Vogel's Textbook of Practical Organic Chemistry*, 5th ed., Longman, Harlow, UK, 1989. (b) Perrin, D. D.; Armarego, W. L. F. *Purification of Laboratory Chemicals*, 3rd ed., Pergamon: Oxford, UK, 1988.
52. Watson, S. C.; Eastham, J. F. *J. Organomet. Chem.* **1967**, *9*, 165.

Chapter Three

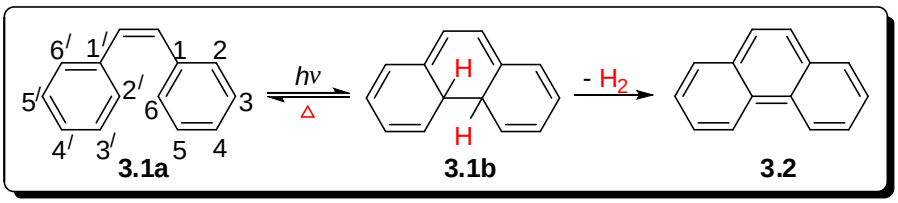
Introduction to Photochromic Diarylperfluorocyclopentene Polymers

Introduction to Photochromic Diarylperfluorocyclopentenes

3.1 Introduction

Photochromism is a reversible change (unimolecular reaction) in a chemical process between two forms having different absorption spectra by light irradiation accompanied with colour change and alterations in the chemical and physical properties of the photochromic material.[1]

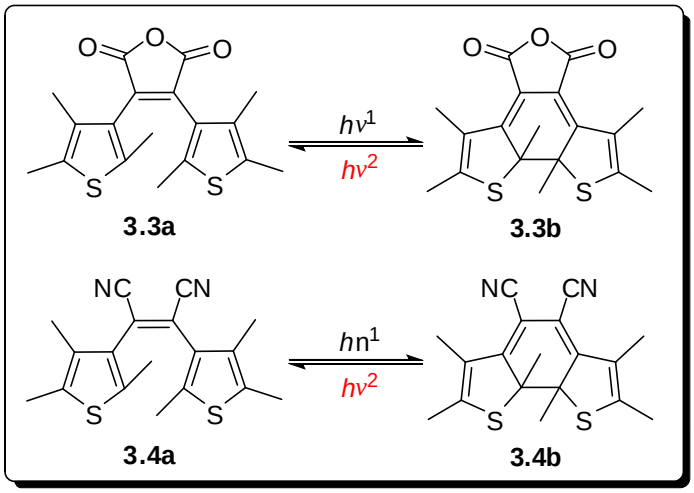
Diarylethenes are compounds that have aromatic groups bonded to each end of a carbon-carbon double bond. Stilbene (**3.1a**), the simplest diarylethene, undergoes a photocyclization reaction to produce dihydrophenanthrene (**3.1b**); in the dark and in a deoxygenated solution **3.1b** returns back to stilbene (**3.1a**), while in the presence of oxygen, **3.1b** undergoes an irreversible hydrogen-elimination reaction (oxidation) to form phenanthrene (**3.2**), acquiring aromaticity (Scheme 3.1).[2-4]



Scheme 3.1

Replacement of the two hydrogen atoms at the 2′- and 6- positions (liable to elimination) of **3.1a** by methyl groups inhibits the elimination reaction and makes the photocyclization reaction a fully reversible process.[2] However, the destruction of the aromatic conjugation increases the ground-state energy of the closed form **3.1b** which makes the energy barrier for the thermal cycloreversion reaction of 1,2-diphenylethene very small; therefore, this photochromic system is thermally unstable and the lifetime of the dihydro-type isomer (closed form) is very short.[2,5] In 1967 Kellogg *et al.*[6] published a paper that developed a photosynthetic route to condensed ring systems including ones with heteroatoms, and within this study they found that replacing the phenyl groups of **3.1a** by heteroaromatics, which generally have lower aromatic stabilization energies than benzene, increases the stability of the closed form. Thiophenes seemed to be particularly effective. In 1988 Irie and Mohri[7] reported the synthesis of compounds **3.3** and **3.4** and presented them as thermally irreversible photochromic diarylethenes (Scheme 3.2), the reason for

such thermal stability is that the energy barrier for the thermal cycloreversion reaction in such compounds is high, leading to more stable photochromic systems.[5,7]



Scheme 3.2

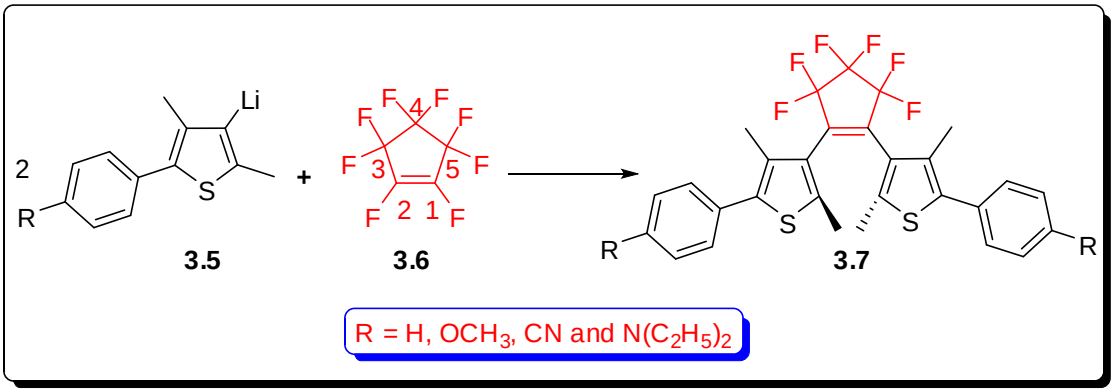
Due to the importance of the photochromic compounds and their potential applications in optical memories and molecular switches,[2,8] researchers have developed a huge number of diarylethenes with heteroaromatics (especially diarylperfluorocyclopentenes with thienyl groups), and the development in this field is still ongoing.

3.2 Synthetic Strategies for Diarylperfluorocyclopentenes

This section shows the reported synthetic strategies for the production of both symmetrical and unsymmetrical types of diarylperfluorocyclopentenes.

3.2.1 Reactions of Aryllithiums with Perfluorocyclopentene

Diarylperfluorocyclopentenes (*e.g.* **3.7**) are the most commonly used diarylethenes.[9] In 1956 Dixon proved that the fluorine atom attached to *sp2*-hybridized carbon atom can be replaced by aryllithium species.[10] This nucleophilic substitution reaction was then successfully applied to the replacement of the fluorine atoms at the 1- and 2- positions of perfluorocyclopentene (**3.6**) by different thienyllithium derivatives (*e.g.* **3.5**) giving various substituted photochromic diarylperfluorocyclopentenes. Scheme 3.3 shows an example for such a synthetic route.[11]

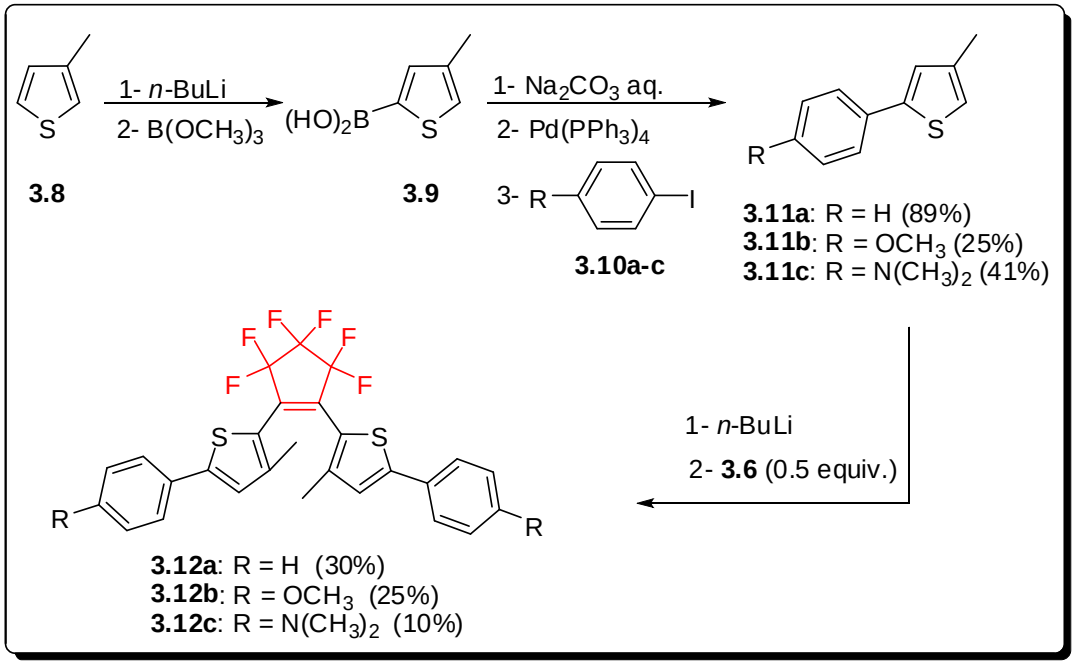


Scheme 3.3

Thienyllithium species (such as **3.5**) are important intermediates which are needed for the synthesis of the starting materials and the final diarylperfluorocyclopentene products. These intermediates can be produced either by the direct lithiation of thiophene derivatives or by lithium-bromine exchange of bromo substituted ones.[12–21]

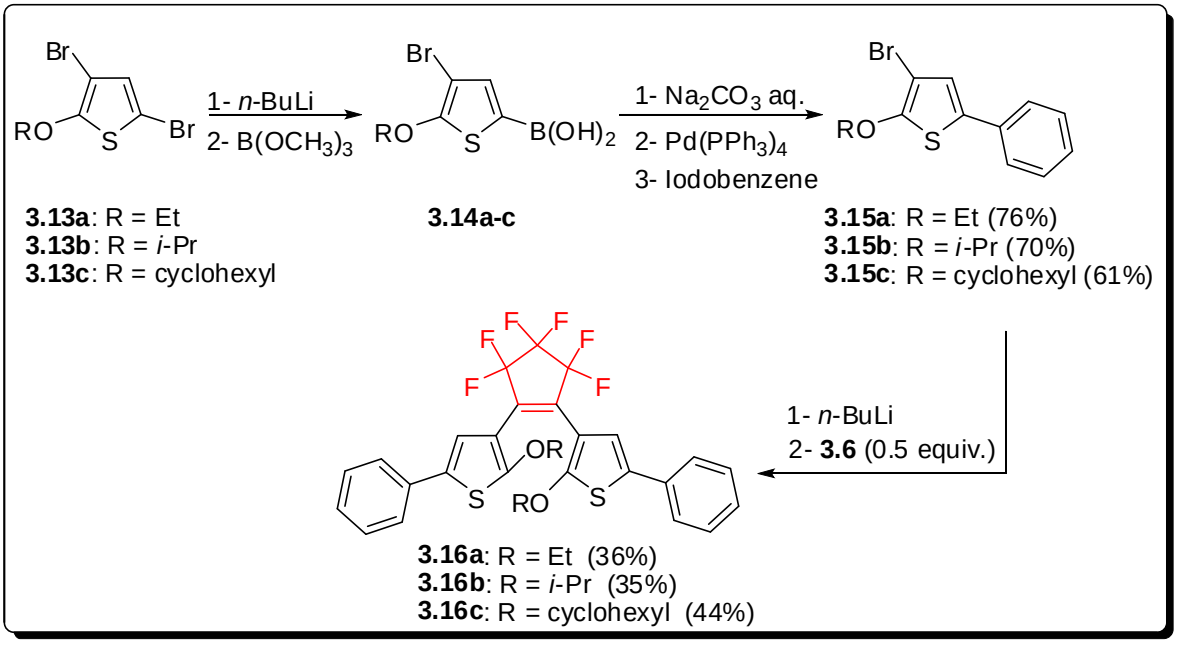
In general reaction of perfluorocyclopentene with 2 mole equivalents of the lithiated thiophene derivatives at low temperature (–78 ^{o}C) is the most common way to produce the desired symmetrical diarylperfluorocyclopentenes. This section will show some examples for such synthetic pathways.[13,14]

In a study of the substituent effect on the photochromic properties of *bis*(2-thienyl)perfluorocyclopentenes (**3.12a-c**), Uchida *et al.*[13] reported the synthesis of **3.12a-c** in two steps (Scheme 3.4) starting with 3-methylthiophene (**3.8**). Compound **3.8** was lithiated (Li–H exchange) and then treated with trimethyl borate to produce 4-methylthiophen-2-ylboronic acid (**3.9**), which is then reacted with different iodobenzene derivatives (**3.10a-c**) in the presence of sodium carbonate and a catalytic amount of tetrakis(triphenylphosphine)palladium(0) to give the desired thiophene derivatives (**3.11a-c**) which were isolated and purified by column chromatography. Lithiation of compounds **3.11a-c** followed by reaction with 0.5 mole equivalent of **3.6** gave the desired products **3.12a-c** in 10–35% isolated yields (Scheme 3.4).



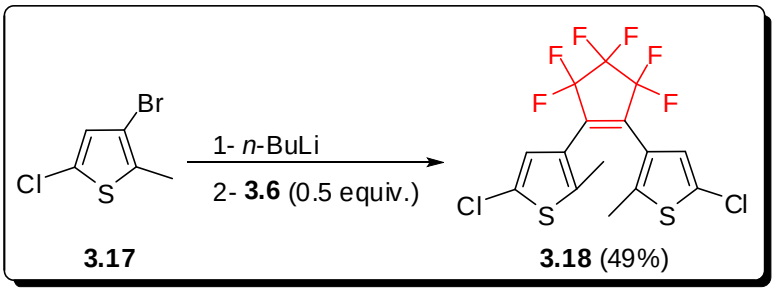
Scheme 3.4

Another example for the synthesis of symmetrical diarylethenes is the synthesis of compounds **3.16a-c**, which was reported by Morimitsu *et al.*[14] In a study of the effect the alkoxy substituents at the 2- and 2′-positions of the thiophene rings on the photochromic properties, these researchers developed synthetic procedures that required two steps (Scheme 3.5). The first step involved bromine-lithium exchange of 2-alkoxy-3,5-dibromothiopenes (**3.13a-c**) followed by reaction with tributyl borate and then with iodobenzene in the presence of sodium carbonate and a catalytic amount of tetrakis(triphenylphosphine)palladium(0) to give thiophene derivatives **3.15a-c** in 61–76% yields (Scheme 3.5). The second step involved a second bromine-lithium exchange of **3.15a-c** followed by reaction with 0.5 mole equivalent of **3.6** to give the desired products **3.16a-c** in 35–44% isolated yields (Scheme 3.5).[14]



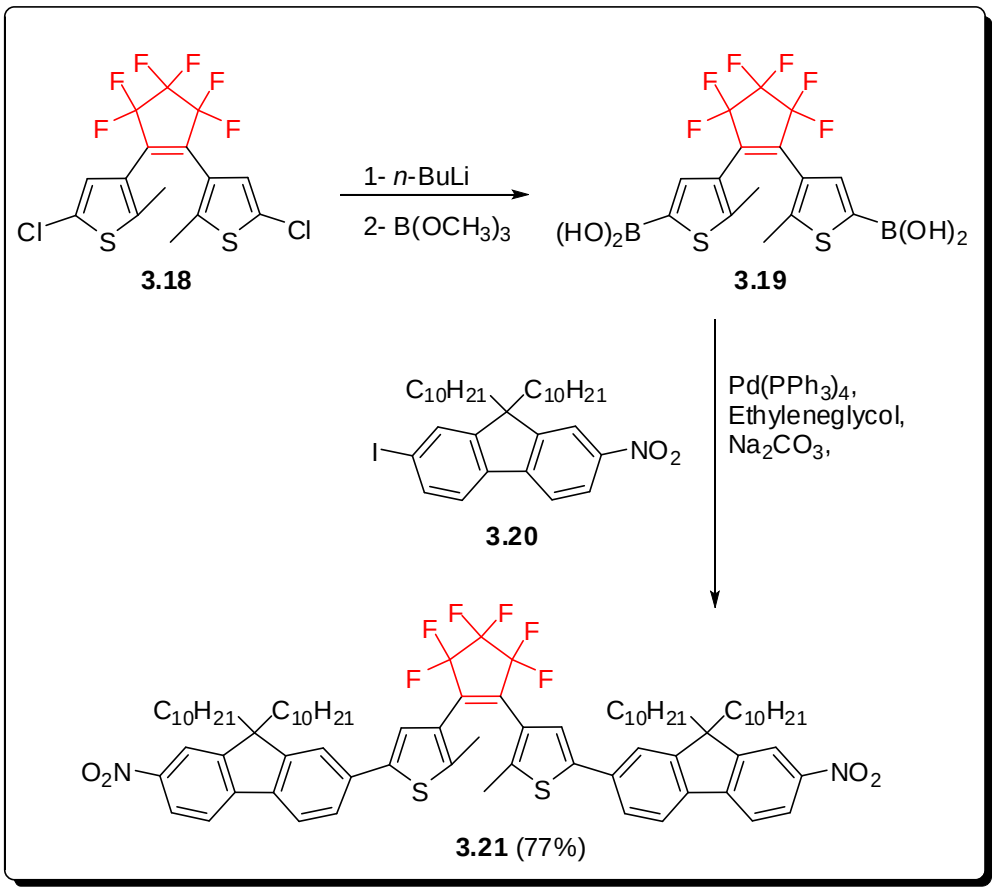
Scheme 3.5

Simple diarylethenes such as compound **3.18** can be synthesized but in moderate yield (49%) by a single step reaction that involves bromine-lithium exchange of compound **3.17** followed by reaction with perfluorocyclopentene (**3.6**; Scheme 3.6).[15]



Scheme 3.6

Compound **3.18** was used as a starting material by Luchita *et al.*[16] to produce the corresponding fluorenyldiarylethene **3.21** in one–pot reaction. The procedure involved the conversion of **3.18** to the corresponding boronic acid *via* bromine–lithium exchange followed by reaction with trimethyl borate to produce **3.19** (Scheme 3.7).[16] Direct coupling of **3.19** with **3.20** in the presence of tetrakis(triphenylphosphine)palladium(0) and ethylene glycol as catalysts gave the desired product **3.21** in 77% yield (Scheme 3.7).[16] This example shows that simple diarylethenes can be modified to produce more complicated ones.

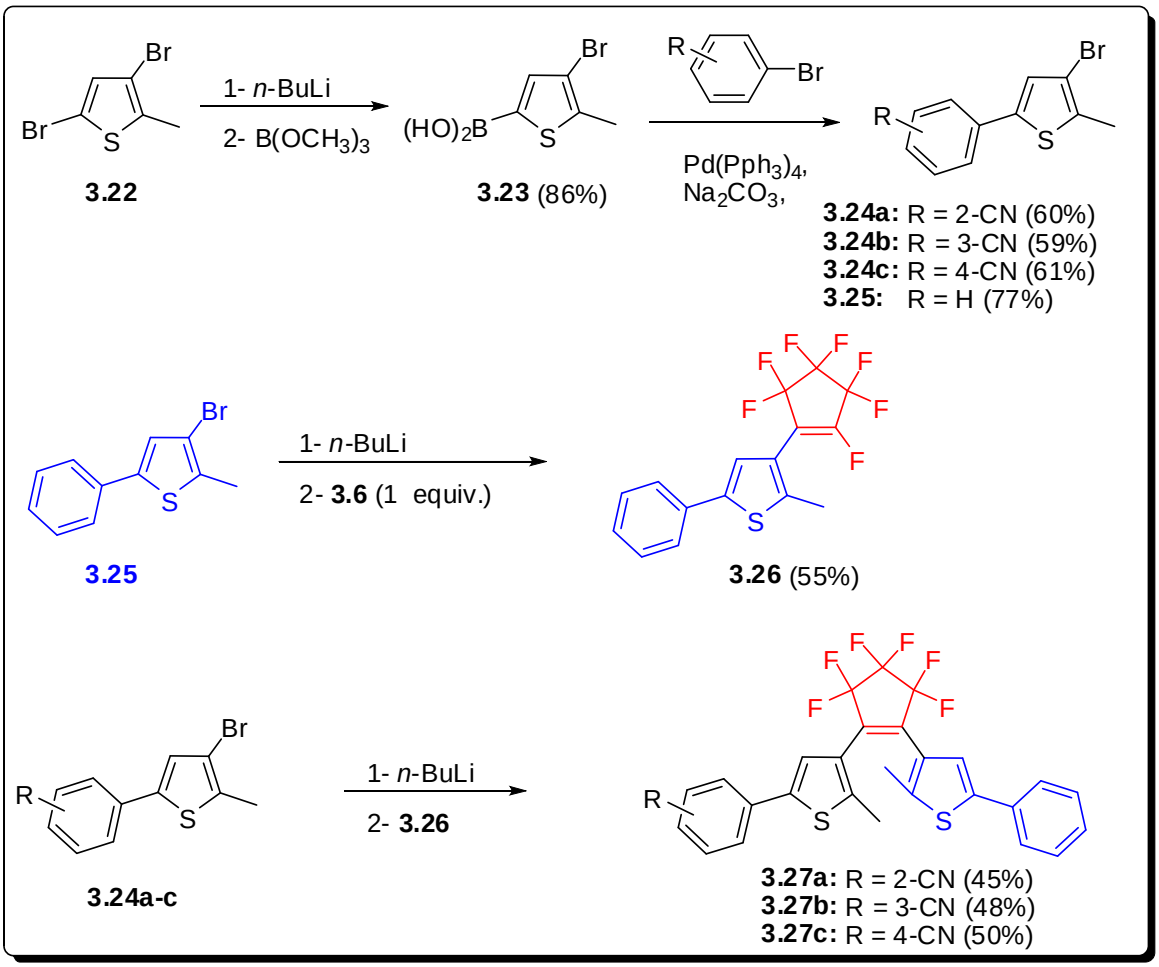


Scheme 3.7

All the examples reported above describe the synthesis of symmetrical diarylethenes. Unsymmetrical diarylethenes are more widely used as photochromic materials. The ability to replace only one of the fluorine atoms (F-1) of perfluorocyclopentene (**3.6**) on reaction with one mole equivalent of a nucleophile allowed synthesis of the corresponding mono-substituted perfluorocyclopentenes. Such derivatives allow the production of unsymmetrical photochromic diarylethenes *via* stepwise synthetic strategies which are more complicated than those for the synthesis of the symmetrical ones since there are extra added steps for the synthesis of the required thiophene derivatives.[17]

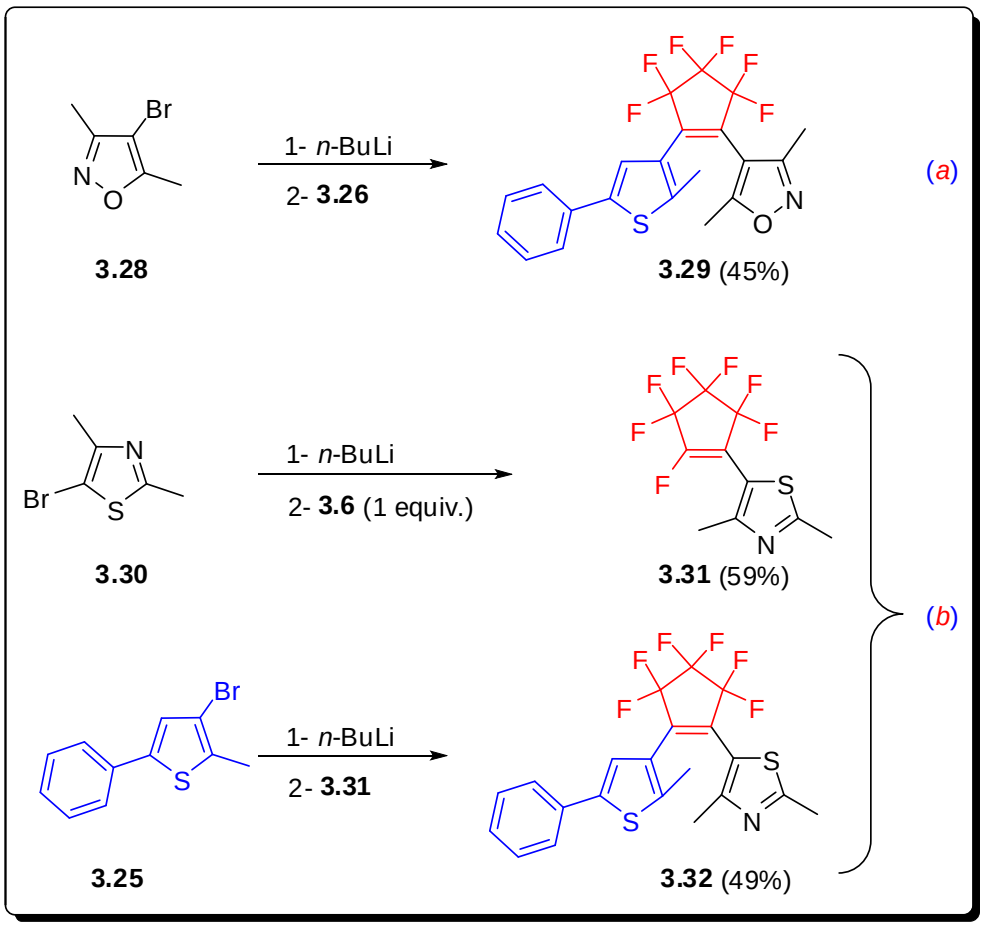
For example, synthesis of compounds **3.27a-c** is reported in Scheme 3.8, which is a typical representation for such synthetic methodology.[18,19] For any of the isomers of **3.27**, the corresponding isomers of compound **3.24** and compound **3.25** should be synthesized in parallel, then lithiation of compound **3.25** followed by reaction with 1.0 mole equivalent of perfluorocyclopentene (**3.6**) gave compound **3.26**. The final step involves bromine–lithium exchange of compounds **3.24a-c** followed by reaction with compound **3.26** to give the

desired unsymmetrical diarylperfluorocyclopentenes **3.27a-c** in 45–50% yields (Scheme 3.8).[18,19]



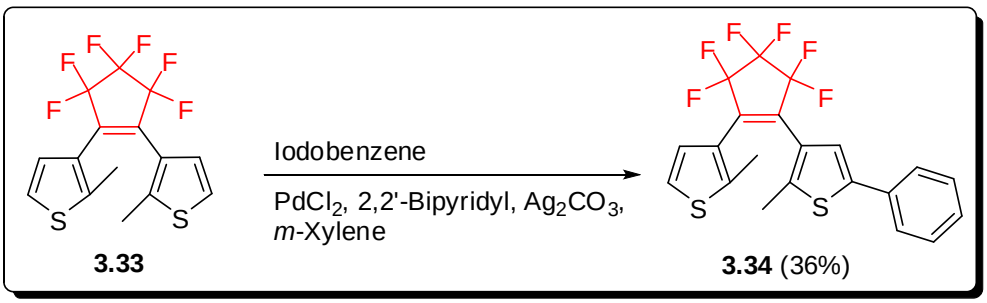
Scheme 3.8

The above strategy is applicable even for the synthesis of unsymmetrical photochromic diarylperfluorocyclopentenes that have other heteroaromatic moieties, such as isoxazole (Scheme 3.9*a*)[19] and thiazole (Scheme 3.9*b*).[20] For example, Scheme 3.9 represents the synthesis of diarylperfluorocyclopentenes **3.29** and **3.32** in moderate yields (45 and 49%, respectively).[20]



Scheme 3.9

In a recent publication Kamiya *et al.*[21] demonstrated a new method for the synthesis of symmetrical and unsymmetrical photochromic diarylethenes by functionalization of the simple diarylethenes *via* palladium–catalyzed regioselective direct arylation. For example, the synthesis of an unsymmetrical diarylethene **3.34** in 36% yield was successful (Scheme 3.10).[21]



Scheme 3.10

Due to the high reactivity of heteroaryllithiums, the lithiation reactions involved in the earlier strategies should be performed at low temperatures, such as –78 °C, which is

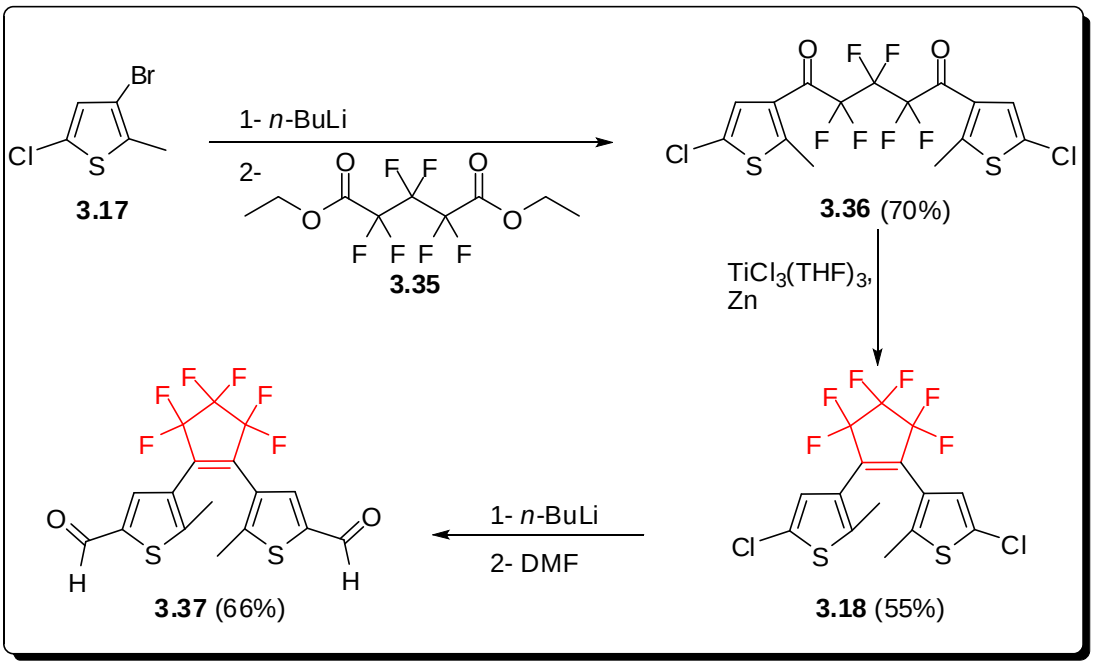
considered as an obstacle for the large scale production of such compounds.[22,23] Therefore, recently, in 2012, Asia *et al.*[23] developed a practical method for the synthesis of symmetrical and unsymmetrical photochromic diarylethenes having thiophene, thiazole, benzothiophene, and benzofuran rings in an integrated flow microreactor *via* halogen-lithium exchange and subsequent reaction with perfluorocyclopentene without using cryogenic conditions. They commented: "*Because several micro chemical plants on pilot scales have already been built, it is hoped that this process will be transformed for industrial production with continuous operation*".[23]

3.2.2 Other Synthetic Methods

Although the strategy of the reactions of aryllithiums with unsubstituted and mono-substituted perfluorocyclopentenes has been successfully and widely applied to the synthesis of a variety of diarylperfluorocyclopentenes,[2] several disadvantages are associated with such processes, which can be summarized in the following points:

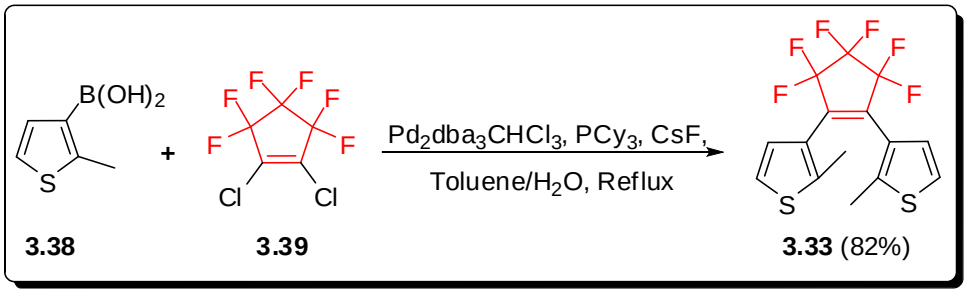
1. The starting material perfluorocyclopentene (**3.6**) is expensive (50 g cost 399.20 EUR form TCI), very volatile (bp 27 ^{o}C) and not easy to handle.
2. The reactions that include a lithiation step require cryogenic and dry conditions.[23]
3. The yields are low to moderate in most cases, and it is hard to conduct large scale reactions.[2,24]
4. The high reactivity of the generated aryllithiums makes the presence of some functional groups such as carbonyl and cyano moieties problematic.[25]

Some efforts have been made by researchers to overcome such disadvantages.[24,25] In 1999 Lucas *et al.*[24] developed an alternative method for the synthesis of symmetrical diarylperfluorocyclopentenes. Their strategy involved the synthesis of compound **3.36** using a cheap starting material such the diethyl ester of hexafluoroglutaric acid (**3.35**) rather than perfluorocylopentene (**3.6**). Bromine–lithium exchange of 2-methyl-3-bromo-5-chlorothiophene (**3.17**) followed by subsequent reaction with the diethyl ester of hexafluoroglutaric acid (**3.35**) gave the corresponding diketone **3.36** in 70% yield (Scheme 3.11). Compound **3.36** underwent a titanium mediated coupling using $TiC1_3(THF)_3$ and Zn in THF at 40 °C (McMurry coupling) to give **3.18** in 55% yield. Compound **3.18** was readily converted to another photochromic diarylperfluorocyclopentene derivative, **3.37**, in 66% yield (Scheme 3.11). The procedure was applicable on a relatively large scale with reasonable yields.[24]



Scheme 3.11

Recently, in 2011, Hiroto *et al.*[25] introduced a new synthetic protocol for diarylethenes through a Suzuki–Miyaura cross-coupling reaction of arylboronic acids and esters with 1,2-dichlorohexafluorocyclopentene (**3.39**) in the presence of the tris(dibenzylideneacetone)dipalladium(0)-chloroform adduct (Pd_2dba_3•$CHCl_3$), with tricyclohexylphosphine as a ligand and cesium fluoride (CsF) as a base. Various diarylethenes were synthesised using such a process, of which an example is shown in Scheme 3.12.[25] The starting material **3.39** is less volatile (bp 90 ^{o}C) than **3.6**, which makes it favoured over the conventional route, no cryogenic conditions are required in this procedure, and no organolilithium reagents are used in this method. Therefore, such a method is applicable for the synthesis of different derivatives having reactive functional groups such as cyano and ester moieties. The yields reported for such derivatives were in the range of 29–91%.[25]



Scheme 3.12

Despite the advantages of the above two procedures they still suffer from a substantial disadvantage in that both of them are limited to the syntheses of symmetrical diarylperfluorocyclopentenes. Based on that, we decided to consider the reactions of aryllithiums with perfluorocyclopentene as a synthetic strategy in this thesis.

3.3 Photochromic Diarylperfluorocyclopentene Polymers

The photochromism of diarylethenes could be achieved in solutions, crystalline states, amorphous forms and polymeric matrices.[26] The uses of such photochromic systems in optical memory and switches, computers, data storage (write and read) and other optical devices stand in need for the material to be in solid films. Photochromic diarylperfluorocyclopentene polymers are favoured over low molecular weight monomeric compounds. Therefore, the production of photochromic diarylethenes became an interesting field that attracted researchers to study and develop such polymeric materials. Very recently, Luo *et al.*[27] published an interesting review about the "recent progress on photochromic diarylethene polymers"; they classified the photochromic diarylethene polymers as shown in Figure 3.1. This section will represent some example which were reported in that review.[27]

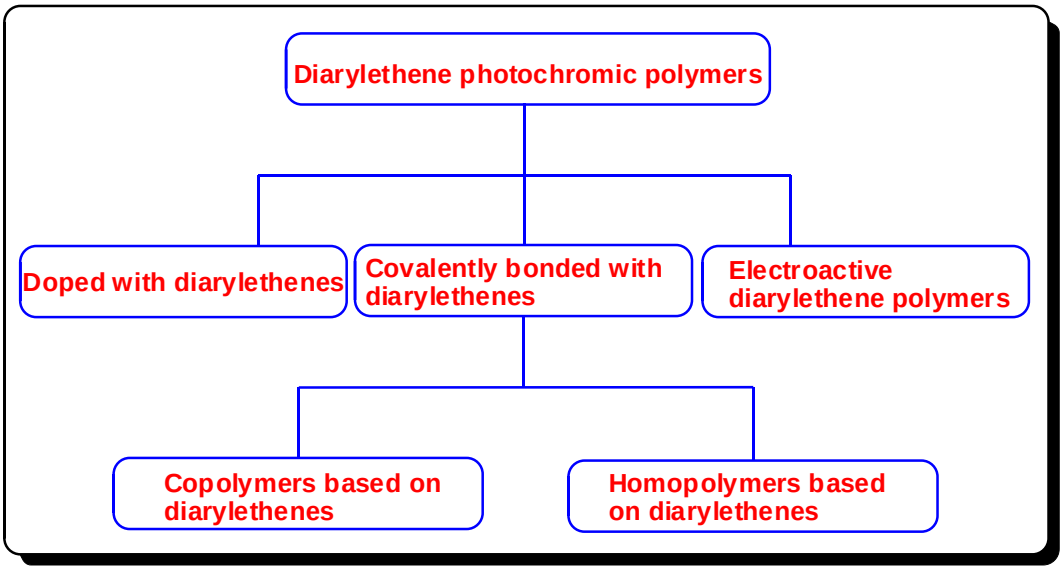


Figure 3.1: Classification of photochromic diarylethene polymers

3.3.1 Photochromic Polymers Doped with Diarylethenes

The easiest way for getting photochromic polymers (films) is to embed the diarylethene derivatives into a polymer matrix.[27] Poly(methyl methacrylate) (*PMMA*) is

one of the commonly used polymers for such purposes. Films can be prepared by a spin coating technique or by making a solution of a mixture of the PMMA and the photochromic diarylethene followed by casting the mixture on a cover glass and drying.[28] The use of other polymers such as polycarbonate of bisphenol-A [29] and poly(*n*-butyl methacrylate) [30] have also been reported.

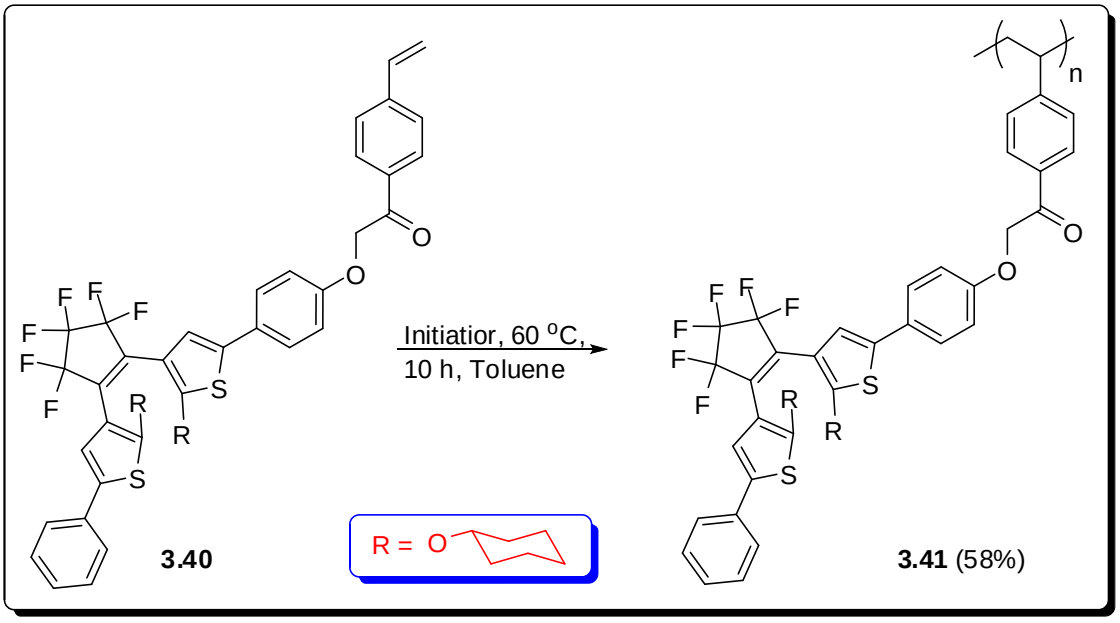
The procedure of making photochromic polymers in such a way (doping a polymer with a photochromic material) is efficient. However, this procedure has some disadvantages such as the effect on the photochromism due to the restriction of the molecular mobility, which may affect the conformational requirements of the photoisomerization reaction, inhomogenity of the matrices and other limitations related to the concentration of the photochromic material in the polymeric matrix.[27] To overcome these disadvantages photochromic polymers with photochromic diarylethenes as a part of their skeletal structure were developed.

3.3.2 Photochromic Polymers Covalently Bonded with Diarylethenes

Photochromic polymers with diarylethene building blocks have several advantages over ones doped with diarylethenes, such as the high concentration of homogeneously distributed photochromic material. They can also be structurally designed to reach the required physical and photochromic properties. There are two types of these polymers: homopolymers that contain only a single type of photochromic diarylethene repeating unit and copolymers that contain a mixture of photochromic diarylethenes with various functional molecules. Photochromic polymers are designed to meet the requirement of the technology in which they are used; good photochromic behaviour and good physical properties.[27] In this thesis we will deal with this topic from the synthetic side in an attempt to develop a convenient synthetic route that can be used to produce new photochromic polymers. Here we will show typical examples of the reported types of photochromic polymers.

3.3.2.1 Photochromic Homopolymers Based on Diarylethenes

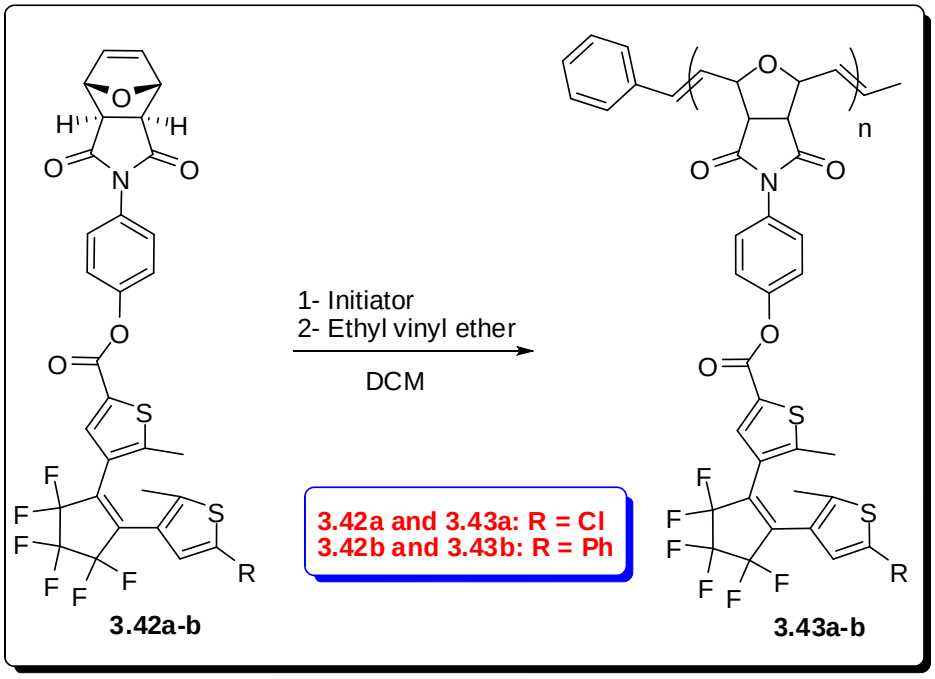
Diarylperfluorocyclopentenes can be designed to have functional groups that are susceptible to polymerization reactions, which allows the use of such photochromic monomers in the synthesis of photochromic polymers. Subjecting a single monomer to suitable polymerization conditions leads to the formation of the required homopolymer. Free radical polymerization and ring-opening metathesis polymerization (ROMP) are among the most commonly used techniques for the production of homopolymers.[31,32] Kobatake and Yamashita[31] have reported the synthesis of photochromic diarylethene polymers for a write-by-light/erase-by-heat recording system. Photochromic compound **3.40** was produced by a multistep synthesis route that involves the use of perflurocyclopentene, lithiation and cross-coupling reactions. Polymer **3.41** was then produced *via* free radical polymerization of **3.40** using 2,2′-azobis(isobutyronitrile) (AIBN) as an initiator in toluene at 60 °C for 10 h (Scheme 3.13). The polymeric material **3.41** was obtained in 58% yield by precipitation in methanol.



Scheme 3.13

Myles and Branda[32] reported the synthesis of the photochromic polymers **3.43a-b**, using a ring-opening metathesis polymerization (ROMP) procedure. They chose this technique because it requires mild reaction conditions, it is compatible with a wide range of functional groups, and it is easy to produce well-ordered homopolymers with low polydispersity. The photochromic compounds **3.42a-b** were synthesised and then used to

produce polymeric materials **3.43a-b**. The procedure involved dissolving the monomers in dry DCM in the presence of *bis*(tricyclohexylphosphine)benzylidineruthenium(IV) dichloride as initiator and the reaction mixture was stirred for 14 h at room temperature, followed by the addition of excess ethyl vinyl ether, and the resulting solutions were stirred while exposed to the atmosphere for 30 min (Scheme 3.14). Polymers **3.43a** and **3.43b** were obtained in 53 and 69% yields, respectively, by precipitation using cold diethyl ether.



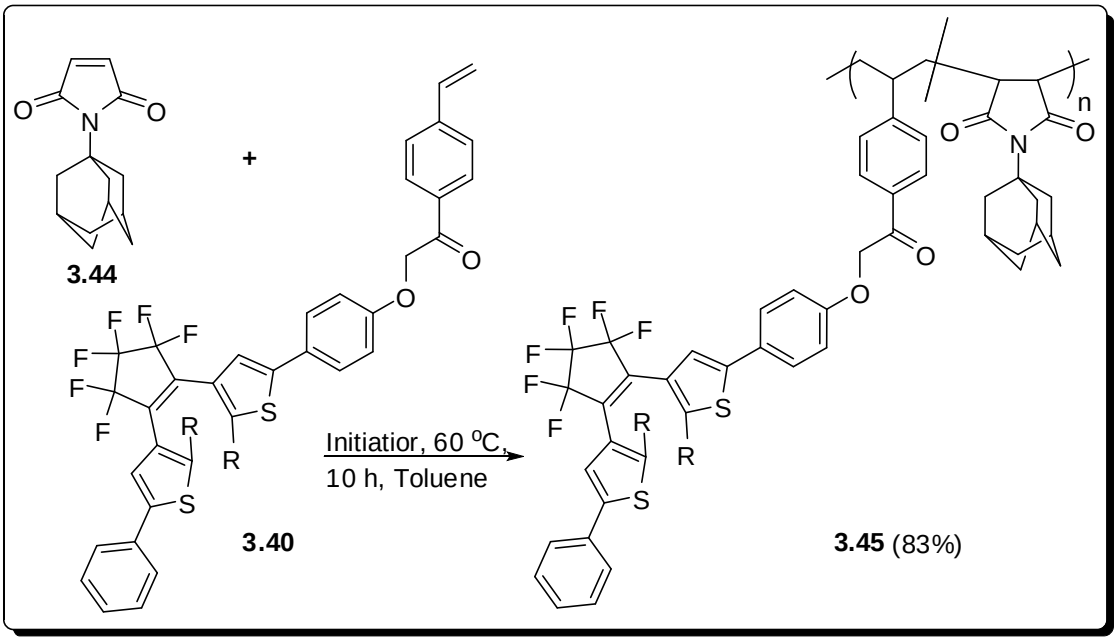
Scheme 3.14

Other techniques such as using Friedel-Crafts acylation and oxidation polymerization have also been reported in the synthesis of photochromic diarylperfluorocyclopentene homopolymers.[33,34]

3.3.2.2 Photochromic Copolymers Based on Diarylethenes

The ability to combine photochromic diarylethenes with multifarious functional molecules in a single polymer opened the gate toward the design and synthesis of different photosensitive polymers.[27,35] In some cases copolymerization has been used to improve the thermal stability of the polymers.[36] For example, to increase the thermal stability of the photochromic homopolymer **3.41** to be used for application to image recordings according to the write-by-light/erase-by-heat system, Kobatake and Yamashita[31] reported that the copolymerization of **3.40** with *N*-1-adamantylmaleimide (**3.44**), gives the photochromic copolymer **3.45**, which has a higher thermal stability than the original homopolymer

(**3.41**). Coplymer **3.45** is produced by free radical polymerization using AIBN as the initiator in toluene at 60 ^{o}C for 10 h (Scheme 3.15). The polymer was then obtained in 83% yield by precipitation in methanol.



Scheme 3.15

Medvedeva *et al.*[37] reported the synthesis of a ternary photochromic copolymer **3.46** containing diarylethene, cholesteric and phenylbenzoate side groups by the radical copolymerization of the corresponding acrylic monomers. They doped this copolymer with a fluorescent material **3.47** and presented it as a photosensitive system (Figure 3.2) which combines the fluorescent and photochromic properties of dyes with the optical properties of the cholesteric polymer matrix. Such a system was considered as promising for the reversible recording of optical information.

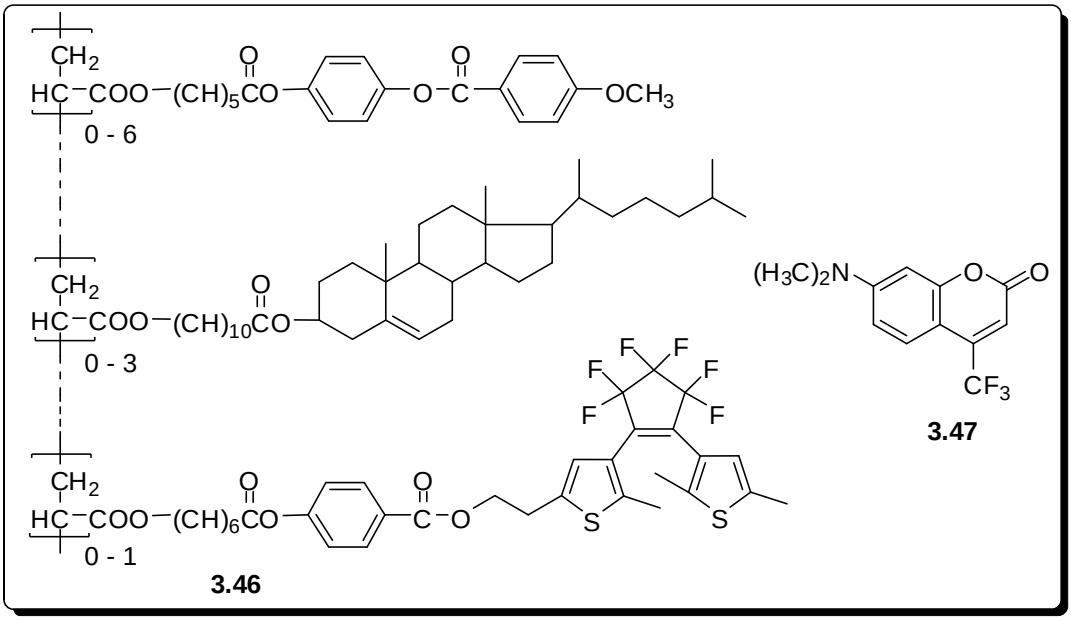
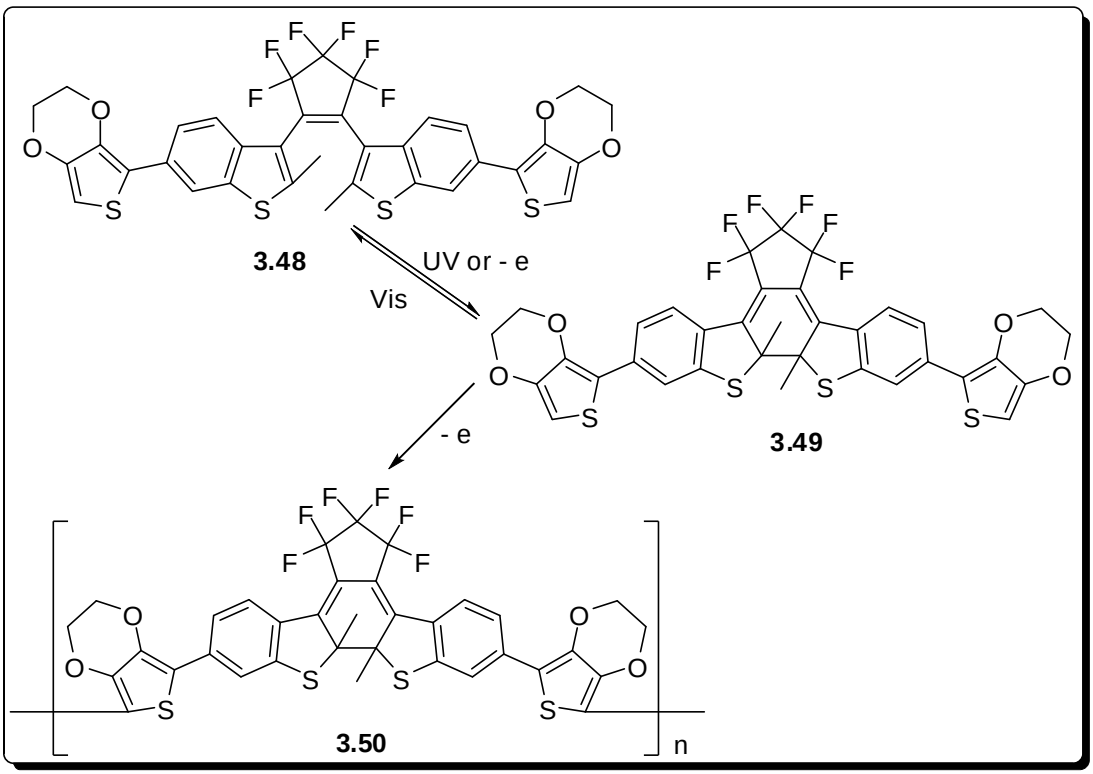


Figure 3.2: photochromic copolymer 3.47 doped with a fluorescent material 3.48

A wide range of diarylethene photochromic copolymers have been reported in the literature,[38] and such materials have recently been used in fabricating nanoparticles.[39]

3.3.3 Diarylethene Electroactive Polymers

The preparation of a photochromic diarylethene film by an electro-deposition technique was first reported by Lee *et al.*[40] in 2007. They reported the synthesis of a diarylethene substituted with 3,4-ethylenedioxythiophene units (**3.48**) as redox active groups that are able to undergo oxidative coupling in the ring-closed isomer **3.49**, leading to anodic polymerization to give **3.50** as a photochromic polymer film (Scheme 3.16).



Scheme 3.16

This procedure is convenient and allows for the direct electro-deposition of diarylethenes as thin films with controllable thickness in a monitored electropolymerization process. However it suffers some disadvantages such as the undesirable side reactions induced by electrolysis.[27] Some other diarylethene photoactive polymers have been reported in the recent literature.[41]

3.4 Conclusion

Photochromic diarylperfluorocyclopentenes are interesting compounds which are expected to have more prevalent applications; from the point of practical applications and manufacturing processes, their polymers are favoured over the low molecular weight monomer. Based on that, a wide range of such polymers has been developed by different processes. Polymers covalently bonded with photochromic diarylperfluorocyclopentenes, have several advantages over other types; they have high photochromic content, good optical homogeneity, better stability and compatibility. In the next chapter we demonstrate a strategy for the synthesis of new poly(alkylene sulfide) that bearing photochromic diarylperfluorocyclopentene moieties.

3.5 References

1. Song, Y.; Zhu, D. *High Density Data Storage: Principle, Technology, and Materials*, World Scientific, London, UK, 2009.
2. Irie, M. *Chem. Rev.* **2000**, *100*, 1685–1716.
3. Waldeck, D. H. *Chem. Rev*. **1991**, *91*, 415–436.
4. Mallory, F. B.; Mallory, C. W. *Org. React.* **1984**, *30*, 1–437.
5. Nakamura, S.; Irie, M. *J. Org. Chem*. **1988**, *53*, 6136–6138.
6. Kellogg, R. M.; Groen, M. B.; Weinberg, H. *J. Org. Chem.* **1967**, *32*, 3093–3100.
7. Irie, M.; Mohri, M. *J. Org. Chem.* **1988**, *53*, 803–808.
8. (a) Pu, S.; Zhang, F.; Xu, J.; Shen, L.; Xiao, Q.; Chen, B. *Mate. Lett.* **2006**, *60*, 485–489. (b) Dulic, D.; Kudernac, T.; Puzys, A.; Feringa, B. L.; Wees, B. J. *Adv. Mater.* **2007**, *19*, 2898–2902.
9. Yokoyama, Y.; Hosoda, N.; Osano, Y. T.; Sasaki, C. *Chem. Lett.* **1998**, 1093–1094.
10. Dixon; S. *J. Org. Chem.* **1956**, *21*, 400–403.
11. Irie, M.; Sakemura, K.; Okinaka, M.; Uchida, K. *J. Org. Chem.* **1995**, *60*, 8305–8309.
12. Joule, J. A.; Mills, K. *Heterocyclic Chemistry*, 5th ed., Wiley, Chichester, UK, 2010.
13. Uchida, K.; Matsuoka, T.; Kobatake, S.; Yamaguchi, T.; Irie, M. *Tetrahedron* **2001**, *57*, 4559–4565.
14. Morimitsu, K.; Shibata, K.; Kobatake, S.; Irie, M. *J. Org. Chem.* **2002**, *67*, 4574–4578.
15. Sevez, G.; Pozzo, J.-L. *Dyes and Pigments* **2011**, *89*, 246–253.
16. Luchita, G.; Bondar, M. V.; Yao, S.; Mikhailov, I. A.; Yanez, C. O.; Przhonska, O. V.; Masunov, A. E.; Belfield, K. D. *ACS Appl. Mater. Interfaces* **2011**, *3*, 3559–3567.
17. See for example: (a) Kobatake, S.; Terakawa, Y.; Imagawa, H. *Tetrahedron* **2009**, *65*, 6104–6108. (b) Cui, S.; Pu, S.; Liu, W.; Liu, G. *Dyes Pigments* **2011**, *91*, 435–441. (c) Liu, G.; Liu, M.; Pu, S.; Fan, C.; Cui, S. *Dyes Pigments* **2012**, *95*, 553–562. (d) Pu, S.; Wang, R.; Liu, G.; Liu, W.; Cui, S.; Yan, P. *Dyes Pigments* **2012**, *94*, 195–206.
18. Pu, S.; Fan, C.; Miao, W.; Liu, G. *Dyes Pigments* **2010**, *84*, 25–35.
19. Pu, S.; Li, H.; Liu, G.; Liu, W.; Cui, S.; Fan, C. *Tetrahedron* **2011**, *67*, 1438–1447.
20. Liu, G.; Pu, S.; Wang, X. *Tetrahedron* **2010**, *66*, 8862–8871.
21. Kamiya, H.; Yanagisawa, S.; Hiroto, S.; Itami, K.; Shinokubo, H. *Org. Lett.* **2011**, *13*, 6394–6397.
22. (a) Clayden, J. *Organolithiums: Selectivity for Synthesis*, Pergamon, Amsterdam, 2002. (b) Rappoport, Z.; Marek, I. *The Chemistry of Organolithium Compounds*, Wiley, Chichester,

2004. (c) Hanazawa, M.; Sumiya, R.; Horikawa, Y.; Irie, M. *J. Chem. Soc. Chem. Commun.* **1992**, 206–207.

23. Asai, T.; Takata, A.; Nagaki, A.; Yoshida, J.–I. *ChemSusChem* **2012**, *5*, 339–350.
24. Lucas, L. N.; Esch, J.–V.; Kellogg, R. M.; Feringa, B. L. *Tetrahedron Lett.* **1999**, *40*, 1775–1778.
25. Hiroto, S.; Suzuki, K.; Kamiya, H.; Shinokubo, H. *Chem. Commun.* **2011**, *47*, 7149–7151.
26. (a) Myles, A. J.; Gorodetsky, B.; Branda, N. R. *Adv. Mater.* **2004**, *16*, 922–925. (b) Irie, M.; *Bull. Chem. Soc. Jpn.* **2008**, *81*, 917–926. (c) Tsujioka, T.; Takagi, R.; Shiozawa, T. *J. Mater. Chem.* **2010**, *20*, 9623–9627. (d) Furukawa, H.; Misu, M.; Ando, K.; Kawaguchi, H. *Macromol. Rapid Commun.* **2008**, *29*, 547–551.
27. Luo, Q.; Cheng, H.; Tian, H. *Polym. Chem.* **2011**, *2*, 2435–2443.
28. (a) Pu, S.; Liu, W.; Liu, G. *Dyes Pigments* **2010**, *87*, 1–9. (b) Pu, S.; Tang, H.; Chen, B.; Xu, J.; Huang, W. *Materials Letters* **2006**, *60*, 3553–3557. (c) Ryo, S.; Ishibashi, Y.; Murakami, M.; Miyasaka, H.; Kobatake, S.; Irie, M. *J. Phys. Org. Chem.* **2007**, *20*, 953–959. (d) Guo, H.; Zhang, F.; Wu, G.-S.; Sun, F.; Pu, S.; Mai, X.; Qi, G. *Opt. Mater.* **2003**, *22*, 269–274. (e) Kitagawa, D.; Yamashita, I.; Kobatake, S. *Chem. Commun.* **2010**, *46*, 3723–3725.
29. Fujimoto, Y.; Ubukata, T.; Yokoyama, Y. *Chem. Commun.* **2008**, 5755–5757.
30. Fukaminato, T.; Umemoto, T.; Iwata, Y.; Yokojima, S.; Yoneyama, M.; Nakamura, S.; Irie, M. *J. Am. Chem. Soc.* **2007**, *129*, 5932–5938.
31. Kobatake, S.; Yamashita, I. *Tetrahedron* **2008**, *64*, 7611–7618.
32. Myles, A. J.; Branda, N. R. *Macromolecules* **2003**, *36*, 298–303.
33. Jeong, Y.-C.; Park, D. G.; Kim, E.; Yang, S. I.; Ahn, K.-H. *Macromolecules* **2006**, *39*, 3106–3109.
34. Uchida, K.; Takata, A.; Ryo, S.; Saito, M.; Murakami, M.; Ishibashi, Y.; Miyasaka, H.; Irie, M. *J. Mater. Chem.* **2005**, *15*, 2128–2133.
35. Wigglesworth, T. J.; Myles, A. J.; Branda, N. R. *Eur. J. Org. Chem.* **2005**, 1233–1238.
36. (a) Matsumoto, A.; Tanaka, S.; Otsu, T. *Macromolecules* **1991**, *24*, 4017–4024. (b) Chern, Y.–T. *Polym. Bull.* **1996**, *36*, 59–65.
37. Medvedeva, D.; Bobrovsky, A.; Boiko, N.; Shibaev, V.; Zavarzin, I.; Kalik, M.; Krayushkin, M. *Macromol. Rapid Commun.* **2005**, *26*, 177–182.
38. (a) Choi, H.; Lee, H.; Kang, Y.; Kim, E.; Kang, S. O.; Ko, J. *J. Org. Chem.* **2005**, *70*, 8291–8297. (b) Kawai, T.; Nakashima, Y.; Irie, M. *Adv. Mater.* **2005**, *17*, 309–314. (c) Wigglesworth, T. J.; Branda, N. R. *Chem. Mater.* **2005**, *17*, 5473–5480. (d) Li, X. C.; Tian, H. *Macromol. Chem. Phys.* **2005**, *206*, 1769–1777. (e) Lim, S. J.; An, B. K.; Park, S. Y. *Macromolecules* **2005**, 38, 6236–6239. (f) Kim, E.; Lee, H. W. *J. Mater. Chem.* **2006**, *16*,

1384–1389. (g) Hayasaka, H.; Tamura, K.; Akagi, K. *Macromolecules* **2008**, *41*, 2341–2346. (h) Hayasaka, H.; Miyashita, T.; Tamura, K.; Akagi, K. *Adv. Funct. Mater.* **2010**, *20*, 1243–1250.

39. (a) Nishi, H.; Kobatake, S. *Macromolecules* **2008**, *41*, 3995–4002. (b) Nishi, H.; Asahi, T.; Kobatake, S. *J. Phys. Chem. C*, **2009**, *113*, 17359–17366. (c) Lim, S.–J.; Carling, C.–J.; Warford, C. C.; Hsiao, D.; Gates, B. D.; Branda, N. R. *Dyes Pigments* **2011**, *89*, 230–235.

40. Lee, J.; Kwon, T.; Kim, E. *Tetrahedron Lett.* **2007**, *48*, 249–254.

41. (a) Wesenhagen, P.; Areephong, J.; Landaluce, T. F.; Heureux, N.; Katsonis, N.; Hielm, J.; Rudolf, P.; Browne, W. R.; Feringa, B. L. *Langmuir* **2008**, *24*, 6334–6342. (b) Areephong, J.; Kudenrnac, T.; Jong, J. J. D.; Carroll, G. T.; Pantorott, D.; Hjelm, J.; Browne, W. R.; Feringa, B. L. *J. Am. Chem. Soc.* **2008**, *130*, 12850–12851.

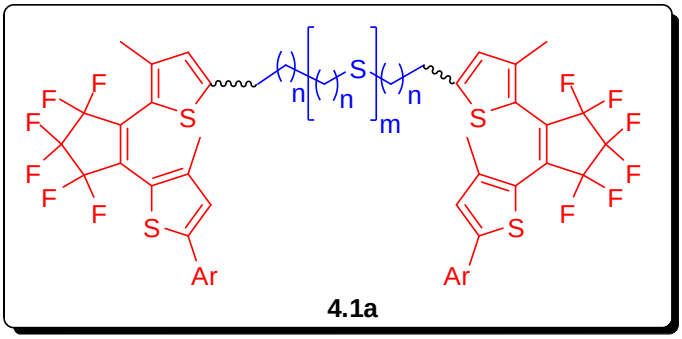
Chapter Four

Synthesis of Poly(alkylene sulfide)s Bearing Photochromic Units

Synthesis of Poly(alkylene sulfide)s Bearing Photochromic Units

4.1 Introduction

In chapter three we have discussed the importance of photochromic materials. We thought that it would be interesting to study the ability of functionalizing the poly(alkylene sulfide)s with photochromic groups to give them such a property (photochromism). The synthesis of such materials could be possible *via* various possible routes. One route could involve synthesis of poly(alkylene sulfide)s with terminal functional groups that can be coupled with a linkable photochromic unit to produce a polymeric material of the general formula **4.1a** (Figure 4.1). In this chapter we shall report our attempts towards the development of this idea and the steps that led to a photochromic model which mimics the target polymer.

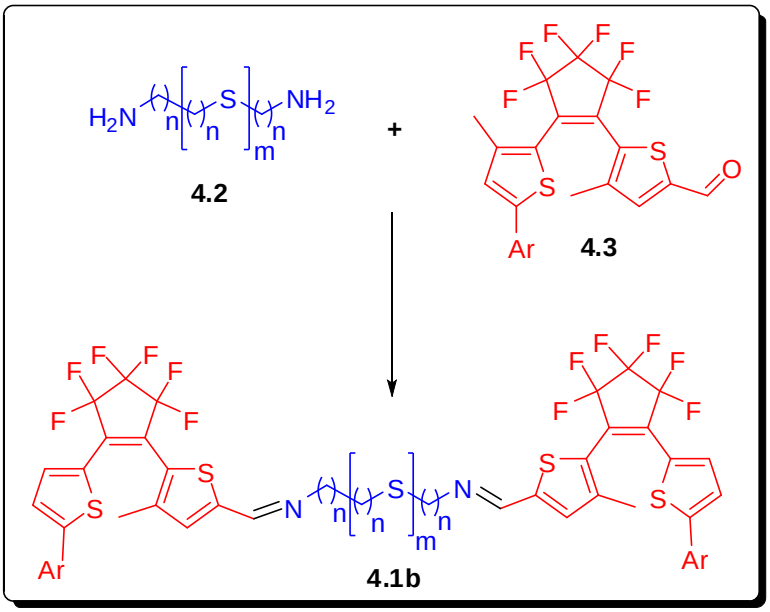


4.1a

Figure 4.1: General formula of 4.1a

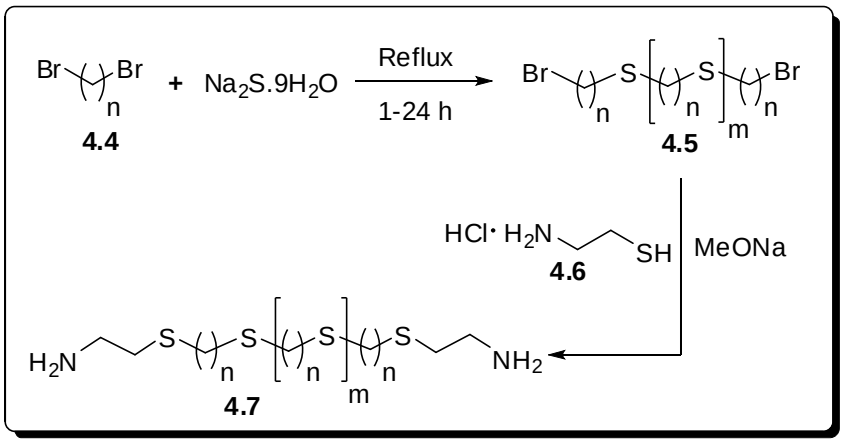
4.2 The Proposed Synthetic Strategy

The strategy that we planned for the synthesis of photochromic poly(alkylene sulfide)s was to prepare polymers **4.2** containing terminal amino groups and allow them to react with a photochromic aldehyde (**4.3**) to produce the corresponding photochromic polymer that contains imine linkages (**4.1b**, Scheme 4.1).



Scheme 4.1

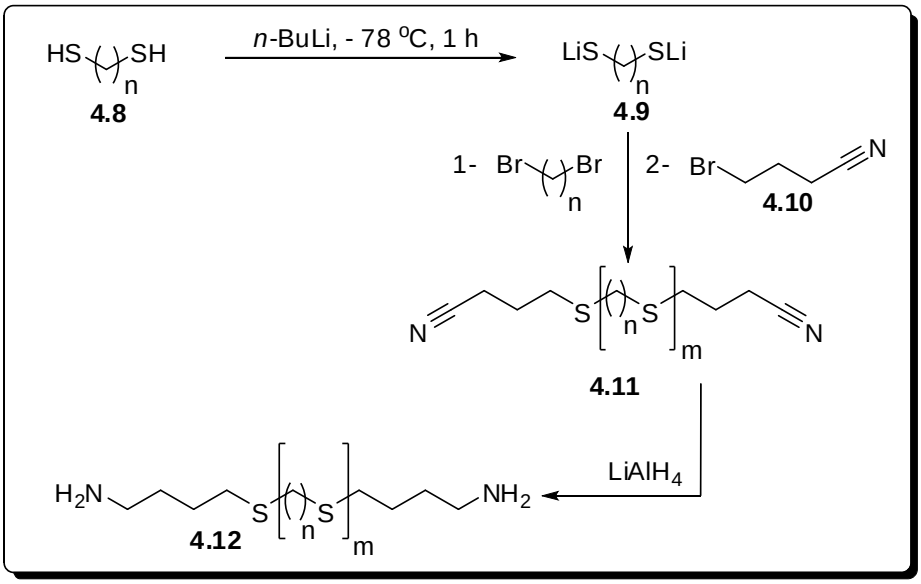
Therefore, the task was to synthesis a poly(alkylene sulfide) with terminal amino groups. Two pathways were proposed for the synthesis of such a polymer. The first route involves preparation of a poly(alkylene sulfide) with terminal bromine atoms by the method mentioned in Chapter 2 (Section 2.2.5), then the bromine atoms could be replaced by aminoalkyl groups using cysteamine hydrochloride (**4.6**) in the presence of sodium methoxide to produce polymeric materials of the general formula of **4.7** (Scheme 4.2).



Scheme 4.2

The second proposed method involves that the polymerization be carried out followed by termination with a compound that gives the desired functional group (*e.g.* NH_2 group) or one (*e.g.* a CN group) that can be modified later to produce the terminal amino groups. The cyano group can be readily reduced to amino group

using a reducing agent such as lithium aluminium hydride ($LiAlH_4$). Therefore, we planned to synthesise poly(alkylene sulfide)s *via* polymerization of lithiated dithiols **4.9** and a dibromoalkane followed by termination with 4-bromobutyronitrile (**4.10**) to produce a polymer (**4.11**) with terminal cyano groups. Reduction of the cyanopolymer should give the desired polymer **4.12** (Scheme 4.3).



Scheme 4.3

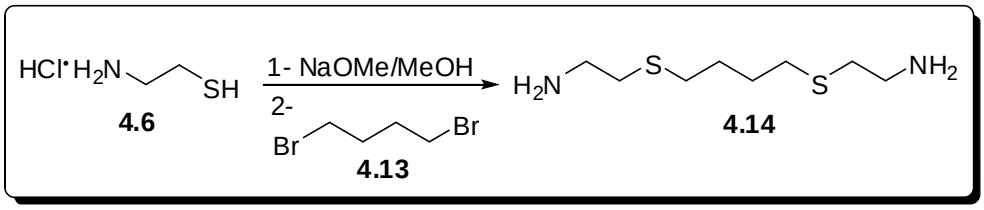
4.3 The Test Model

Before proceeding with the synthesis of the polymeric material and the multistep synthesis of the photochromic aldehyde we decided to test the idea by making a model that resembles the polymeric materials to check the applicability of the theory we proposed. Accordingly, we determined to prepare a diamine which simulates the polymer and react it with a simple aldehyde (*e.g.* benzaldehyde) to see whether it will work in such a way or not.

4.3.1 Synthesis of 1,4-*Bis*(2-aminoethylthio)butane (4.14)

Compound **4.14** is a compound that mimics our polymeric material target. Therefore, we decided to prepare such a material from 1,4-dibromobutane. The synthesis of **4.14** by alkylation of cysteamine hydrochloride (**4.6**) with 1,4-dibromobutane (**4.13**) was reported by Wanichacheva *et al.* (Scheme 4.4).[1] The procedure includes activation of **4.6** with sodium methoxide in methanol followed by the addition of **4.13**. The mixture was

then stirred for 10 h at 40 °C under an inert atmosphere. After evaporation of solvent the reaction mixture was treated with aqueous sodium hydroxide and stirred overnight. The crude product was then extracted with DCM to give a yellow oily material after evaporation of the solvent. No purification method was described to isolate **4.14** as pure material and the reported yield was only 63%. However, we decided to carry out this reaction on the hope that we could isolate the product in pure form. Unfortunately, while the yield was similar to the reported one, the separation of the product was not successful. The ^{1}H NMR analysis of the crude product showed a mixture of the product and starting material with other unidentified impurities.

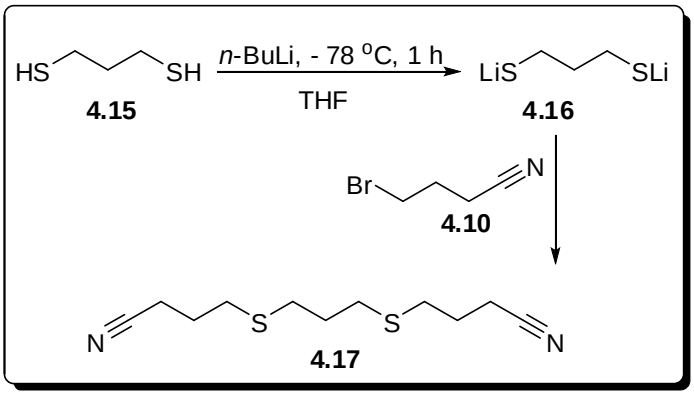


Scheme 4.4

4.3.2 Synthesis of 1,3-*Bis*(4-aminobutylthio)propane (4.18)

The next model that we decided to prepare was **4.18**, which simply represents the monomer of the target polymer with the two ends capped as proposed for the polymer itself. The proposed way involves producing **4.17** (Scheme 4.5). To a solution of 1,3-propanedithiol (**4.15**) in anhydrous tetrahydrofuran (THF), *n*-butyllithium (*n*-BuLi) was added at −78 °C under an inert atmosphere. The mixture was stirred for 1 h and the cooling bath was removed, upon which a white precipitate was formed due to the formation of dilithium propane-1,3-dithiolate (**4.16**). The precipitate disappeared upon addition of 4-bromobutyronitrile (**4.10**) and the mixture was stirred overnight at room temperature and then worked up to give the crude product as an oily material. The first indication for the completion of the reaction was the disappearance of the stench of 1,3-propanedithiol. The ^{1}H NMR spectrum of the crude product showed that the characteristic triplet signals of 4-bromobutyronitrile that resonated at δ = 3.6 ppm had disappeared and that signals corresponding to what would be expected from the methylene groups of the desired product (**4.17**) were present; in the aliphatic region it showed three triplet and two pentet signals with coupling constant 7.0 Hz. The ^{13}C NMR spectrum also showed a signal at δ = 119.2 ppm which represents the cyano group along with five other signals in the up-field region due to the methylene groups. A DEPT experiment confirmed the types of the carbon

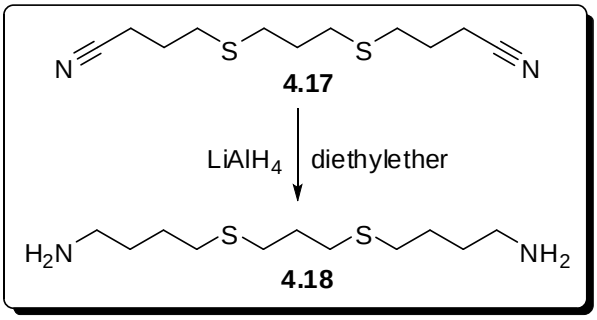
atoms and showed that the carbon signal resonating at δ = 119.2 ppm was quaternary (CN) and the other carbons were secondary (CH_2). A strong band at 2245 cm^{-1} was observed in the FT-IR spectrum of the product which was attributed to the nitrile group stretching (see experimental section for more details). The molecular formula of the desired product was confirmed by high resolution mass spectrometry (HRMS). It showed a peak at *m/z* = 242.0905 which correlates well with the calculated value for $C_{11}H_{18}N_2S_2$ (M^+ of **4.17**), which is 242.0911. It was clear that the product was obtained in high purity and in high yield (95%; Scheme 4.5), for which no purification was needed.



Scheme 4.5

Having successfully prepared pure **4.17**, the next step was the synthesis of **4.18**. Compound **4.18** can be obtained by reduction of **4.17** using $LiAlH_4$ (Scheme 4.6). The procedure involves the addition of **4.17** to a solution of $LiAlH_4$ in dry diethyl ether under an inert atmosphere. The mixture was stirred for 48 h at room temperature and then quenched with water, acidified with concentrated H_2SO_4 and basified with NaOH. The product was extracted with dichloromethane and the crude product was obtained after evaporation of solvent. The FT-IR spectrum of the crude product showed two medium absorption bands at 3300 and 3361 cm^{-1} due to NH_2 group stretching. Also, it showed no absorption bands within the region of 2245 cm^{-1}, indicating that no cyano groups of the starting material **4.17** remained. The ^1H NMR spectrum of the product showed three triplets, a pentet and a multiplet signals, as well as a broad exchangeable signal corresponding to the protons of two amino groups. The chemical shift and the multiplicity of such signals were reasonably consistent with the ones predicted by ChemDraw for the product **4.18**. The ^{13}C NMR spectrum confirmed the absence of cyano group carbons and showed six signals corresponding to what was predicted for the methylene groups of **4.18** (see experimental section for details). Finally the HRMS confirmed the formula for the

molecular ion peak of **4.18** as $C_{11}H_{26}N_2S_2$ (M^+ of **4.18**). According to this method compound **4.18** was obtained as pure material in 88% yield.



Scheme 4.6

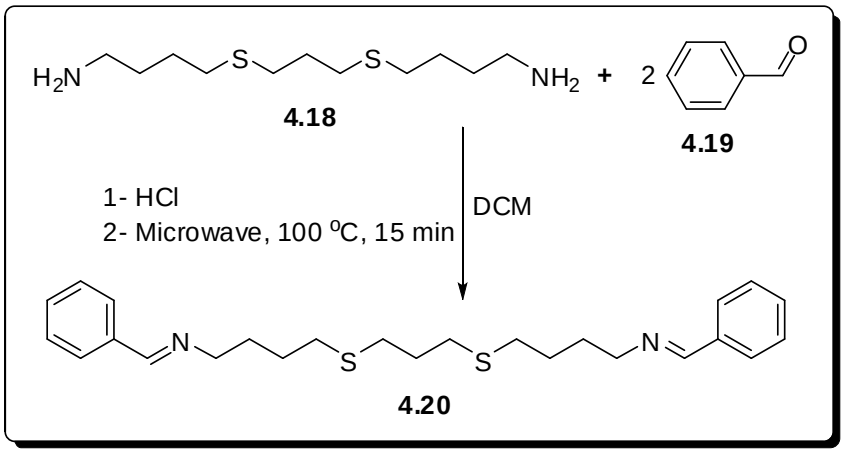
4.3.3 Synthesis of 1,3-*Bis*[4-(*N*-benzylideneamino)butylthio]propane (4.20)

Primary amines react with aldehydes in the presence of an acid catalyst to produce imines (Schiff bases).[2] These well known reactions are commonly carried out in an alcohol (ethanol or methanol) as a solvent in the presence of a catalytic amount of acid (*e.g.* HCl) under reflux conditions to give the corresponding product, which crystallise on cooling of the reaction mixture.

Having successfully produced **4.18**, we next attempted its conversion to the target model. Therefore, reaction of benzaldehyde (**4.19**) and diamino compound **4.18** was carried out in an attempt to produce **4.20** (Scheme 4.7). DCM is not a common solvent for such reactions, however, because of the poor solubility of **4.18** in alcohols we decided to use DCM. Due to the low boiling point of DCM (40 °C) we thought to do the reaction under high pressure. Therefore, we decided to use the microwave reactor rather than the conventional heating, by this technique the reaction temperature could be raised to 100 °C. Also, the reaction time could be shortened and the minimum amount of solvent could be used.

The reaction was attempted on a small scale in which a mixture of compound **4.18** (1.9 mmol) and of benzaldehyde (**4.19**; 4.0 mmol) in DCM (4 ml) was treated with a dry HCl solution in diethyl ether as a catalyst. The mixture was then subjected to microwave irradiation (using a microwave reactor) at 100 °C for 15 minutes. The solvent was then removed to give an oily material. The unreacted benzaldehyde (**4.19**) was distilled off under high vacuum. The ^{1}H NMR spectrum of the isolated material showed that the singlet

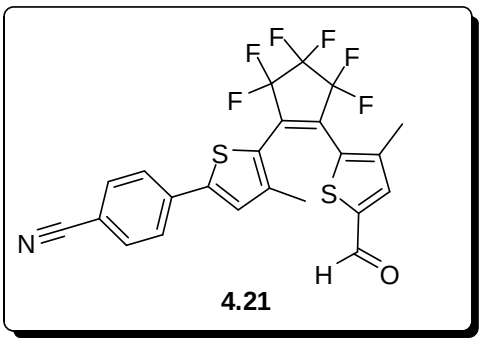
signal corresponding to the aldehydic proton had disappeared and the patterns of the aliphatic protons were different from those of **4.18**. Signals which are well correlated to the structure of **4.20** were present, including signals in the aromatic area. The ^{1}H NMR spectrum also showed two characteristic signals that resonated at δ = 8.20 ppm (singlet) and 3.55 ppm (triplet) corresponding to CH=N and CH_2N protons, respectively. The ^{13}C NMR spectrum of the crude product confirmed the presence of CH=N and CH_2N carbons resonating at δ = 161.1 ppm (doublet) and 61.2 ppm (triplet), respectively. It also showed all other expected carbons for product **4.20**. The FT-IR spectrum showed a strong band at 1645 cm^{-1} due to C=N stretching and showed the absence of the absorption bands within the region of 3300 cm^{-1} corresponding to the NH_2 stretching of **4.18**. The electron impact mass spectrum of the product (EI-MS) showed a molecular ion peak at *m/z* = 426 (see experimental section for details). The HRMS spectrum confirmed the formula of the molecular ion peak as $C_{25}H_{34}N_2S_2$ (M^+ of **4.20**). It was clear that the product produced was **4.20** as a pure material in a good yield (85%).



Scheme 4.7

4.4 Synthesis of a New Photochromic Aldehyde

In order to produce the target, a photochromic unit is needed. A photochromic aldehyde that can be condensed with diamino polymeric materials to produce the target product would be appropriate. In the literature,[3] there are some photochromic diarylethenes that have an aldehyde group. However, based on previous experience within our research group we designed a novel diarylethene that meets all the requirements needed to produce the target material. The compound proposed was 1-[5-(formyl)-3-methyl-2-thienyl]-2-[5-(4-cyanophenyl)-3-methyl-2-thienyl]perfluorocyclopentene (**4.21**; Figure 4.2).



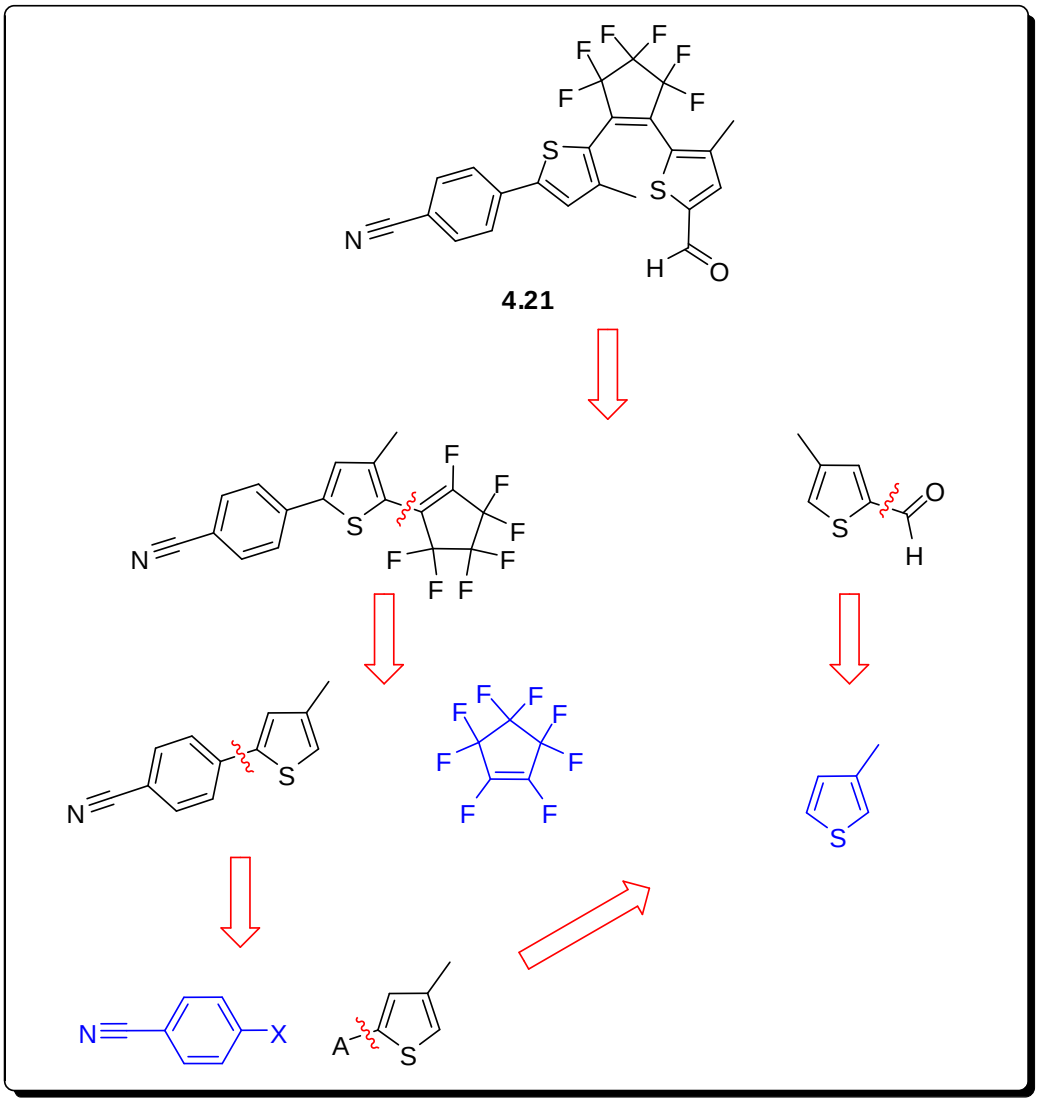
4.21

Figure 4.2: Structure of 4.21

Diarylethenes with an electron-withdrawing cyano substituent are interesting photochromic compounds; these compounds have started to attract researchers to study the effect of such a group on the photochromic behavior.[4] The compound we are introducing is also unique in its geometry, in terms of the connection positions between thienyl groups (C-2 rather than C-3) and the hexafluorocyclopentene moiety.

4.4.1 Disconnection of 4.21

The disconnection of **4.21** is shown in Scheme 4.8.



Scheme 4.8

It is clear that the required starting materials are 3-methylthiophene, perfluorocyclopentene and 4-halobenzonitrile. In the next sections we discuss the multi-step synthesis of **4.21** starting from these materials.

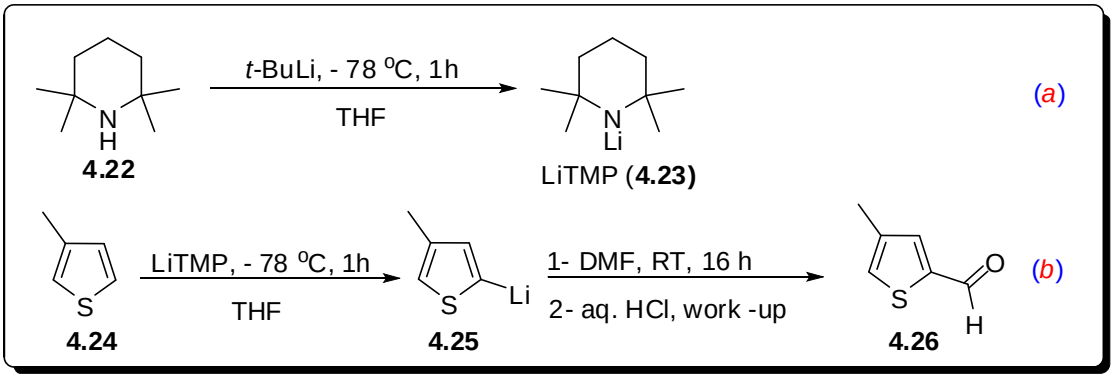
4.4.2 Synthesis of 4-Methylthiophene-2-carboxaldehyde (4.26)

The first step in the synthesis of **4.21** would involve synthesis of **4.26**. In 2006 K. Smith and M. Barratt[5] reported an efficient procedure for the synthesis of compound **4.26** as an example of a highly selective substitution of 3-methylthiophene *via* directed lithiation. They developed the method to overcome problems associated with the

substitution of 3-methylthiophene, such as the poor selectivity that lead to mixtures of different isomers due to competitive substitution at different positions on the thiophene ring.[5]

Lithium 2,2,6,6-tetramethylpiperidide (LiTMP, **4.23**) was used as the lithiating reagent to lithiate 3-methylthiophene (**4.24**), at the 5-postion followed by reaction with an electrophile to give high yields of the corresponding 2,4-disubstituted thiophenes. The reaction was found to be selective at the 5-position even when unhindered electrophiles were used. Such regioselectivity could be attributed to the bulkiness of LiTMP, which attacks the less hindered position.[5]

The procedure involved the *in-situ* generation of LiTMP from reaction of 2,2,6,6-tetramethylpiperidine (**4.22**) with *t*-BuLi at –78 °C (Scheme 4.9*a*) followed by the addition of 3-methylthiophene (**4.24**). The reaction mixture was stirred for 1 h at that low temperature (to form **4.25**), followed by addition of 2 mol. equivalents of *N*,*N*-dimethylformamide (DMF) (Scheme 4.9*b*) and the resulting mixture was stirred for 16 h at room temperature and was then worked-up with an acid to remove the reformed TMP, followed by extraction with diethyl ether. The solvent was removed under reduced pressure to give the crude product as an oily material.



Scheme 4.9

The ^{1}H NMR spectrum of the crude product showed a singlet at δ = 9.79 ppm corresponding to the expected aldehyde proton as well as the other expected signals for the two aromatic protons. It also showed a singlet at δ = 2.24 ppm due to the methyl protons. The ^{13}C NMR spectrum of the product showed a singlet signal at δ = 183.2 ppm corresponding to the carbonyl group carbon. The FT-IR spectrum showed a strong band at 1667 cm^{-1} corresponding to C=O stretching (see experimental section for details). The

elemental formula of **4.26** was confirmed as C_6H_6OS by the high resolution mass spectrometry analysis of its molecular ion peak .

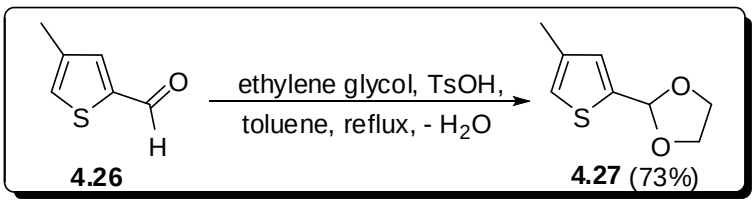
4.4.3 Synthesis of 2-(4-Methyl-2-thienyl)-1,3-dioxolane (4.27)

Further substitution of **4.26** might be problematic in the presence of the CHO group that could undergo nucleophilic addition with any nucleophile in the reaction mixture. Such side reactions could lead to undesired products. Therefore, the carbonyl group of **4.26** should be protected first before attempting any further substitution on the thiophene ring.

One of the simple transformations that can be carried out on the carbonyl group of aldehydes is the formation of cyclic acetals. The acetal can be easily converted back to the aldehyde by simple reaction with hydrochloric acid in THF. Such a process is very common for the protection of CHO groups and has been applied on substrates that are structurally related to compound **4.26**.[6,7]

The most important point that pushed us to follow this method is the stability of the cyclic acetals in the presence of organolithium reagents, so such a method would allow us to carry on to do further lithiation reaction on the protected aldehyde.

The protection of **4.26** was attempted based on a standard procedure.[8] The procedure involved reaction of **4.26** with ethylene glycol in toluene as a solvent in the presence of *para*-toluenesulfonic acid (TsOH) as a dehydrating reagent under reflux conditions (Scheme 4.10) using a Dean and Stark apparatus for 16 h. The mixture was worked-up with aqueous sodium hydrogen carbonate solution and the product was extracted with ethyl acetate. Evaporation of solvent provided the crude product as a dark brown oily material, which was treated with charcoal to give yellow oil.



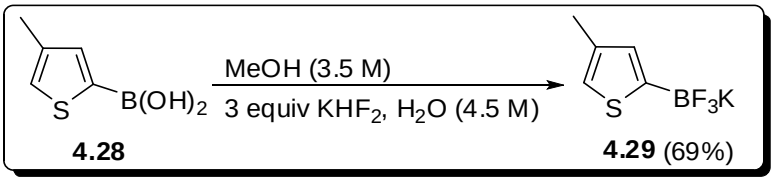
Scheme 4.10

The ^{1}H NMR spectrum of the product showed that the signal corresponding to the aldehyde proton of **4.26** had disappeared. It showed the appearance of a singlet that

resonated at δ = 4.59 and a multiplet that resonated at δ = 4.03-3.87 ppm corresponding to the CH and CH_2 groups of the cyclic 1,3-dioxolan-2-yl group of **4.27** respectively. The ^{13}C NMR spectrum showed that the signal at δ = 183.2 ppm in **4.26** had disappeared and showed all the carbons expected for the structure **4.27**. The EI-MS of the product showed a molecular ion peak at *m/z* = 170 and the HRMS confirmed the molecular formula for the molecular ion as $C_8H_{10}O_2S$, which is consistent with the structure of **4.27** (see experimental section for details).

4.4.4 Synthesis of 2-(4-Cyanophenyl)-4-methylthiophene (4.34)

The disconnection of our target molecule (Scheme 4.8) led us to look for a method for the synthesis of **4.34**. This compound has been reported in a couple of publications.[9, 10] In 2009 Molander *et al.*[9] prepared different bench-stable potassium heteroaryltrifluoroborates and developed a general method for their cross-coupling to aryl and heteroaryl halides. They managed to obtain the cross-coupled products in good to excellent yields.[7] One of those products was **4.34**. Synthesis of **4.34** took place in two steps. The first step (Scheme 4.11) involved reaction of 4-methyl-2-thienylboronic acid (**4.28**) with aqueous potassium bifluoride (KHF_2) in methanol at 0 °C. The reaction mixture was stirred at room temperature for 10 min to give **4.29**. Following work-up and purification by continuous Soxhlet extraction, 4-methyl-2-thienyltrifluoroborate (**4.29**) was obtained in 69% yield.

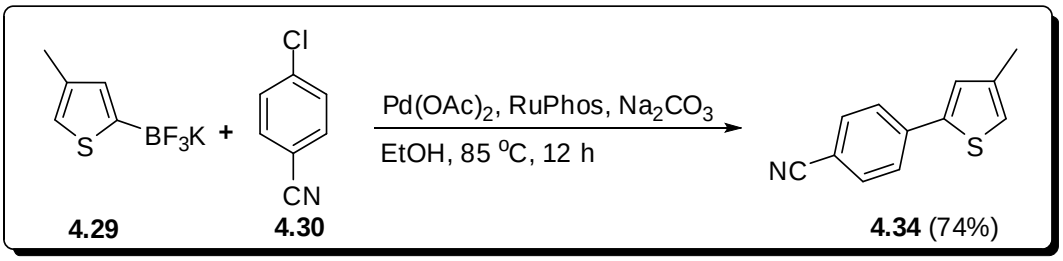


Scheme 4.11

It was found that the recrystallization of commercially obtained **4.28** from $CHCl_3$ immediately prior to use can afford **4.29** in excellent yield (95%) possibly because **4.28** is not very stable and undergoes protodeboronation.

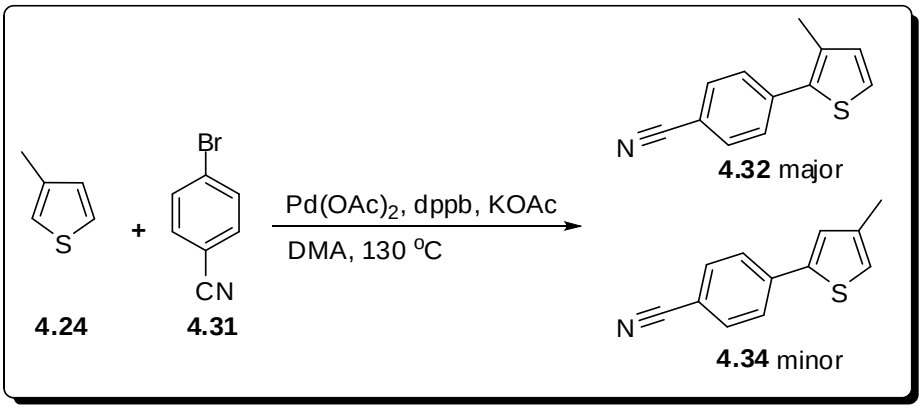
The second step (Scheme 4.12) involved production of **4.34** by a Suzuki-Miyaura cross-coupling reaction of **4.29** with 4-chlorobenzonitrile (**4.30**). The procedure involved use of a mixture of $Pd(OAc)_2$, 2-dicyclohexylphosphino-2′,6′-diisopropoxybiphenyl (RuPhos) and Na_2CO_3 as catalysts. The mixture was placed in a vial with ethanol, then

evacuated, purged with nitrogen and sealed. The mixture was heated at 85 °C for 12 h. After cooling down to room temperature the crude product was collected by filtration. Purification of the crude product by column chromatography gave pure **4.34** in 74% yield.



Scheme 4.12

In 2011 Dong *et al.*[10] reported a palladium-catalysed C-2 or C-5 direct arylation of 3-substituted thiophenes with aryl bromides. 3-Methylthiophene (**4.24**) was one of the substrates of interest. They found that the reaction of **4.24** with 4-bromobenzonitrile (**4.31**) in the presence of $Pd(OAc)_2$/1,4-bis(diphenylphosphino)butane (dppb) as a catalytic system, KOAc as a base and dimethylacetamide (DMA) as a solvent at 130 °C gave 2-(4-cyanophenyl)-3-methylthiopene (**4.32**) as the major product along with a low yield of **4.34** (Scheme 4.13). The ratio of **4.32**:**4.34** was 87:13 and product **4.32** was isolated in 65% yield. This method cannot be considered as a convenient procedure for the synthesis of **4.34** since a mixture of products was obtained and required separation.

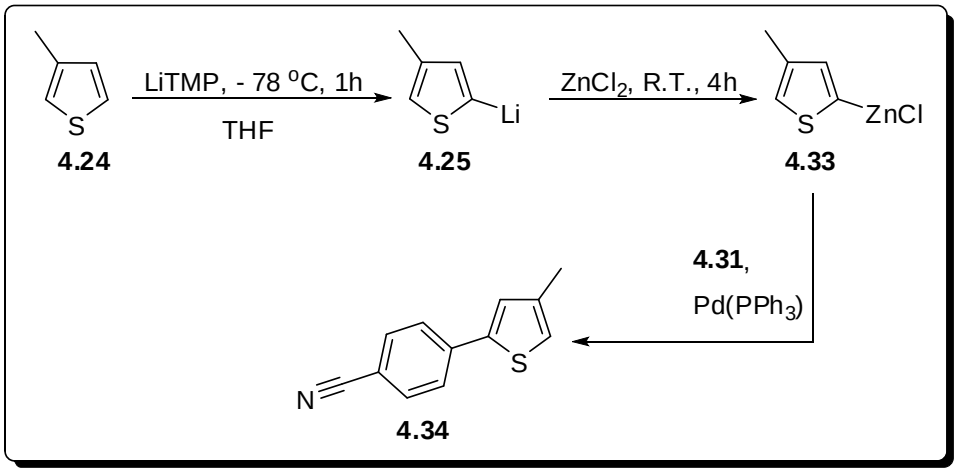


Scheme 4.13

In conclusion, the method developed by Molander *et al.*[9] is the only convenient reported method for the synthesis of **4.34**. However, we decided to find a better procedure in which we could produce **4.34** in a single step starting with stable, cheap and commercially available 3-methylthiophene (**4.24**).

Thienylzinc chlorides that could be prepared from reaction of thienyllithium with anhydrous zinc chloride, can be used for the arylation of thiophenes through the Negishi coupling reaction. In such a reaction, thienylzinc chlorides cross-couple to aryl halides in the presence of palladium(0) as catalyst.[11,12]

From that we designed an experiment for the production of **4.34** by the selective lithiation of 3-methylthiophene (**4.24**) using LiTMP (**4.23**) followed by the addition of anhydrous zinc chloride ($ZnCl_2$) to form 3-methyl-2-thienylzinc chloride (**4.33**) which then cross-couples with 4-bromobenzonitrile (**4.31**) in the presence of tetrakis(triphenylphosphine)palladium(0) as catalyst to give **4.35** (Scheme 4.14).



Scheme 4.14

By applying the conditions shown in Scheme 4.14, we have conducted a number of experiments in which **4.33** was prepared *in-situ* and reacted with one mole equivalent of 4-bromobenzonitrile (**4.31**). The ^{1}H NMR spectrum of the crude product revealed that compound **4.34** was successfully produced in *ca.* 70% yield along with residual **4.31**. The problem was the purification process, because both **4.31** and **4.34** have similar polarity and run very close to each other on a column. From TLC we found that the best eluent to be used for isolation of **4.34** was a mixture of petroleum ether/ethyl acetate in the ratio of 98/2 by volume. However, the first fraction indicated that about 20% of **4.34** eluated as a mixture with **4.31**. The best isolated yield of the pure product was 50%. Attempts to improve the yield by increasing reaction time for the formation **4.33** and the temperature for the formation of **4.34** were not successful. Therefore, the molar ratio of **4.33/4.31** was increased in an attempt to improve the yield so that the loss of product during purification by column chromatography could be avoided. It was found that 1.6/1.0 was the optimised

ratio, by use of which no **4.31** was observed in the crude product. As a result product **4.34** was isolated in 95% yield based on **4.31** after purification by flash column chromatography (silica gel; hexane/diethyl ether 1/1 by volume).

The ^{1}H NMR spectrum of the isolated product showed signals at chemical shifts that correlated well with what would be expected for the structure of **4.34**. Signals corresponding to H-3, H-5 and CH_3 of **4.34** are expected to be singlets, however, we noticed that the signals of H-3 and H-5 appeared as doublets and the signal of CH_3 as triplet. Therefore we decided run a correlation spectroscopy (COSY) experiment for **4.34**. The COSY spectrum (Figure 4.3) showed that both H-3 and H-5 couple with the CH_3 protons.

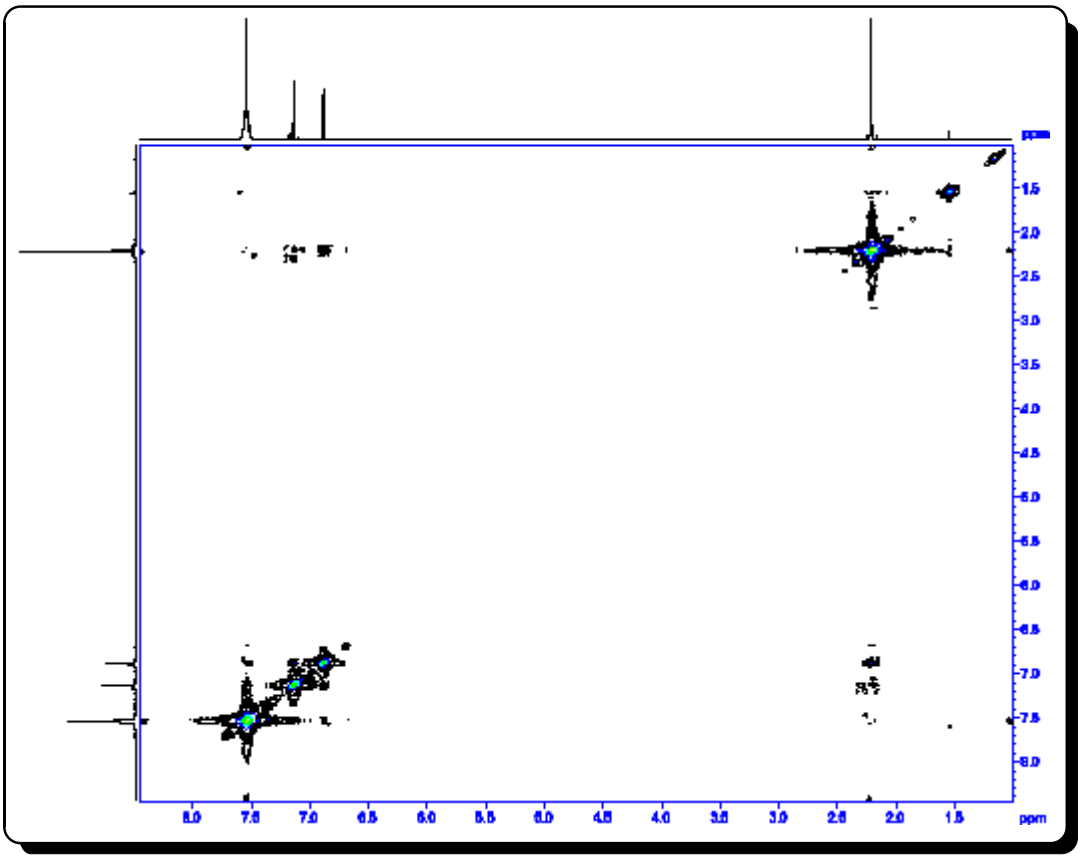


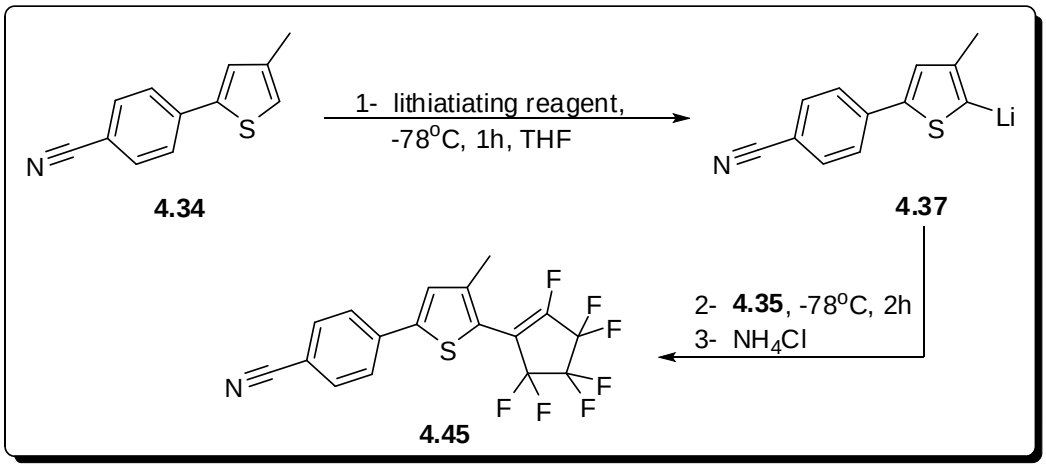
Figure 4.3: COSY Spectrum of 4.34

The ^{13}C NMR spectrum of the product also showed the expected signals corresponding to the 10 different types of carbon atoms of **4.34**. FT-IR spectroscopy showed a strong absorption band at 2225 cm^{-1} for the C≡N stretching. The EI-MS showed a molecular ion peak at *m/z* = 199 and the HRMS confirmed the formula of the molecular ion as $C_{12}H_9NS$ (see experimental section for details).

It is clear that compound **4.34** can be produced in excellent yield starting with **4.24** which is cheap and commercially available. Also, the purification process was straightforward and provided pure **4.34** in 95% yield based on **4.31**. The procedure is more convenient than the one reported by Molander *et al.*[9] The latter one involved synthesis and/or purification of **4.28,** which then had to be converted into **4.29**, with an extra purification process required to give a 69% yield; then, the reaction of **4.31** with **4.29** in the presence of $Pd(OAc)_2$/RuPhos as a catalytic system was required, to give **4.34** in 74% yield.

4.4.5 Proposed Synthesis of 1-[5-(4-Cyanophenyl)-3-methyl-2-thienyl] perfluorocyclopentene (4.45) *via* Direct Lithiation

Replacement of F–1 of perfluorocyclopentene (**4.35**) by a thienyl group could in principle be achieved by reaction of the appropriate thienyllithium derivative with **4.35** at low temperature (–78 °C).[13] 3,5–Disubstituted thiophenes undergo direct α–lithiation upon treatment with *n*–butyllithium.[12,14] The proposed synthesis of **4.45** is therefore shown in Scheme 4.15.

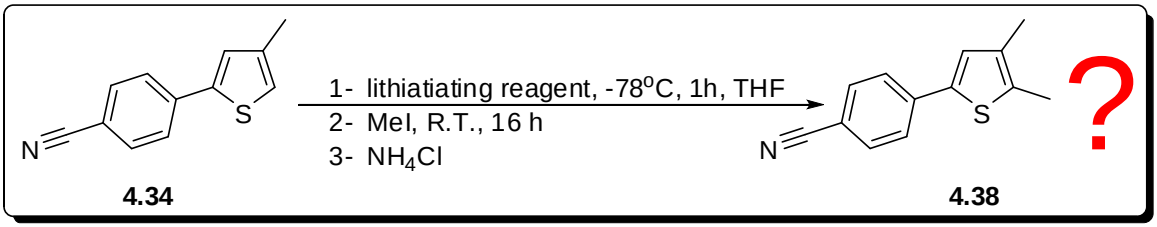


Scheme 4.15

4.4.6 Synthesis of 5-(4-Cyanophenyl)-2,3-dimethylthiophene (4.38) *via* Direct Lithiation

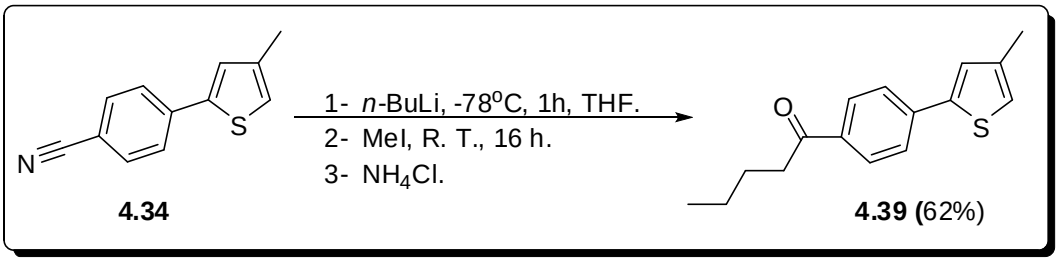
Perfluorocyclopentene (**4.35**) is a volatile liquid material with a very low boiling point (27 °C), which makes it difficult to handle, and it is an expensive material (€ 399.20 for 50.0 g from TCI). Therefore, it was proposed to use a cheap material like iodomethane

as an electrophile instead of **4.35** in a reaction to test whether lithium reagent **4.37** was formed successfully. However, the reaction of **4.37** with iodomethane could probably be carried out over a longer time or at a higher temperature (*e.g.* room temperature) than one with a compound such as **4.35**, where it would be necessary to avoid a second substitution at C-2 of **4.35**. Reaction of **4.34** with *n*-BuLi was carried out at –78 °C for 1 h followed by reaction with iodomethane for 16 h at room temperature (Scheme 4.16). The expected product was 5-(4-cyanophenyl)-2,3-dimethylthiophene (**4.38**; Scheme 4.16). Following work-up, a solid material was obtained, TLC of which indicated the formation of a new product along with residual **4.34** and other impurities.



Scheme 4.16

The crude product was purified by column chromatography and subjected to various spectroscopic techniques to elucidate its structure. The ^{1}H NMR spectrum of the product showed signals corresponding to the phenyl and thienyl protons. However, it also showed five sets of signals in the aliphatic region at δ = 2.87 (t, J = 7.4 Hz, 2 H), 2.21 (s, 3 H), 1.64 (app. pent., J = 7.4 Hz, 2 H), 1.33 (app. sext, J = 7.4 Hz, 2 H) and 0.88 (t, J = 7.4 Hz, 3 H), which clearly indicated the presence of *n*–butyl and methyl groups. The source of the butyl group should be *n*-BuLi. It seemed likely that nucleophilic addition of *n*-BuLi took place at the nitrile group, followed by hydrolysis to give a butylcarbonyl group and the product could be 2-(4-pentanoylphenyl)-4-methylthiophene (**4.39**; Scheme 4.17). Therefore the spectra of the product were analysed to establish its structure.



Scheme 4.17

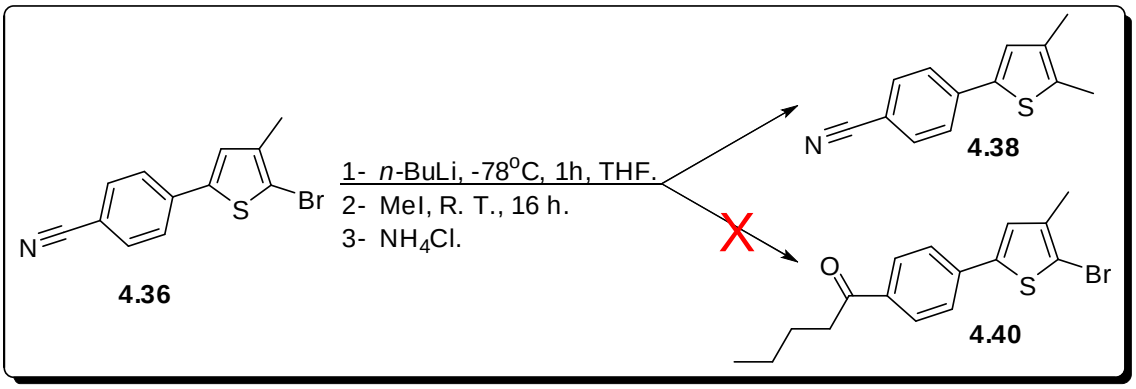
The ^{13}C NMR spectrum of the product showed the absence of a nitrile carbon (at δ = 119.0 ppm for **4.34**) and showed the presence of a carbonyl carbon that resonated as a singlet at δ = 199.8 ppm. The FT–IR spectrum showed no absorption band within the region of 2225 cm^{-1} due to CN group and showed instead a strong absorption band at 1676 cm^{-1} due to the carbonyl group. Clearly compound **4.39** was the product obtained according to Scheme 4.17 and was obtained in 62% yield. Furthermore, the low and high resolution mass spectra confirmed the structure of **4.39**. The mass spectrum showed a pseudo molecular ion peak at m/z = 259 and the HRMS confirmed the formula of the pseudo molecular ion as $C_{16}H_{19}OS$ (MH^+ of **4.39**) (see experimental section for more details).

A different process was needed to produce 5-(4-cyanophenyl)-3-methyl-2-thienyllithium (**4.37**) by avoiding the nucleophilic addition of the lithium reagent at the nitrile group. Therefore, the reaction was attempted with the less nucleophilic and more hindered lithium regent lithium diisopropylamide (LDA) under the conditions used with *n*–BuLi. The TLC for the crude solid product obtained showed the presence of residual starting material and a new product along with highly polar impurities. The product was purified by column chromatography and subjected to NMR and MS analysis.

The ^1H NMR spectrum of the pure product clearly indicated that H-5 of the thienyl of **4.34** had been replaced by a methyl group. It showed that one of the signals of the two aromatic protons of the thienyl group of **4.34** had disappeared and a new signal corresponding to a methyl group had appeared, indicating the formation of **4.38**. The ^{13}C NMR spectrum showed all the carbons that would be expected for **4.38**. The presence of the cyano group was also confirmed by FT-IR spectroscopy which showed an absorption band at 2225 cm^{-1}. Finally, The EI-MS showed a molecular ion peak at *m/z* = 213 and the HRMS confirmed the formula of the molecular ion as $C_{13}H_{11}NS$ (M^+ of **4.38**). Clearly, product **4.38** was produced as the major product under the conditions tried and was obtained in 66% yield. Various attempts were made to try to find conditions under which yield of **4.38** could be improved. The reaction was attempted by varying the reaction time and temperature (*e.g.* –40 °C) for the lithiation step. However, no significant improvement in the yield was achieved. Therefore, we decided to attempt synthesis of **4.38** *via* bromine-lithium exchange of 2-bromo-5-(4-cyanophenyl)-3-methylthiophene (**4.37**), which needed to be prepared first, followed by reaction with iodomethane.

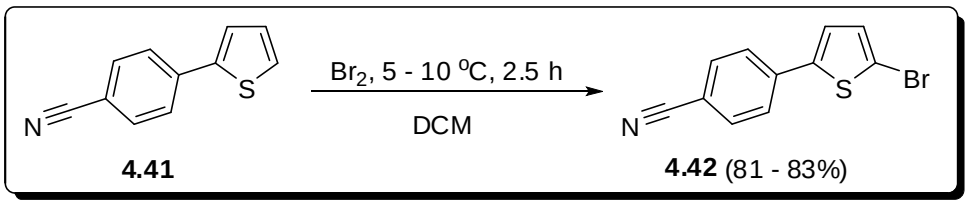
4.4.7 Synthesis of 2-Bromo-5-(4-cyanophenyl)-3-methylthiophene (4.36)

Bromothiophenes react rapidly with alkyllithiums at low temperatures (−78 °C) to give the corresponding thienyllithium *via* bromine–lithium exchange.[15] In general this reaction is preferred over direct lithiation on the thiophene ring (deprotonation).[16] Hence, we determined to synthesize 2-bromo-5-(4-cyanophenyl)-3-methylthiophene (**4.36**), which was expected to undergo bromine–lithium exchange rather than reaction at the C≡N (giving **4.40**) by treatment with *n*–BuLi (Scheme 4.18).



Scheme 4.18

Bromination, and electrophilic aromatic substitution of thiophene in general, occur preferentially at C-2.[17] In the literature,[18] it was reported that treatment of 2-(4-cyanophenyl)thiophene (**4.41**) with one molar equivalent of bromine (Br_2) gives 2-bromo-5-(4-cyanophenyl)thiophene (**4.42**) in 81 to 83% yield (Scheme 4.19).



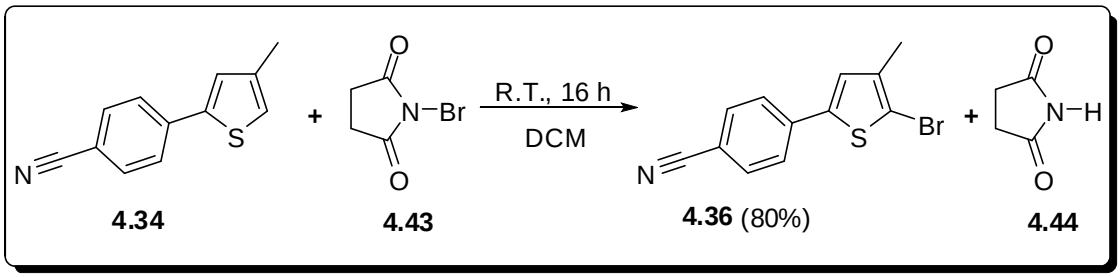
Scheme 4.19

The structures of **4.41** and **4.34** are very similar, thus we expected that applying the reported bromination procedure on **4.34** would allow us to produce **4.36** in a very good yield.

N-Bromosuccinimide (NBS, **4.43**) can be used for the bromination of thiophenes.[19] Bromination of **4.34** was first attempted using NBS as a brominating reagent (Scheme

4.20). A solution of NBS (1.2 molar equivalents) in DCM was added slowly at 0 °C to a solution of **4.34** in DCM and then the mixture was stirred for 16 h at room temperature. Following work-up the obtained crude solid was checked by TLC which showed that all the starting material **4.34** was consumed and a new product was formed. The crude material was then purified by column chromatography to give the pure product.

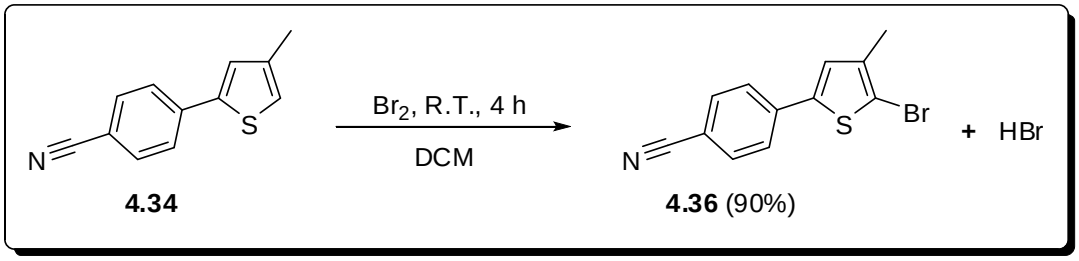
The ^{1}H NMR spectrum of the pure product showed two distinct doublet signals at δ = 7.57 and 7.51 ppm, corresponding to H-2/H-3 and H-5/H-6 of 4-cyanophenyl, respectively. Such patterns were different than those for the corresponding protons in starting material **4.34**, which appeared as a multiplet at δ = 7.68-7.63 ppm. Also, it showed that one of the signals of the thiophene protons had disappeared. The ^{13}C NMR spectrum showed that the C-5 thienyl signal of **4.34** at δ = 122.6 ppm had disappeared, and a new signal at δ = 110.8 ppm had appeared. The DEPT experiment confirmed that the new signal belongs to a quaternary carbon while the one that disappeared was for a secondary carbon which confirms that H-5 of the thienyl unit of **4.34** has been replaced. The mass spectrum of the product showed two molecular ion peaks at *m/z* = 279 ([M^{81}Br]$^{+}$, 34) and 277 ([M^{79}Br]$^{+}$, 35) and the HRMS confirmed the formula of the molecular ion at *m/z* = 277 was $C_{12}H_8BrNS$ ([M^{79}Br]$^{+}$ of **4.36**). Clearly, the spectroscopic data confirmed the structure of the product as **4.36** (see experimental section for details). 2-Bromo-5-(4-cyanophenyl)-3-methylthiophene (**4.36**) was obtained in 80% yield (Scheme 4.20) after purification.



4.34 **4.43** **4.36** (80%) **4.44**

Scheme 4.20

The 80% yield of **4.36** was a good yield; however, we aspired to improve it further by using bromine instead of NBS (Scheme 4.21)



Scheme 4.21

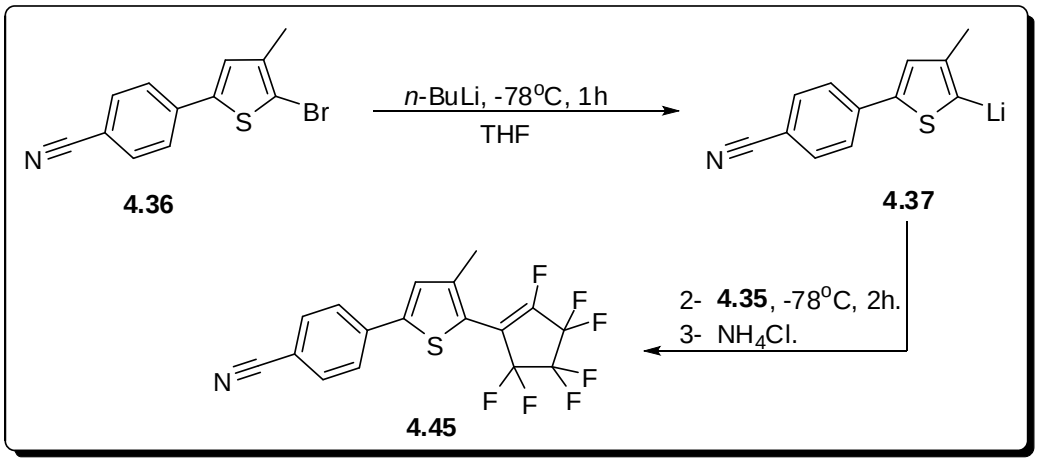
To a solution of **4.34** in DCM a solution of bromine (1.2 molar equivalents) in DCM was added slowly at 0 °C followed by stirring at room temperature. The reaction was followed up by TLC. The reaction was worked-up after completion (4 h) to provide the crude product as a single component as indicated by the TLC. Compound **4.36** was obtained in 90% yield as pure material without the need for a purification process. Therefore, bromine is recommended as a brominating reagent for such reaction over NBS.

4.4.8 Synthesis of 5-(4-Cyanophenyl)-2,3-dimethylthiophene (4.38) *via* Bromine–Lithium Exchange

Having successfully synthesized **4.36**, the next step was the synthesis of **4.38** *via* bromine–lithium exchange. To a cooled (–78 °C) solution of **4.34** in dry THF *n*–BuLi (1.1 molar equivalents) was added slowly and the mixture was then stirred for 1 h at that low temperature. Iodomethane was added to the mixture and the cooling bath was removed and the mixture was stirred for 16 h at room temperature. After work up, TLC of the crude product showed a light spot for the starting material and a dark spot for the product along with some impurities. The product was isolated by column chromatography and subjected to characterization. analysis and has been proved to be **4.38**, which was obtained in 86% yield (Scheme 4.18).

4.4.9 Synthesis of 1-[5-(4-Cyanophenyl)-3-methyl-2-thienyl]perfluorocyclopentene (4.45) *via* Bromine–Lithium Exchange

At this stage we realized that formation of **4.37** should be relatively easy *via* bromine–lithium exchange of **4.36** rather than direct lithiation of **4.34**. Bromine–lithium exchange of **4.36** could be favoured over the reaction of *n*–BuLi with C≡N of **4.36**, which if successful would lead to the formation of **4.37** which could be trapped to produce **4.45** (Scheme 4.22).



Scheme 4.22

To a solution of **4.37** in THF (prepared as described in 4.4.8), an excess (about 1.4 molar equivalent) perfluorocyclopentene (**4.35**) was added in one portion at −78 °C and the reaction mixture was stirred for 2 h and then quenched with ammonium chloride at that low temperature. The cooling bath was removed and the mixture was stirred while warming to room temperature. The product was extracted with diethyl ether, dried and the solvent was removed to provide the crude product.

The TLC of the crude product showed three spots, the first one of which was for 2-(4-cyanophenyl)-4-methylthiopene (**4.34**) due to debromination of **4.36**. The other two spots (one dark and one light) represented new products. The two products were then isolated by column chromatography.

^{1}H NMR spectrum of the major product showed two singlet signals in the aromatic area at δ = 7.59 and 7.20 ppm, corresponding to the 4 protons of the phenyl group and H-3 of the thienyl ring, respectively, of the expected product **4.45**. It also showed a doublet with a small coupling constant (3 Hz) at δ = 2.24 ppm due to the methyl protons. In the ^{13}C NMR spectrum the signal at δ = 110.8 ppm, which corresponded to C-2 of the thienyl unit of **4.36**, had disappeared; otherwise, the spectrum showed signals which were similar to those of **4.36**. The EI-MS of the major product showed a molecular ion peak at *m/z* = 391 and the HRMS confirmed the formula of the molecular ion as $C_{17}H_8F_7NS$ (M^+ of **4.45**). The ^{19}F NMR spectrum showed four signals that correlate well to the structure of **4.45**. Finally, the structure of **4.45** was confirmed further by X-ray crystallography (Figure 4.4). Compound **4.45** was obtained in 71% isolated yield. Detailed characterization data are reported fully in the experimental section.

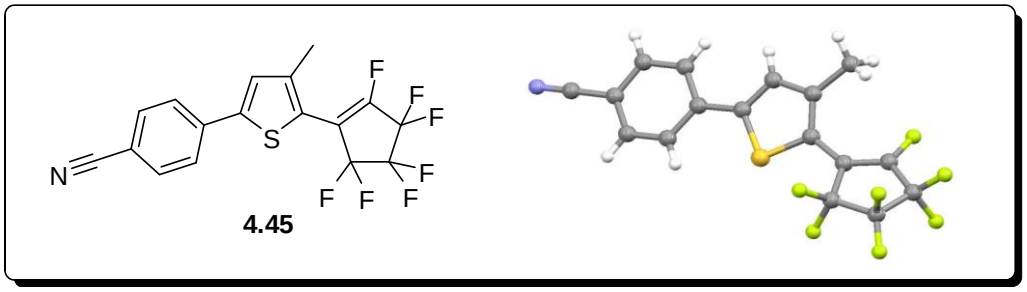


Figure 4.4: X-Ray structure of 4.45

The ^{1}H NMR spectrum of the minor product appeared to be very similar to that of **4.45**; the only difference was that the signal in the aliphatic area was a singlet rather than a doublet. The ^{13}C NMR spectrum showed a signal at δ = 124.4 ppm which was attributed to C-1/C-2 of hexafluorocyclopentene. The ^{19}F NMR spectrum showed only two signals, which indicated that symmetrical 1,5-disubstitiuted perfluorocyclopentene has been formed. The MS analysis showed a molecular ion peak at *m/z* 570 which correlated well to the molecular weight of 1,5-bis[5-(4-cyanophenyl)-3-methyl-2-thienyl]perfluorocyclopentene (**4.46**, Figure 4.5) which is expected to be the side product. The HRMS showed that the calculated mass for $C_{29}H_{16}F_6N_2S_2$ (M^+ of **4.46**) is 570.0664, and the found one was 570.0659. Clearly the side product was identified as **4.46**, which was obtained in 10% yield. Finally, the structure of **4.46** was confirmed by X-ray crystallography (Figure 4.5) (see experimental section for the detailed analysis of the structure of **4.46**).

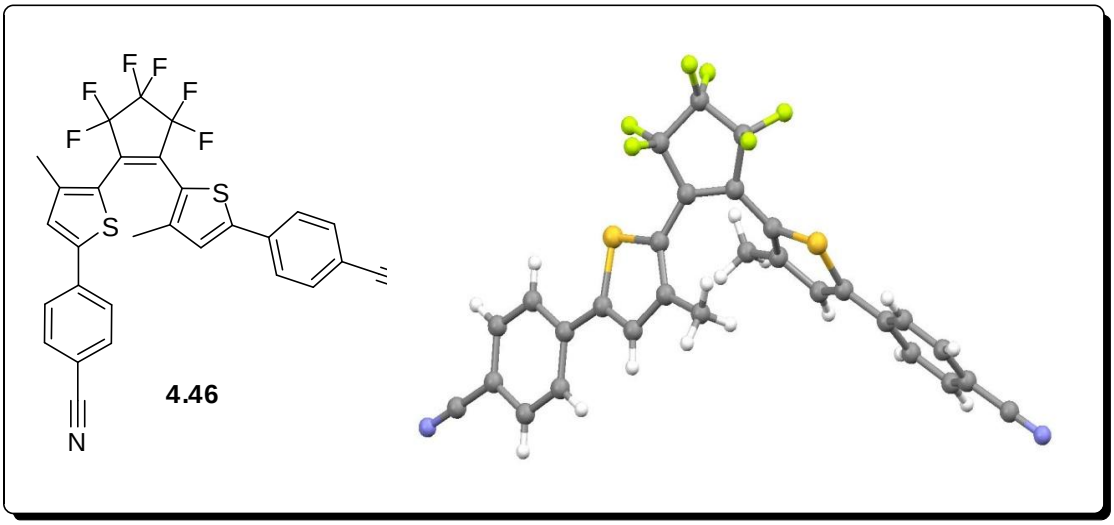
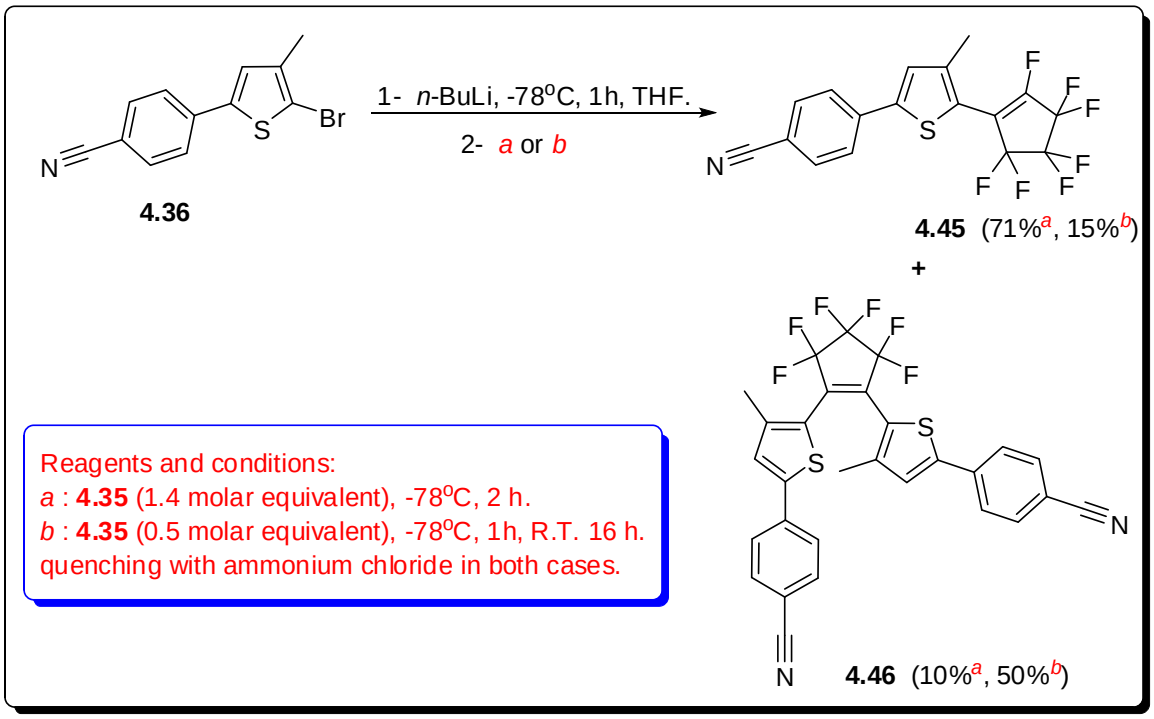


Figure 4.5: X-Ray structure of 4.46

Compound **4.46** is a novel one; we thought that it was worthwhile to find the proper conditions for its production in a good yield. Therefore, synthesis of **4.46** was attempted by

using **4.36** and 0.5 molar equivalents of **4.35** under conditions shown in Scheme 4.23. Following work-up and purification by column chromatography **4.46** was obtained in 50% yield based on **4.36**, along with 15% of **4.45**.

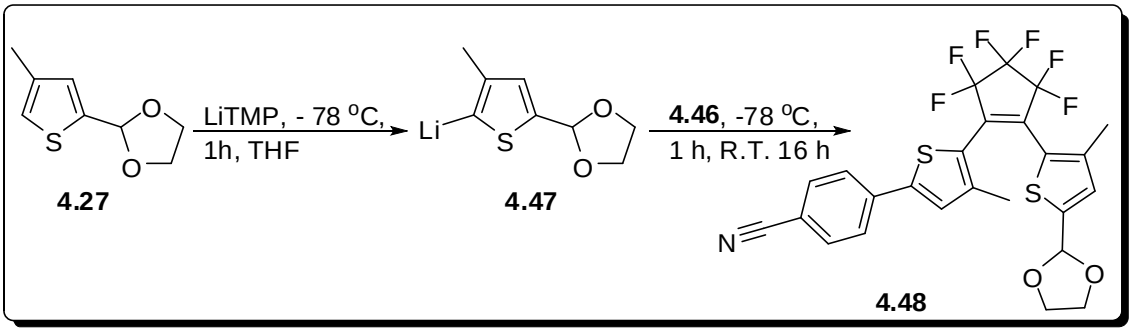


Scheme 4.23

4.4.10 Synthesis of 1-[5-(2-[1,3]Dioxolanyl)-3-methyl-2-thienyl]-2-[5-(4-cyanophenyl)-3-methyl-2-thienyl]perfluorocyclopentene (4.48)

Having successfully synthesized **4.27** and **4.45** our attention was next turned to join these two molecules together to produce **4.48**. In this reaction F-5 of **4.45** should be replaced by the thienyl group of **4.47** which could be produced by the direct lithiation of **4.27**. From previous experience within our research group it was known that lithiation of **4.27** using *n*–BuLi or *t*–BuLi gives a mixture of isomeric products due to direct lithiation at the 3-position of **4.27** besides other side products. However, lithiation of **4.27** with LiTMP (**4.23**) at –78 °C took place at the 3-position to give a single product along with a little bit of the starting material present.[20] Based on that we used **4.23** as the lithiating reagent for the synthesis of **4.48**.

To the freshly prepared **4.23**, compound **4.27** was added slowly and the mixture was stirred for 1 h at –78 °C followed by the addition of a solution of **4.45**. The reaction mixture was stirred for 2 h at –78 °C then over night at room temperature (Scheme 4.24).



Scheme 4.24

After aqueous workup using saturated NH_4Cl, a crude solid product was obtained. The TLC showed that it was a mixture of the starting materials and a product, which was then isolated by column chromatography. The ^1H NMR spectrum of the pure product showed a combination of the signals of **4.27** and **4.45** with a little shift, and the signal at δ = 6.88 ppm, which corresponds to H-5 of **4.27**, had disappeared, which correlated well to what would be expected for **4.48**. The DEPT ^{13}C NMR spectrum also showed a similar combination of signals, with the exception that one of the doublet signals in the aromatic area at δ = 121.6 ppm (corresponding to C-5 of **4.27**) has disappeared and an extra singlet signal in the aromatic region had appeared, proving the substitution of H-2 of **4.27** to give **4.48**. The ^{19}F NMR spectrum showed three signals that correlated well to the structure of **4.48**. The EI-MS showed a molecular ion peak at *m/z* = 541 and the formula was confirmed by the HRMS as $C_{19}H_{13}F_6NO_2S_2$ (M^+). Finally, X-ray crystallography (Figure 4.6) confirmed the structure of **4.48** which was obtained in 68% isolated yield. The detailed characterization data for compound **4.48** are presented in the experimental section.

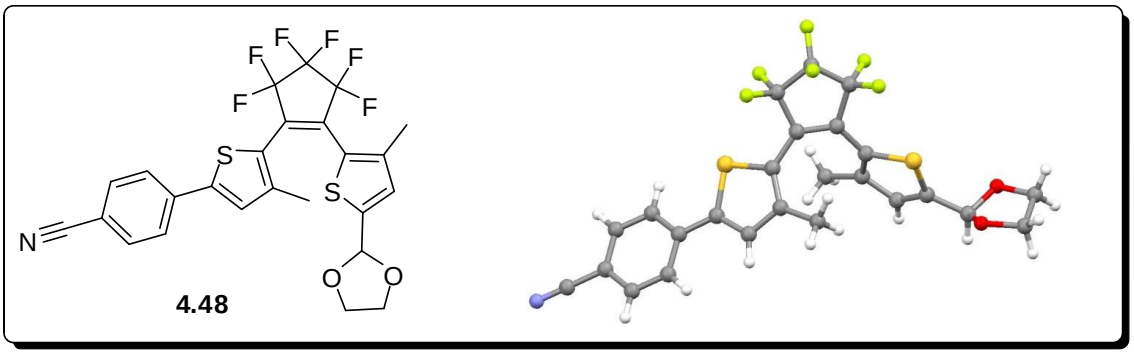
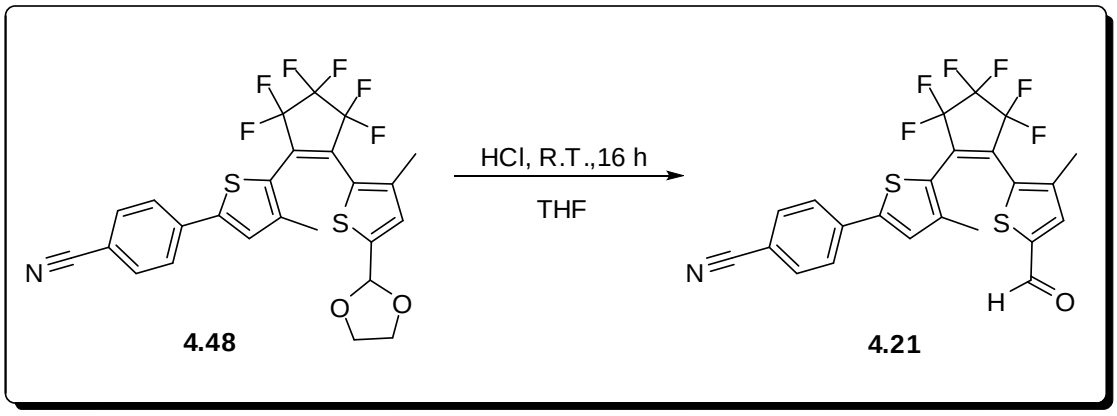


Figure 4.6: X-Ray structure of 4.48

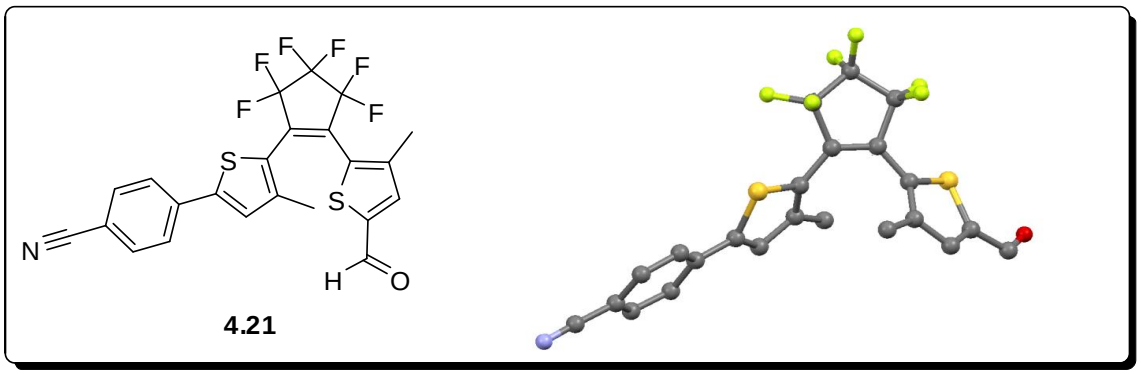
4.4.11 Synthesis of 1-[5-(Formyl)-3-methyl-2-thienyl]-2-[5-(4-cyanophenyl)-3-methyl-2-thienyl]perfluorocyclopentene (4.21)

Compound **4.48** is the protected form of **4.21**. Treatment of a solution of pure **4.48** in THF with aqueous HCl for 16 h followed by basification and aqueous workup resulted in the production of a solid material for which the TLC analysis showed a single component (Scheme 4.25).



Scheme 4.25

The FT-IR spectrum showed a strong absorption band at 1674 cm^{-1} related to C=O group stretching. The ^{1}H NMR analysis showed a characteristic singlet signal at δ = 9.8 ppm corresponding to the aldehyde proton. It also showed that signals corresponding to the 1,3-dioxolan-2-yl group had disappeared and showed the other expected signals for **4.21**. The ^{13}C NMR analysis showed a singlet signal at δ = 182.4 ppm corresponding to the carbonyl group carbon and also showed the absence of CH and CH_2 units of the 1,3-dioxolan-2-yl group present in **4.48**. The ^{19}F NMR spectrum showed three signals that correlated well to the structure of **4.21**. The EI-MS showed a molecular ion peak at *m/z* = 497 and the HRMS confirmed the formula of the molecular ion as $C_{23}H_{13}F_6NOS_2$ (M^+ of **4.21**). Finally X-ray crystallography (Figure 4.7) confirmed the structure of **4.21**, which was obtained in 93% isolated yield. The detailed characterization data are reported in the experimental section.



4.21

Figure 4.7: X-Ray structure of 4.21

4.4.12 Synthesis of 1,3-*Bis*[*N*-(3-methyl-2-(1-(5-(4-cyanophenyl)-3-methyl-2-thienyl)-3,3,4,4,5,5-hexafluorocyclopenten-2-yl)-5-thienylmethylidene)aminobutylthio]propane (4.49)

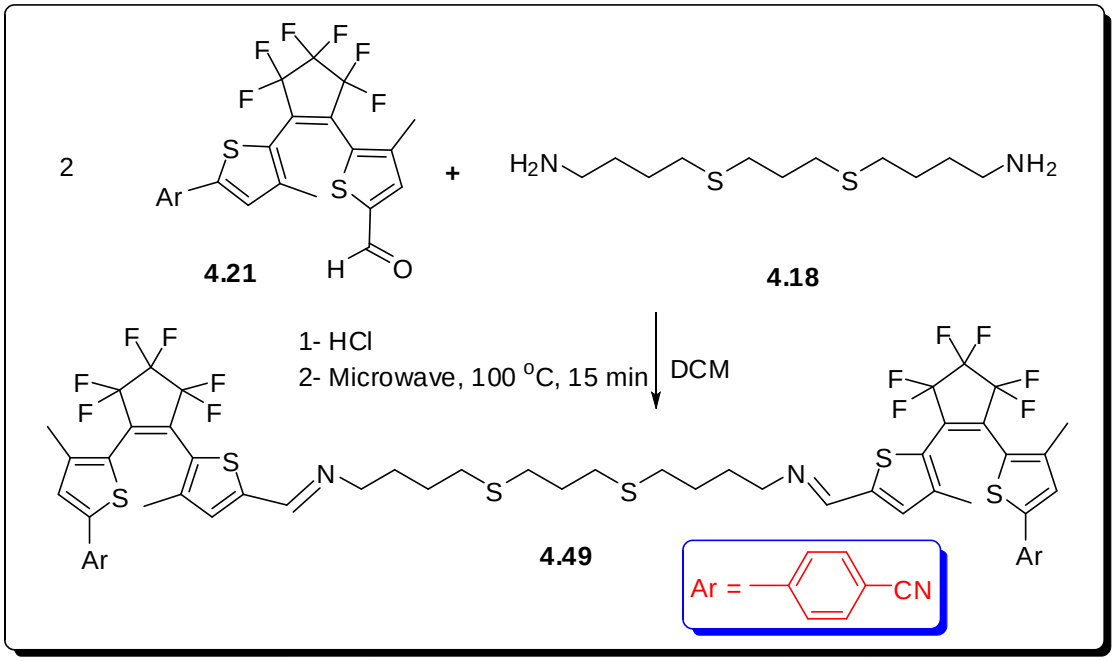
At this stage our aim was to produce the photochromic model **4.49**. In Section 4.3.3 we showed that benzaldehyde can be used successfully in a test case to produce **4.20** on reaction with **4.18**. Consequently we studied and designed a synthetic route for the production **4.21**. The quantity of **4.21** produced after the multistep synthesis was limited. Scaling up the reactions was problematic and a low yield was obtained; therefore, even with repeating the experiments under the optimized conditions, within the available time the amount of the final target was limited. Therefore, an attempt to produce **4.49** was carried out on a small scale.

In a microwave 10 ml vial, a mixture of **4.18** and **4.21 (**2 molar equivalents) in DCM containing a drop of dry HCl solution in diethyl ether was heated under microwave irradiation (using a microwave reactor) at 100 °C for 30 min (Scheme 4.26).

The ^{1}H NMR analysis of the isolated material showed that the signal corresponding to the aldehyde proton of **4.21** had diminished and the patterns of the aliphatic protons were different than those of **4.18**. Two characteristic signals were observed, a singlet at δ = 8.20 ppm and a triplet δ = 3.55 ppm, corresponding to the protons of HC=N and CH_2N protons, respectively. It also showed all other expected signals, which were well correlated to the structure of **4.49**. The ^{13}C NMR spectrum showed signals at δ = 153.3 (doublet) and 60.9 ppm (triplet) corresponding to the carbons of C=N and CH_2N, respectively. It also showed the presence of methylene carbons. It also showed that the signal at δ = 182.4, corresponding to the carbonyl group carbon in **4.21**, had disappeared. The ^{19}F NMR

spectrum of **4.49** showed three signals that correlated well to the structure. The FT-IR analysis showed an absorption band at 1631 cm^{-1} due to the C=N stretching, while the N–H stretching absorption bands at 3300 and 3361 cm^{-1} for **4.18** had disappeared and the C=O stretching band at 1674 cm^{-1} had diminished.

Due to the high molecular weight of **4.49** (1209.4 g/mol), its molecular ion couldn't be detected using MS (EI) technique. The highest ion was observed at *m/z* = 583.1. The MALDI-TOF technique enabled us to see the molecular ion (M^+). The EI-HRMS confirmed the structure of one of the ions ($C_{27}H_{21}F_6N_2S_3$); it showed a peak at *m/z* = 583.0768, correlating well to the ion of the formula $C_{27}H_{21}F_6N_2S_3$, for which the exact calculated mass is 583.0771. Compound **4.49** was obtained in 93% yield.



Scheme 4.26

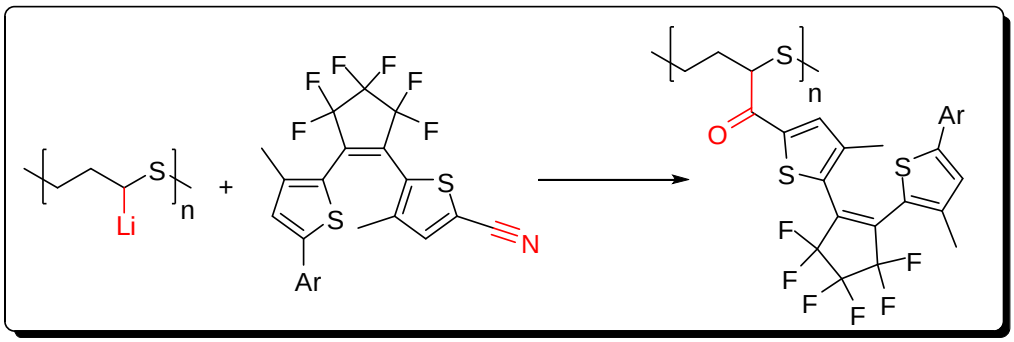
4.5 Conclusions

1,3-*Bis*(4-aminobutylthio)propane (**4.18**) has been synthesized in two steps. The first step involves reaction of lithium propane-1,3-*bis*(thiolate) (**4.16**) with 4-bromobutyronitrile (**4.10**) to give 1,3-*bis*(3-cyanopropylthio)propane (**4.17**). The second step involved reduction of **4.17** to give the corresponding diamino compound **4.18**. Reaction of benzaldehyde with diamino compound **4.18** gave 1,3-*bis*(4-(*N*-benzylideneamino)butylthio)propane (**4.20**), which can be used as a simple model for a synthetic pathway that could be used as a route for the production of functionalized

poly(alkylene sulfide)s. We have designed and synthesized a new photochromic diarylethene aldehyde (**4.21**) and this has been used to produce the corresponding novel photochromic oligomeric material **4.49**.

Three novel compounds - **4.48**, **4.21** and **4.49** - were synthesised and showed photochromic behaviour when their dilute solutions were exposed to a simple UV lamp. A colour change was observed and their UV spectra before and after exposure to the UV light were different; all the changes were reversible. However, such results are not reported in the thesis and will be fully investigated in the near future by the use of the proper instrumentation to establish the detailed photochromic properties of such new compounds. These compounds are interesting and their use in different applications such as optical memories and molecular switches should be the next step (future work).

Future work will also aim at the production of various polymeric sulfides with high concentrations of the photochromic units, possibly by the activation of the methylene groups next to sulfur in the backbone of the poly(alkylene sulfide). Such activation could perhaps be achieved by lithiation of the pre-prepared polymers followed by reaction with appropriately reactive photochromic materials (Scheme 4.27).



Scheme 4.27

Apart from that, and with a view toward green chemistry, we have made a start with the use of poly(propylene sulfide) as a replacement for dimethyl sulfide (DMS) in Corey–Kim oxidation (oxidation of primary and secondary alcohols to aldehydes and ketones respectively). We have already investigated a number of reactions and modest yields were obtained. Therefore, we are planning to increase the yields and try to find conditions under which the yields become quantitative.

4.6 Experimental

4.6.1 General

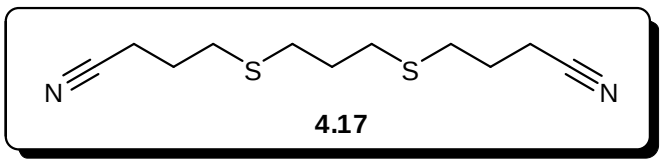
See Chapter 2, Section 2.12.1.

4.6.2 Instruments

Microwave reactions were carried out using CEM Discover microwave reactor. ^{19}F NMR spectra were recorded on Jeol Eclipse 300 FT NMR Spectrometer. MALDI-TOF spectra were performed with a Waters MALDI Micro MX spectrometer. X-Ray crystal structure determination was made in Cardiff using a Bruker-Nonius Kappa CCD area-detector diffractometer equipped with an Oxford Cryostream low temperature cooling device operating at 150(2) K (λ = 0.71073 Å). Details about the other instruments are shown in Chapter 2, Section 2.12.2.

4.6.3 Synthesis of 1,3-*Bis*(3-cyanopropylthio)propane (4.17)

In an oven dried 50 mL flask, flushed with nitrogen and protected by a rubber septum, was placed freshly distilled THF (25 mL). 1,3-Propanedithiol (0.54 g; 5.00 mmol) was added and the mixture was cooled to –78 °C under nitrogen. *n*-Butyllithium (6.25 mL of 1.60 M solution in hexane; 10.0 mmol) was added over 10 min. The reaction mixture was stirred at -78 °C for 1 h and the cooling bath was removed to allow the mixture to warm up to room temperature. 4-Bromobutyronitrile (1.48 g; 10.0 mmol) was added by syringe and the reaction mixture was stirred at room temperature overnight. A saturated aqueous solution of ammonium chloride (NH_4Cl; 10 mL) and water (10 mL) were added subsequently, followed by extraction with chloroform (2 × 50 mL). The organic layer was washed with brine (100 mL) and dried over anhydrous magnesium sulfate. The solvent was evaporated under reduced pressure to give **4.17** (1.10 g; 4.54 mmol; 91%) as a colourless oil.

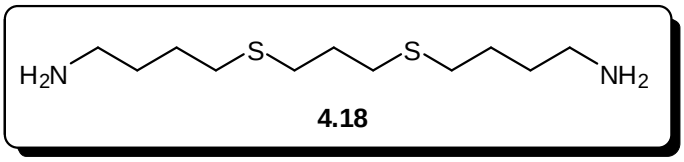


4.17

^{1}H NMR (400 MHz, $CDCl_3$), δ (ppm): 2.54 (t, J = 7.0 Hz, 4 H, SCH_2CH_2CH_2S), 2.51 (t, J = 7.0 Hz, 4 H, 2 × CH_2CH_2CH_2CN), 2.41 (t, J = 7.0 Hz, 4 H, 2 × CH_2CN), 1.83 (app. p, J = 7.0 Hz, 4 H, 2 × CH_2CH_2CH_2CN), 1.75 (pentet, J = 6.9 Hz, 2 H, SCH_2CH_2CH_2S).
^{13}C NMR (100 MHz, $CDCl_3$), δ (ppm): 119.2 (s, CN), 30.6 (t, CH_2CH_2CH_2CN), 30.5 (t, SCH_2CH_2CH_2S), 28.9 (t, SCH_2CH_2CH_2S), 25.2 (t, CH_2CH_2CN), 16.0 (t, CH_2CN).
MS-EI (*m/z*, %): 242 (M^+, 52), 176 (12), 175 (38), 174 (100).
HRMS (EI): calcd for $C_{11}H_{18}N_2S_2$ (M^+) 242.0911; found, 242.0905.
FT–IR, ν_{max}: 2923, 2245, 1447, 1423 cm^{-1}.

4.6.4 Synthesis of 1,3-*Bis*(4-aminobutylthio)propane (4.18)

In an oven dried 50 mL flask, flushed with nitrogen and protected by a rubber septum, was placed dry diethyl ether (50 mL). The flask was cooled in a water/ice bath and lithium aluminum hydride (6.0 mL of 2.40 M solution in THF, 14.4 mmol) was then added slowly followed by the dropwise addition of **4.17** (0.80 g; 3.30 mmol). The cooling bath was removed and the mixture was stirred 48 h at room temperature. After quenching by the careful addition of water (5.0 mL), the mixture was acidified with concentrated H_2SO_4 then basified with 6 N NaOH. DCM (300 mL) was added to the mixture and the combined layers were filtered. The organic layer was separated, washed with brine and dried over anhydrous magnesium sulfate. The solvent was removed under reduced pressure to give **4.18** (0.70 g, 2.79 mmol; 85%) as a colourless oily material.



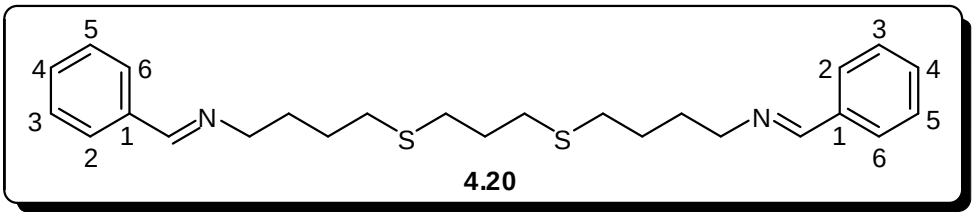
4.18

^{1}H NMR (400 MHz, $CDCl_3$), δ (ppm): 2.64 (t, J = 7.1 Hz, 4 H, 2 × C$H_2$$NH_2$), 2.55 (t, J = 7.1 Hz, 4 H, 2 × CH_2CH_2CH_2C$H_2$$NH_2$), 2.46 (t, J = 7.1 Hz, 4 H, SCH_2CH_2CH_2S), 1.79 (pentet, J = 7.1 Hz, 2 H, SCH_2CH_2CH_2S), 1.60–1.44 (m, 8 H, 2 × CH_2CH_2CH_2C$H_2$$NH_2$), 1.32 (br s, exch., 4 H, 2 NH_2).
^{13}C NMR (100 MHz, $CDCl_3$), δ (ppm): 39.3 (t, CH_2NH_2), 30.5 (t, CH_2CH_2CH_2C$H_2$$NH_2$), 29.4 (t, C$H_2CH_2$$NH_2$), 28.4 (t, SC$H_2CH_2CH_2$S), 26.8 (t, SC$H_2CH_2CH_2$S), 24.5 (t, C$H_2CH_2CH_2CH_2$$NH_2$).
MS-EI (*m/z*, %): 250 (M^+, 40), 179 (38), 178 (98), 161 (75), 147 (90), 104 (88), 87 (99), 73 (100).

HRMS (EI): calcd for $C_{11}H_{26}N_2S_2$ (M^+) 250.1537; found, 250.1529.
FT–IR, ν_{max}: 3361, 2925, 2851, 1661, 1593 cm^{-1}.

4.6.5 Synthesis of 1,3-*Bis*(4-(*N*-benzylideneamino)butylthio)propane (4.20)

In a 10 mL microwave vial charged with a magnetic bar, were placed benzaldehyde (0.34 g; 3.2 mmol) and compound **4.18** (0.40 g; 1.6 mmol). DCM (4 mL) and dry HCl (0.15 mL of 1 M solution in diethyl ether, 0.15 mmol) were added to the mixture and the vial was sealed and subjected to microwave irradiation at 100 °C for 20 min. The mixture was cooled, then decanted into a 50 mL round bottomed flask and the solvent was evaporated under reduced pressure. The unreacted benzaldehyde was distilled off under high vacuum to give **4.20** (0.58 g; 1.36 mmol; 85%) as a yellow oil.



4.20

^{1}H NMR (400 MHz, $CDCl_3$), δ (ppm): 8.2 (s, 2 H, 2 × HC=N), 7.66-7.63 (m, 4 H, 2 × H2/H6 of phenyl), 7.34–7.32 (m, 6 H, 2 × H3/H4/H5 of phenyl), 3.55 (t, J = 7.2 Hz, 4 H, 2 × CH_2N), 2.54–2.46 (m, 8 H, 2 × CH_2SCH_2), 1.80–1.70 (m, 8 H, 2 × CH_2CH_2CH_2N), 1.63–1.55 (m, 2 H, SCH_2CH_2CH_2S).
^{13}C NMR (100 MHz, $CDCl_3$), δ (ppm): 161.1 (d, *C*=N), 136.2 (s, C-1 of phenyl), 130.6 (d, C-4 of phenyl), 128.6 (d, C2/C6 of phenyl), 128.1 (d, C3/C5 of phenyl), 61.2 (t, CH_2N), 31.9 (t, *C*H_2CH_2CH_2CH_2N), 30.9 (t, S*C*H_2CH_2*C*H_2S), 30.1 (t, *C*H_2CH_2N), 29.4 (t, SCH_2*C*H_2CH_2S), 27.4 (t, *C*H_2CH_2CH_2N).
MS-EI (*m/z*, %): 426 (M^+, 5), 321 (12), 266 (93), 192 (99), 159 (100), 132 (96), 87 (95).
HRMS (EI): calcd for $C_{25}H_{34}N_2S_2$ (M^+) 426.2163; found, 426.2150.
FT–IR, ν_{max}: 2928, 2844, 1645 cm^{-1}.

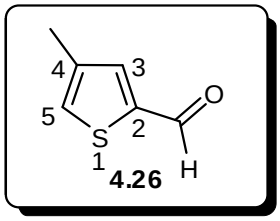
4.6.6 Preparation of Lithium 2,2,6,6-tetramethylpiperidide (LiTMP; 4.23)

In an oven dried 50 mL flask, flushed with nitrogen and protected by a rubber septum, was placed 2,2,6,6-tetramethylpiperidine (TMP, 0.45 g ; 3.2 mmol) and freshly distilled THF (20.0 mL). The solution was cooled in a dry ice–acetone bath under a stream

of nitrogen and stirred for 30 min. *tert*-Butyllithium (2.00 mL of 1.70 M solution in hexane; 3.40 mmol) was added drop wise *via* a syringe. The mixture was stirred for 1 h at that low temperature to get LiTMP (**4.23**; 3.20 mmol).

4.6.7 Synthesis of 4-Methylthiophene-2-carboxaldehyde (4.26)

Lithium 2,2,6,6-tetramethylpiperidide (**4.23**, LiTMP; 3.2 mmol) was prepared according to the above described procedure. 3-Methylthiophene (**4.24**; 0.29 g; 3.0 mmol) was added and the mixture was stirred for another 1 h to produce 4-methyl-2-thienyllithium (**4.25**). *N*,*N*-dimethylformamide (DMF; 0.57 g; 7.7 mmol) was added by a syringe. The cooling bath was removed and the mixture was stirred at room temperature overnight. The reaction was quenched by the addition of aqueous HCl (2 M; 20 mL) followed by efficient extraction with diethyl ether (3 × 100 mL). The combined organic layer was washed with a saturated aqueous solution of sodium bicarbonate ($NaHCO_3$, 50 mL) and brine (50 mL) followed by drying over anhydrous magnesium sulfate. The solvent was evaporated under reduced pressure to get **4.26** (0.35 g, 2.77 mmol; 92%) as a yellow oily material.



4.26

^{1}H NMR (400 MHz, $CDCl_3$), δ (ppm): 9.79 (s, 1 H, CHO), 7.50 (s, 1 H, H-5), 7.28 (s, 1 H, H-3), 2.24 (s, 3 H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$), δ (ppm): 183.2 (d, CHO), 143.6 (s, C-2), 139.2 (s, C-4), 138.2 (d, C-3), 131.1 (d, C-5), 15.5 (q, CH_3).

MS-EI (*m/z*, %): 126 (M^+, 83), 125 (100), 79 (29).

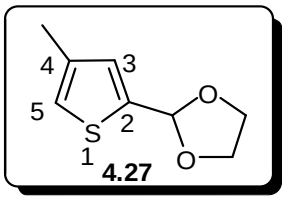
HRMS (EI): calcd for C_6H_6OS (M^+) 127.0135; found, 127.0139.

FT–IR, ν_{max}: 3510, 3318, 3087, 2926, 2822, 1797, 1667 cm^{-1}.

4.6.8 Synthesis of 2-(4-Methyl-2-thienyl)-1,3-dioxolane (4.27)

In a 250 mL flask fitted with a Dean and Stark trap and condenser, 4-methylthiophene-2-carboxaldehyde (**4.26**; 5.55 g; 44.00 mmol), ethylene glycol (5.83 g;

94.00 mmol) and *para*-toluenesulfonic acid monohydrate (0.84 g; 4.40 mmol) were dissolved in toluene (100 mL). The reaction mixture was refluxed overnight. After the point at which water stopped to accumulate in the trap, the mixture was allowed to cool down to the room temperature. The mixture was filtered and a saturated aqueous solution of sodium bicarbonate (100 mL) was added followed by extraction with ethyl acetate (6 × 100 mL). The organic layer was washed with brine (3 × 200 mL) and dried over anhydrous magnesium sulfate, then treated with charcoal (2 g, stirred at room temperature for 30 min then filtered). The solvent was evaporated under reduced pressure to give **4.27** (5.50 g; 32.3 mmol; 73 %) as a light yellow oil.



4.27

^{1}H NMR (400 MHz, $CDCl_3$), δ (ppm): 6.88 (s, 1 H, H-5), 6.80 (s, 1 H, H-3), 5.59 (s, 1 H, CH of 1,3-dioxolan-2-yl), 4.03-3.87 (m, 4 H, 2 × CH_2 of 1,3-dioxolan-2-yl), 2.14 (s, 1 H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$), δ (ppm): 141.5 (s, C-2), 137.2 (s, C-4), 128.5 (d, C-3), 121.6 (d, C-5), 100.3 (d, C-2 of 1,3-dioxolan-2-yl), 65.2 (t, C-4 and C-5 of 1,3-dioxolan-2-yl), 15.7 (q, CH_3).

MS-EI (*m/z*, %): 170 (M^+, 100), 169 (64), 110 (13), 86 (30), 85 (57), 84 (93), 83 (50).

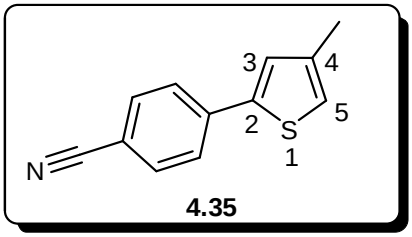
HRMS (EI): calcd for $C_8H_{10}O_2S$ (M^+) 170.0397; found, 170.0402.

FT–IR, ν_{max}: 3091, 2951, 2886, 1669, 1563 cm^{-1}.

4.6.9 Synthesis of 2-(4-Cyanophenyl)-4-methylthiopene (4.34)

In an oven dried 50 mL flask, flushed with nitrogen and protected by a rubber septum (flask A), 4-methyl-2-thienyllithium (20.0 mmol) was prepared as described for the synthesis of 4-methylthiophene-2-carboxaldehyde. Zinc chloride ($ZnCl_2$; 20 mL 1.00 M solution in diethyl ether; 20 mmol) was added. The mixture was stirred for 4 h at room temperature. In another oven dried 100 mL 2 necked flask fitted with a condenser (flask B), flushed with nitrogen and protected with a rubber septum, 4-bromobenzonitrile (2.25 g; 12.4 mmol) and tetrakis(triphenylphosphine)palladium(0) (0.15 g; 0.13 mmol) were dissolved in freshly distilled THF (10 mL). The contents of flask A were transferred slowly

via a double ended needle to flask B. The mixture was stirred for 2 h at 50 °C, then the oil bath was removed and stirring was continued overnight at room temperature. Water (50 mL) was added followed by extraction with diethyl ether (2 × 100 mL). The combined organic layer was washed with brine (2 × 50 mL) then dried over anhydrous magnesium sulfate. The solvent was evaporated under reduced pressure to get a crude yellow solid material, which was purified by column chromatography (silica gel; hexane/diethyl ether; 50/50) to give **4.34** (2.34 g; 11.7 mmol; 95 %) as a light yellow solid material.



4.35

Mp: 105–106 °C, (lit.[9] 101–103 °C)

^{1}H NMR (400 MHz, $CDCl_3$), δ (ppm): 7.68–7.63 (m, 4 H, H-2/H-3/H-5/H-6 of 4-cyanophenyl), 7.25 (d, J = 1.1 Hz, 1 H, H-5), 7.00 (d, J = 1.1 Hz, 1 H, H-3), 2.32 (app. t, J = 0.7 Hz, 3 H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$), δ (ppm): 141.7 (s, C-2), 139.3 (s, C-1 of 4-cyanophenyl), 138.8 (s, C-4), 132.7 (d, C-3/C-5 of 4-cyanophenyl), 127.4 (d, C-3), 125.8 (d, C-2/C-6 of 4-cyanophenyl), 122.6 (d, C-5), 119.0 (s, CN), 110.3 (s, C-4 of 4-cyanophenyl), 15.8 (q, CH_3).

MS-EI (*m/z*, %): 199 (M^+, 70), 85 (63), 84 (100).

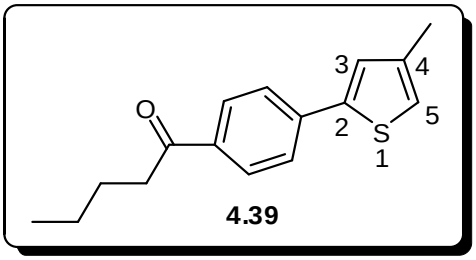
HRMS (EI): calcd for $C_{12}H_9NS$ (M^+) 199.0458; found, 199.0456.

FT–IR, ν_{max}: 3081, 2924, 2359, 2342, 2225, 1605, 1505 cm^{-1}.

4.6.10 Synthesis of 2-(4-Pentanoylphenyl)-4-methylthiophene (4.39)

n-Butyllithium (0.70 mL of 1.60 M solution in hexane; 1.12 mmol) was added drop wise to a stirred cooled (–78 °C) solution of 2-(4-cyanophenyl)-4-methylthiopene (**4.34**; 0.20 g; 1.0 mmol) in freshly distilled THF (20 mL) and the mixture was stirred at that low temperature for 1 h. The cooling bath was removed to let the mixture warm up to room temperature. A saturated aqueous solution of ammonium chloride (NH_4Cl; 10 mL) and water (10 mL) were added subsequently followed by extraction with diethyl ether (2 × 50 mL). The organic layer was washed with brine (100 mL) and dried over anhydrous

magnesium sulphate. Solvent was evaporated under reduced pressure to get solid crude material, which was purified by column chromatography (silica gel; diethyl ether/hexane; 1/10) to give **4.39** (0.16 g; 0.62 mmol; 62 %) as a light green solid.



4.39

Mp: 82–83 ^{o}C.

^{1}H NMR (400 MHz, $CDCl_3$), δ (ppm): 7.86 (d, J = 8.4 Hz, 2 H, H-3/H-5 of 4-pentanoylphenyl), 7.56 (d, J = 8.4 Hz, 2 H, H-2/H-6 of 4-pentanoylphenyl), 7.2 (s, 1 H, H-5), 6.85 (s, 1 H, H-3), 2.87 (t, J = 7.4 Hz, 2 H, CH_2CH$_2$CH$_2$CH$_3$), 2.21 (s, 3 H, CH$_3$), 1.64 (app. pentet., J = 7.4 Hz, 2 H, CH$_2$CH_2CH$_2$CH$_3$), 1.33 (app. sextet, J = 7.4 Hz , 2 H, CH$_2$CH$_2$CH_2CH$_3$), 0.88 (t, J = 7.4 Hz, 3 H, CH$_2$CH$_2$CH$_2$CH_3).

^{13}C NMR (100 MHz, $CDCl_3$), δ (ppm): 199.8 (s, C=O), 142.6 (s, C-2), 139.1 (s, C-1 of 4-pentanoylphenyl), 138.7 (s, C-4), 135.5 (s, C-4 of 4-pentanoylphenyl), 128.8 (d, C-3/C-5 of 4-pentanoylphenyl), 126.9 (d, C-3), 125.4 (d, C-2/C-6 of 4-pentanoylphenyl), 121.9 (d, C-5), 38.3 (t, CH$_2$CH$_2$CH$_2$CH$_3$), 26.6 (t, CH$_2$$CH_2CH_2CH_3$), 22.6 (t, CH$_2CH_2$$CH_2CH_3$), 15.9 (q, CH$_3$), 14.0 (q, CH$_2CH_2CH_2$$CH_3$).

MS-CI (*m/z*, %): 300 [(M + MeCNH)$^{+}$, 35], 260 (20), 259 (MH^{+} 100).

HRMS (EI): calcd for $C_{16}H_{19}OS$ (MH^{+}) 259.1155; found 259.1157.

FT–IR, ν_{max}: 2947, 2924, 2865, 1676, 1596 cm^{-1}.

4.6.11 Synthesis of 2-Bromo-5-(4-cyanophenyl)-3-methylthiophene (4.36)

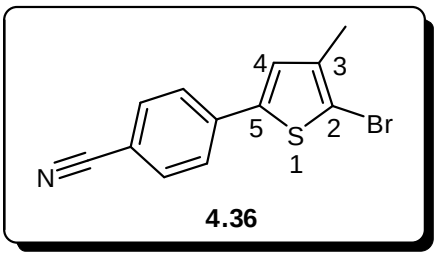
Procedure 1

2-(4-Cyanophenyl)-4-methylthiopene (**2.35**, 0.20 g; 1.0 mmol) was dissolved in DCM (10 mL) and cooled to 0 ^{o}C. A solution of bromine (0.19 g; 1.2 mmol) in DCM (15 mL) was added using a dropping funnel over a period of 30 min. The reaction mixture was stirred at room temperature for 4 h (the reaction was followed by TLC). A saturated aqueous solution of sodium thiosulfate (1 mL) was added followed by neutralization (pH 7) using a saturated aqueous solution of sodium bicarbonate. The mixture was extracted

with chloroform (25 mL). The organic layer was then washed with brine (3 × 25 mL). The organic layer was dried over anhydrous magnesium sulfate. The solvent was evaporated under reduced pressure to get **4.36** (0.25 g; 0.90 mmol ; 90%) as a white solid.

Procedure 2:

2-(4-Cyanophenyl)-4-methylthiopene (**4.34**, 0.20 g; 1.0 mmol) was dissolved in dichloromethane (DCM; 10 mL) and cooled to 0 ^{o}C. A solution of *N*-bromosuccinimide (NBS; 0.21 g; 1.2 mmol) in DCM (15 mL) was added using a dropping funnel over a period of 30 min. the reaction mixture was stirred overnight at room temperature then it was cooled down to 0 ^{o}C and filtered. Chloroform (25 mL) was added followed by washing with HCl (20 mL; 2 M), aqueous saturated sodium bicarbonate solution (25 mL) and water (3 × 25 mL). The organic layer was dried over anhydrous magnesium sulfate. The solvent was evaporated under reduced pressure to get a crude solid, which was purified by column chromatography (silica gel; hexane/diethyl ether; 50/50) to give **4.36** (0.22 g; 0.80 mmol; 80 %) as a white solid.



4.36

Mp: 110–111 ^{o}C.

^{1}H NMR (400 MHz, $CDCl_3$), δ (ppm): 7.57 (d, J = 8.6 Hz, 2 H, H-3/H-5 of 4-cyanophenyl), 7.51 (d, J = 8.6 Hz, 2 H, H-2/H-6 of 4-cyanophenyl), 7.15 (s, 1 H, H-4), 2.37 (s, 3 H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$), δ (ppm): 141.0 (s, C-3), 138.9 (s, C-5), 137.8 (s, C-1 of 4-cyanophenyl), 132.8 (d, C-3/C-5 of 4-cyanophenyl), 126.9 (d, C-4), 125.5 (d, C-2/C-6 of 4-cyanophenyl), 118.8 (s, CN), 111.4 (s, C-4 of 4-cyanophenyl), 110.8 (s, C-2), 15.1 (q, CH_3).

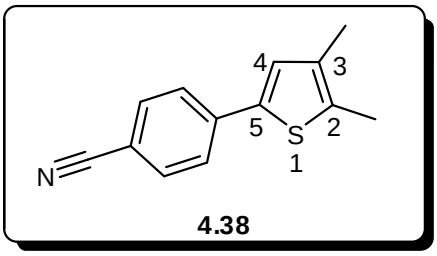
MS-EI (*m/z*, %): 279 ($[M^{81}Br]^+$, 34), 277 ($[M^{79}Br]^+$, 35), 198 (20), 86 (63), 84 (100).

HRMS (EI): calcd for $C_{12}H_8BrNS$ $[M^{79}Br]^+$ 276.9569; found, 276.9561.

FT–IR, ν_{max}: 3069, 2921, , 2229, 1653, 1604, 1558, 1504 cm^{-1}.

4.6.12 Synthesis of 5-(4-Cyanophenyl)-2,3-dimethylthiophene (4.38)

2-Bromo-5-(4-cyanophenyl)-3-methylthiophene (**4.36**; 0.20 g; 0.72 mmol) was dissolved in freshly distilled THF (25 mL) and cooled to –78 ^{o}C under nitrogen. *n*-Butyllithium (0.50 mL of 1.60 M solution in hexane; 0.80 mmol) was added in a dropwise manner. The reaction mixture was stirred for 1 h at that low temperature. Iodomethane (0.14 g; 1.00 mmol) was added and the cooling bath was removed to let the reaction mixture warm up to room temperature and the stirring was continued for 16 h. The reaction was worked up and purification was carried out as described for the synthesis of 2-(4-pentanoylphenyl)-4-methylthiophene (**3.39**, Section 4.6.10) to give **4.38** (0.13 g; 0.62 mmol; 86%) as a yellow solid.



4.38

Mp: 136–137 ^{o}C.

^{1}H NMR (400 MHz, $CDCl_3$), δ (ppm): 7.60–7.50 (m, 4 H, H-2/H-3/H-5/H-6 of 4-cyanophenyl), 7.06 (s, 1 H, H-4), 2.31 (s, 3 H, C-2-CH_3), 2.09 (s, 3 H, C-3-CH_3).

^{13}C NMR (100 MHz, $CDCl_3$), δ (ppm): 138.9 (s, C-1 of 4-cyanophenyl), 136.8 (s, C-5), 135.6 (s, C-3), 134.9 (s, C-2), 132.6 (d, C-3/C-5 of 4-cyanophenyl), 128.1 (d, C-4), 125.3 (d, C-2/C-6 of 4-cyanophenyl), 119.1(s, CN), 109.7 (s, C-4 of 4-cyanophenyl), 13.7 (q, C-3-*C*H_3), 13.4 (q, C-2-*C*H_3).

MS-EI (*m/z*, %): 213 (M^+, 100), 212 (57), 198 (87), 86 (43), 84 (65).

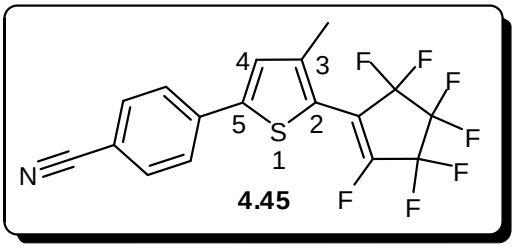
HRMS (EI): calcd for $C_{13}H_{11}NS$ (M^+) 213.0605; found, 213.0612.

FT–IR, ν_{max}: 3061, 2919, 2860, 2225, 1603, 1506 cm^{-1}.

4.6.13 Synthesis of 1-[5-(4-Cyanophenyl)-3-methyl-2-thienyl]perfluorocyclopentene (4.45)

2-Bromo-5-(4-cyanophenyl)-3-methylthiophene (**4.36**; 0.50 g; 1.8 mmol) was dissolved in freshly distilled THF (25 mL) and cooled to –78 ^{o}C under nitrogen. *n*-Butyllithium (1.31 mL of 1.60 M solution in hexane; 2.10 mmol) was added in a

dropwise manner. The reaction mixture was stirred for 1 h at that low temperature. Perfluorocyclopentene (**3.35**, 0.50 g 2.5 mmol) was added. The mixture was stirred at –78 ^{o}C for 2 h. Work up was carried out as described for the synthesis of 2-(4-pentanoylphenyl)-4-methylthiophene (**3.39**, Section 4.6.10). The crude product obtained was purified by column chromatography (silica gel; starting with just hexane then diethyl ether was gradually added to the eluent) and the isolated product was crystallized from diethyl ether to give **4.45** (0.50 g; 1.28 mmol; 71%) as a crystalline yellow material.



4.45

Mp: 114–115 ^{o}C.

^{1}H NMR (400 MHz, $CDCl_3$), δ (ppm): 7.59 (app. s, 4 H, H-2/H-3/H-5/H-6 of 4-cyanophenyl), 7.2 (s, 1 H, H-3), 2.24 (d, J = 3.0 Hz, 3 H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$), δ (ppm): 145.7 (s, C-5 of thienyl), 143.8 (s, C-3 of thienyl), 137.1 (s, C-1 of 4-cyanophenyl), 132.9 (d, C-3 and C-5 of 4-cyanophenyl), 128.8 (d, C-4 of thienyl), 126.3 (d, C-2 and C-6 of 4-cyanophenyl), 118.4 (s, CN), 111.9 (s, C-4 of 4-cyanophenyl), 15.6 (q, CH_3).

^{19}F NMR (282.2 MHz, $CDCl_3$), δ (ppm): –107.7, –117.4, –124.3, –129.3.

MS-EI (*m/z*, %): 391 (M^+, 100), 86 (52), 84 (82).

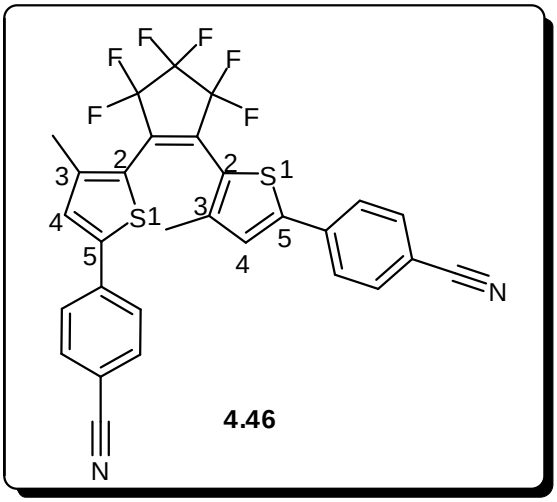
HRMS (EI): calcd for $C_{17}H_8F_7NS$ (M^+) 391.0265; found, 391.0266.

FT–IR, ν_{max}: 2223, 1682, 1605 cm^{-1}.

Selected crystallographic data: Empirical formula = $C_{17}H_8F_7NS$, formula weight = 391.30, temperature = 296(2) K, λ = 0.71073 Å, monoclinic, P21/a , unit cell dimensions: a = 10.9237(8) Å, b = 12.5421(10) Å, c = 13.0352(9) Å, α = 90°, β = 112.043(5) °, γ = 90°, V = 1655.4(2) $Å^3$, Z = 4, density (calculated) = 1.570 Mg/m^3, absorption coefficient = 0.269 mm^{-1}, F(000) = 784, crystal size = 0.40 x 0.30 x 0.06 mm^3, theta range for data collection = 3.25 to 20.88°, Reflections collected = 5525, independent reflections = 1736 [R (int) = 0.0532], final R indices [I>2σ (I)] = R1 = 0.0896, wR2 = 0.2456, R indices (all data) = R1 = 0.1096, wR2 = 0.2670, extinction coefficient = 0.059(11)·

4.6.14 Synthesis of 1,5-*Bis*[5-(4-cyanophenyl)-3-methyl-2-thienyl]perfluorocyclopentene (4.46)

2-Bromo-5-(4-cyanophenyl)-3-methylthiophene (0.50 g; 1.80 mmol) was dissolved in freshly distilled THF (25 mL) and cooled to –78 °C under nitrogen. *n*-Butyllithium (1.31 mL of 1.60 M solution in hexane; 2.10 mmol) was added in a dropwise manner. The reaction mixture was stirred for 1 h at that low temperature. Perfluorocyclopentene (0.90 mmol) was added and the mixture was stirred at –78 °C for 2 h and then at room temperature for 16 h. Workup was carried out as described for the synthesis 2-(4-pentanoylphenyl)-4-methylthiophene (**3.39**, Section 4.6.10). The crude product obtained was purified as described for compound **4.45** (Section 4.6.13). Compound **4.46** (0.26 g; 0.45 mmol; 50%) was obtained as an orange crystalline material.



4.46

Mp: 214–1215 °C.

^{1}H NMR (400 MHz, $CDCl_3$), δ (ppm): 7.6 (app. s, 8 H, 2 × H-2/H-3/H-5/H-6 of 4-cyanophenyl), 7.1 (s, 2 H, 2 × H-4), 1.8 (s, 6 H, 2 × CH_3).

^{13}C NMR (100 MHz, CDCl3), δ (ppm): 145.5 (s, C-5 of thienyl), 142.7 (s, C-3 of thienyl), 137.2 (s, C-1 of 4-cyanophenyl), 132.9 (d, C-3 and C-5 of 4-cyanophenyl), 128.5 (d, C-4 of thienyl), 126.2 (d, C-2/C-6 of 4-cyanophenyl), 124.4 (s, C-1/C-2 of hexafluorocyclopentenyl), 118.5 (s, CN), 111.7 (s, C-4 of 4-cyanophenyl), 15.6 (q, CH_3).

^{19}F NMR (282.2 MHz, $CDCl_3$), δ (ppm): –108.9, –140.9.

MS-EI (*m/z*, %): 570 (M^+, 100), 388 (40), 368 (99), 348 (57), 328 (40), 268 (53), 146 (25).

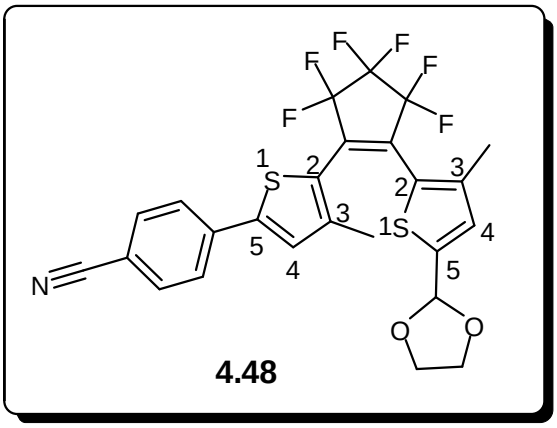
HRMS (EI): calcd for $C_{29}H_{16}F_6N_2S_2$ (M^+) 570.0664; found, 570.0659.

FT–IR, ν_{max}: 2227, 1604 cm^{-1}.

Selected crystallographic data: Empirical formula = $C_{29.5}H_{16.5}Cl_{1.5}F_6N_2S_2$, Formula weight = 630.24,temperature = 293(2) K, wavelength = 0.71073 Å, monoclinic, space group C2/c, unit cell dimensions a = 18.4237(4) Å, b = 15.7594(6) Å, c = 20.9299(7) Å, α = 90°, β = 113.280(2)°, γ = 90°, volume = 5582.2(3) $Å^3$, Z = 8, density (calculated) = 1.500 Mg/m^3, absorption coefficient = 0.398 mm^{-1}, F(000) = 2552, theta range for data collection = 2.79 to 27.44°, reflections collected = 10636, independent reflections = 6329 [R(int) = 0.0423], final R indices = [I>2σ (I)], R1 = 0.0658, wR2 = 0.1389, R indices (all data), R1 = 0.1053, wR2 = 0.1608.

4.6.15 Synthesis of 1-[5-(2-[1,3]Dioxolanyl)-3-methyl-2-thienyl]-2-[5-(4-cyanophenyl)-3-methyl-2-thienyl]perfluorocyclopentene (4.48)

Lithium 2,2,6,6-tetramethylpiperidide (LiTMP; 1.90 mmol) was prepared according to the procedure reported in Section 4.6.6. 2-(4-Methyl-2-thienyl)-1,3-dioxolane (**4.27**, 0.30 g; 1.8 mmol;) was dissolved in freshly distilled THF (5 mL) under nitrogen, cooled to –78 ^oC and transferred to the LiTMP solution by a double ended needle. The mixture was stirred at –78 ^oC for 1 h. 1-[5-(4-cyanophenyl)-3-methyl-2-thienyl]perfluorocyclopentene (**4.45**, 0.66 g; 1.7 mmol; dissolved in 5.0 mL of freshly distilled THF under nitrogen) was transferred slowly to the reaction mixture by a double ended needle. The reaction mixture was stirred at –78 ^oC for 2 h, then the cooling bath was removed, and the mixture was stirred at room temperature overnight. Work-up was carried out as described for the synthesis of 2-(4-pentanoylphenyl)-4-methylthiophene (**3.39**, Section 4.6.10). The crude product was purified by column chromatography (silica gel; hexane/diethyl ether in the ratio of 50/50 by volume) and the isolated product was washed with hexane and crystallized from diethyl ether to give **4.48** (0.62 g; 1.14 mmol; 68%) as a light brown crystalline material.



4.48

Mp: 142–143 ^{o}C.

^{1}H NMR (400 MHz, $CDCl_3$), δ (ppm): 7.62–7.57 (m, 4 H, H-2/H-3/H-5/H-6 of 4-cyanophenyl), 7.09 (s, 1 H, H-4 of 4-cyanophenyl substituted thienyl), 6.85 (s, 1 H, H-4 of 1,3-dioxolan-2-yl substituted thienyl), 5.97 (s, 1 H, CH of 1,3-dioxolan-2-yl), 4.07–3.93 (m, 4 H, 2 × CH_2 of 1,3-dioxolan-2-yl), 1.73 (s, 3 H, CH_3), 1.71 (s, 3 H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$), δ (ppm): 146.1 (s), 145.2 (s), 142.6 (s), 141.1(s), 137.3 (s), 132.9 (d, C-3 and C-5 of 4-cyanophenyl), 129.4 (d), 128.4 (d), 126.1 (d, C-2/ C-6 of 4-cyanophenyl), 124.4 (s), 123.5 (s), 118.6 (s, CN), 111.6 (s), 99.7 (d, C-2 of 1,3-dioxolan-2-yl), 65.4 (t, C-4/C-5 of 1,3-dioxolan-2-yl), 15.5 (q, CH_3), 15.4 (q, CH_3).

^{19}F NMR (282.2 MHz, $CDCl_3$), δ (ppm): –108.8, –109.2, –131.0.

MS-EI (*m/z*, %): 541 (M^+, 40), 469 (84), 465 (49), 64 (100).

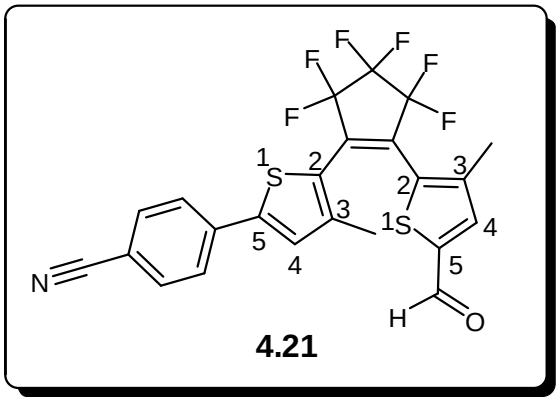
HRMS (EI): calcd for $C_{19}H_{13}F_6NO_2S_2$ 465.0295; found, 465.0292.

FT–IR, ν_{max}: 2892, 2227, 1604 cm^{-1}.

Selected crystallographic data: Empirical formula = $C_{25}H_{17}F_6NO_2S_2$, formula weight = 541.52, temperature = 150(2) K, wavelength = 0.71073 Å, crystal system = monoclinic, space group = P21/a, unit cell dimensions: a = 8.7227(3) Å, b = 12.4633(5) Å, c = 21.7574(10) Å, α = 90°, β = 94.108(2) °, γ = 90°, volume = 2359.25(17) Å3, Z = 4, density (calculated) = 1.525 Mg/m3, absorption coefficient = 0.298 mm-1, F(000) = 1104, crystal size = 0.40 x 0.35 x 0.05 mm^3, theta range for data collection = 2.49 to 20.82°, reflections collected = 4754, independent reflections = 2457 [R (int) = 0.0424], final R indices [I>2σ (I)] = R1 = 0.0869, wR2 = 0.2143, R indices (all data) = R1 = 0.1004, wR2 = 0.2218, extinction coefficient = 0.016(2).

4.6.16 Synthesis of 1-[5-(Formyl)-3-methyl-2-thienyl]-2-[5-(4-cyanophenyl)-3-methyl-2-thienyl]perfluorocyclopentene (4.21)

Compound **4.47** (0.25 g; 0.46 mmol) was dissolved in THF (5 mL) and a solution of aqueous HCl (10 %, 5 mL) was added and then the reaction mixture was stirred for 16 h at room temperature. The mixture was neutralized with solid sodium hydrogen carbonate and extracted with ethyl acetate (4 × 30 mL). The combined organic layer was washed with brine (50 mL) and dried over anhydrous magnesium sulfate. Solvent was evaporated under vacuum to get a yellow solid which upon crystallization from diethyl ether gave **4.21** (0.21 g; 0.42 mmol; 92%) as a yellow crystalline material.



4.21

Mp: 192–193 ^{o}C.

^{1}H NMR (400 MHz, $CDCl_3$), δ (ppm): 9.8 (1 H, CHO), 7.62–7.57 (m, 4 H, H2/H3/H5/H6 of 4-cyanophenyl), 7.46 (s, 1 H, H4 of formyl substituted thienyl), 7.11 (s, 1 H, H-4 of 4-cyanophenyl substituted thienyl), 1.85 (s, 3H, CH_3), 1.79 (s, 3H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$), δ (ppm): 182.4 (d, CHO), 146.1 (s), 145.5 (s), 143.0 (s), 141.8 (s), 137.9 (d), 137.0 (s), 132.9 (d, C-3/C-5 of 4-cyanophenyl substituted thienyl), 131.8 (s), 128.6 (d), 126.2 (d, C-2/C-6 of 4-cyanophenyl substituted thienyl), 123.5 (s), 118.4 (s, CN), 112.0 (s), 15.6 (q, CH_3), 15.2 (q, CH_3).

^{19}F NMR (282.2 MHz, $CDCl_3$), δ (ppm): –108.9, –109.3, –131.1.

MS-EI (*m/z*, %): 497 (M^+, 100), 355 (10), 218 (8), 149 (15).

HRMS (EI): calcd for $C_{23}H_{13}F_6NOS_2$ (M^+) 497.0343; found, 497.0353.

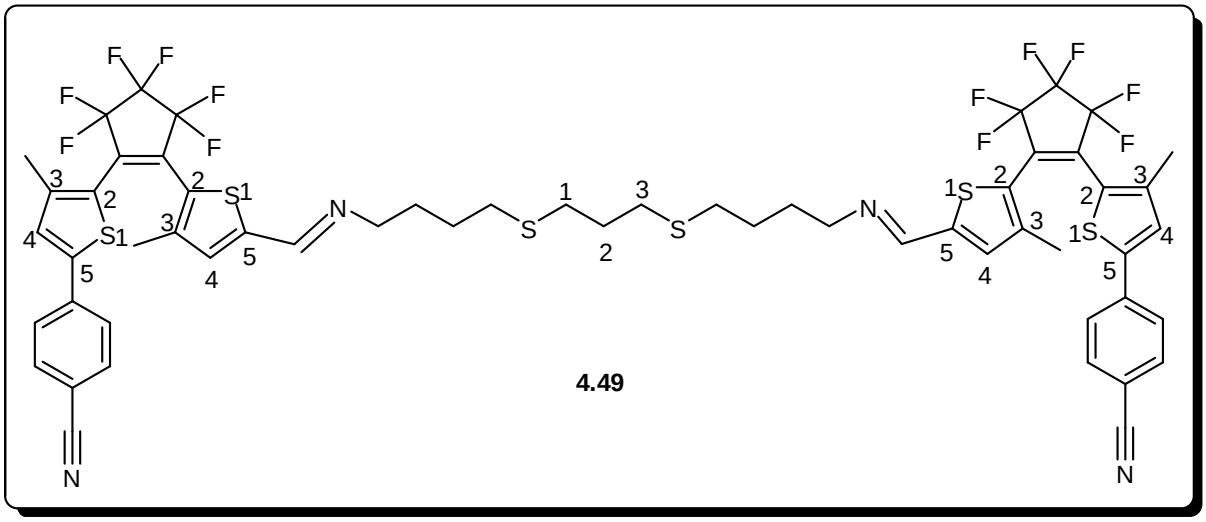
FT–IR, ν_{max}: 2959, 2226, 1674 cm^{-1}.

Selected crystallographic data: Empirical formula = C_{23} H_{13} F_6 N O S_2, formula weight = 497.46, temperature = 293(2) K, wavelength = 0.71073 Å, crystal system = monoclinic, space group P21/a, unit cell dimensions:a = 8.6773(7) Å a = 90°, b = 12.7605(11) Å, c = 20.1076(11) Å, α = 90°, β = 98.733(4)°, γ = 90°, volume = 2200.6(3) Å^3, Z = 4, density

(calculated) = 1.501 Mg/m^{3,} absorption coefficient = 0.309 mm$^{-1,}$ F(000) = 1008, theta range for data collection 1.02 to 20.82°, reflections collected 4474, independent reflections 2306 [R(int) = 0.1071], final R indices [I>2σ (I)] = R1 = 0.1131, wR2 = 0.2766, R indices (all data) = R1 = 0.1957, wR2 = 0.3313, extinction coefficient = 0.008(3).

4.6.17 Synthesis of 1,3-*Bis*[4-(*N*-(3-methyl-2-(2-(5-(4-cyanophenyl)-3-methyl-2-thienyl)-3,3,4,4,5,5-hexafluorocyclopenten-1-yl)-5-thienylmethylidene)aminobutylthio]propane (4.49)

In a 10 mL microwave vial charged with a magnetic bar were placed compounds **4.21** (40 mg; 0.080 mmol) and **4.18** (12 mg; 0.048 mmol). DCM (2 mL) was added to dissolve the mixture and dry HCl (0.01 mL of 1 M solution in diethyl ether, 0.01 mmol) was then added. The vial was sealed and subjected to microwave irradiation at 100 ºC for 30 min. The mixture was decanted into a 50 mL round bottomed flask and the solvent was evaporated under reduced pressure to give **4.49** (54.0 mg; 0.045 mmol; 93%) as a brownish yellow solid material.



4.49

Mp: 142–144 ^{o}C.

^{1}H NMR (500 MHz, $CDCl_3$), δ (ppm): 8.20 (s, 2 H, 2 × CH=N), 7.63–7.55 (m, 8 H, 2 × H2/H3/H5/H6 of 4-cyanophenyl), 7.10 (s, 2 H, 2 × H-4 of imino substituted thienyl), 6.97 (s, 2 H, 2 × H-4 of 4-cyanophenyl substituted thienyl), 3.52 (t, J = 6.5 Hz, 4 H, 2 × CH_2N), 2.54 (t, J = 7.2 Hz, 4 H, $CH_2SCH_2CH_2CH_2SCH_2$), 2.48 (t, J = 7.2 Hz, 4 H, $SCH_2CH_2CH_2S$), 1.81–1.69 (m, 18 H, 2 × $CH_2CH_2CH_2N$, $SCH_2CH_2CH_2S$ and 4 × CH_3), 1.61–1.54 (m, 4 H, 2 × CH_2CH_2N).

^{13}C NMR (125 MHz, $CDCl_3$), δ (ppm): 153.3 (d, CHN), 145.6 (s), 145.4 (s), 142.7 (s), 141.3 (s), 137.2 (d), 132.9 (d, , C-3/C-5 of 4-cyanophenyl), 132.8 (d), 128.5 (d), 126.2 (d, C-2/C-6 of 4-cyanophenyl), 125.6 (s), 124.3 (s), 118.5 (s, CN), 111.8 (s), 60.9 (t, CH_2N), 32.0 (t, $CH_2CH_2CH_2CH_2N$), 31.0 (t, $SCH_2CH_2CH_2S$), 30.3 (t, CH_2CH_2N), 29.4 (t, $SCH_2CH_2CH_2S$), 27.4 (t, $CH_2CH_2CH_2N$), 15.6 (q, CH_3), 15.4 (q, CH_3).

^{19}F NMR (282.2 MHz, $CDCl_3$), δ (ppm): –108.9, –131.0.

MALDI-TOF (*m/z*, %): 1210.2 (M^+ + 1, 50), 1209.2 (M^+, 70), 1208.2 (M^+ – 1, 100)

MS-EI (*m/z*, %): 583 (62), 550 (63), 509 (100), 482 (52).

HRMS (EI): calcd for $C_{27}H_{21}F_6N_2S_3$ 583.0771; found, 583.0768.

FT–IR, ν_{max}: 2923, 2856, 2226, 1631 cm^{-1}.

4.7 References

1. Wanichacheva, N.; Watpathomsub, S.; Lee, S. V.; Grudpan, K. *Molecules* **2010**, *15*, 1798–1810.
2. Kürti, L.; Czakó, B. *Strategic Applications of Named Reactions in Organic Synthesis*, Elsevier Academic Press, Burlington MA, USA, 2005.
3. (a) Kodani, T.; Matsuda, K.; Yamada, T.; Kobatake, S.; Irie, M. *J. Am. Chem. Soc.* **2000,** *122,* 9631–9637. (b) Aubert, V.; Guerchais, V.; Ishow, E.; Hoang–Thi, K.; Ledoux, I.; Nakatani, K.; Bozec, H. L. *Angew. Chem. Int. Ed.* **2008**, *47*, 577 –580. (c) Sevez, G.; Pozzo, J.–L. *Dyes and Pigments* **2011**, *89*, 246–253.
4. Pu, S.; Liu, W.; Liu, G. *Dyes and Pigments* **2010**, *87*, 1–9.
5. Smith, K.; Barratt, M. L. *J. Org. Chem.* **2007**, *72*, 1031–1034.
6. (a). Gallagher, Jr. B. M.; Zhao,H.; Pesant, M.; Fang, F. G. *Tetrahedron Lett.* **2005**, *46*, 923–926. (b) Marson, C. M.; Pucci, S. *Tetrahedron Lett*. **2004**, *45*, 9007–9010.
7. Zheng, C.; Pu, S.; Xu, J.; Luo, M.; Huang, D.; Shen, L. *Tetrahedron* **2007**, *63*, 5437–5449.
8. Clayden, J.; Greeves, N.; Warren, S.; Wothers, P. *Organic Chemistry*, Oxford University Press, New York, USA, 2008.
9. Molander, G. A.; Canturk, B.; Kennedy, L. E. *J. Org. Chem.* **2009**, *74*, 973–980.
10. Dong, J. J.; Roy, D.; Roy, R. J.; Ionita, M.; Doucet, H. *Synthesis* **2011**, 3530–3546.
11. Takahashi, K.; Suzuki, T.; Akiyama, K.; Ikegami, Y.; Fukazawat Y. *J. Am. Chem. Soc.* **1991**, *113*, 4576–4583.
12. Irie, M.; Sakemura, K.; Okinaka, M.; Uchida, K. *J. Org. Chem.* **1995**, *60*, 8305–8309.

13. See for example: (a) Uchida, K.; Matsuoka, T.; Kobatake, S.; Yamaguchi, T.; Iri, M. *Tetrahedron* **2001**, *57*, 4559–4565. (b) Pu, S.; Fan, C.; Miao, W.; Liu, G. *Dyes and Pigments* **2010**, *84*, 25–35. (c) Boyer, J.–C.; Carling, C.–J.; Gates, B. D.; Branda, N. R. *J. Am. Chem. Soc.* **2010**, *132*, 15766–15772. (d) Yoshida, J.; Kim, H.; Nagaki, A. *ChemSusChem* **2011**, *4*, 331–340.

14. (a) Uchida, K.; Irie, M. *Chem. Lett.* **1995**, 969–970. (b) Sun, F.; Zhang, F.; Guo, H.; Zhou, X.; Wang, R.; Zhao, F. *Tetrahedron* **2003**, *59*, 7615–7621.

15. See for example: See for example: (a) Kobatake, S.; Terakawa, Y.; Imagawa, H. *Tetrahedron* **2009**, *65*, 6104–6108. (b) Cui, S.; Pu, S.; Liu, W.; Liu, G. *Dyes Pigments* **2011**, *91*, 435–441. (c) Liu, G.; Liu, M.; Pu, S.; Fan, C.; Cui, S. *Dyes Pigments* **2012**, *95*, 553–562. (d) Pu, S.; Wang, R.; Liu, G.; Liu, W.; Cui, S.; Yan, P. *Dyes Pigments* **2012**, *94*, 195–206.

16. Hegasy, A. S. PhD Thesis, *Directed Lithiation of Substituted Benzylamines*, Cardiff University, **2009**.

17. Joule, J. A.; Mills, K. *Heterocyclic Chemistry*, 5th ed., Wiley, Chichester, UK, 2010.

18. (a) Brendle, J. J.; Outlaw, A.; Kumar, A.; Boykin, D. W.; Patrick, D. A.; Tidwell, R. R.; Werbovetz K. A. *Antimicrob. Agents Chemother.* **2002**, *46*, 797–807. (b) Chaires, J. B.; Ren, J.; Hamelberg, D.; Kumar, A.; Pandya, V.; Boykin, D. W.; Wilson, W. D. *J. Med. Chem.* **2004**, *47*, 5729–5742.

19. Morimitsu, K.; Shibata, K.; Kobatake, S.; Irie, M. *J. Org. Chem.* **2002**, *67*, 4574–4578.

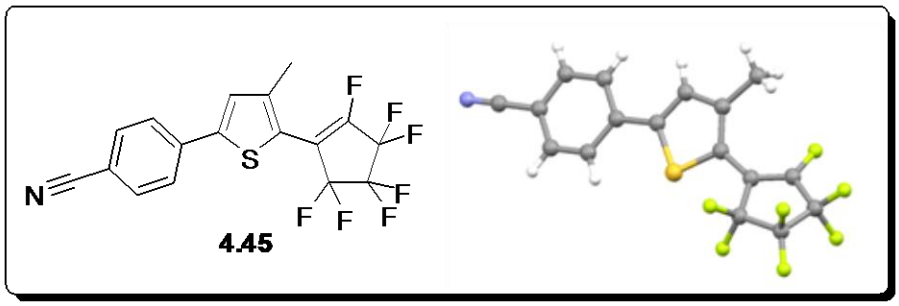
20. Barrat, M. L. PhD Thesis, *Synthesis of a Photoswitchable Acceptor Molecule*, Swansea University, **2006**.

Appendix

X-Ray Data Tables

X-Ray Data Tables

Table A1: Crystal data and structure refinement for 4.45.



Identification code	4.45	
Empirical formula	C_{17} H_8 F_7 N S	
Formula weight	391.30	
Temperature	296(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P21/a	
Unit cell dimensions	a = 10.9237(8) Å	α= 90°.
	b = 12.5421(10) Å	β= 112.043(5)°.
	c = 13.0352(9) Å	γ = 90°.
Volume	1655.4(2) $Å^3$	
Z	4	
Density (calculated)	1.570 Mg/m^3	
Absorption coefficient	0.269 mm^{-1}	
F(000)	784	
Crystal size	0.40 x 0.30 x 0.06 mm^3	
Theta range for data collection	3.25 to 20.88°.	
Index ranges	-10<=h<=10, -12<=k<=12, -13<=l<=13	
Reflections collected	5525	
Independent reflections	1736 [R(int) = 0.0532]	
Completeness to theta = 20.88°	99.2 %	
Max. and min. transmission	0.9840 and 0.9001	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	1736 / 0 / 237	
Goodness-of-fit on F^2	1.037	
Final R indices [I>2sigma(I)]	R1 = 0.0896, wR2 = 0.2456	
R indices (all data)	R1 = 0.1096, wR2 = 0.2670	
Extinction coefficient	0.059(11)	
Largest diff. peak and hole	0.787 and -0.302 e.$Å^{-3}$	

Table A2: Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^{2}x 10^3) for 4.45. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
C(1)	6329(8)	-1338(6)	5376(7)	86(2)
C(2)	7139(6)	-1001(6)	4782(6)	74(2)
C(3)	7933(9)	-1708(6)	4526(7)	101(2)
C(4)	8708(9)	-1386(6)	3992(7)	97(2)
C(5)	8737(6)	-343(5)	3677(5)	68(2)
C(6)	7956(7)	379(6)	3962(7)	94(2)
C(7)	7163(7)	47(6)	4521(7)	95(2)
C(8)	9572(6)	27(5)	3095(5)	69(2)
C(9)	9764(7)	1017(6)	2820(6)	81(2)
C(10)	10630(7)	1122(5)	2253(6)	80(2)
C(11)	11111(7)	144(5)	2101(5)	76(2)
C(12)	11020(9)	2195(6)	1926(8)	118(3)
C(13)	12022(7)	-109(6)	1577(5)	77(2)
C(14)	13012(9)	-982(7)	1942(7)	99(2)
C(15)	13903(13)	-841(9)	1274(9)	126(3)
C(16)	13222(10)	-76(8)	397(7)	112(3)
C(17)	12137(9)	329(7)	697(7)	103(2)
N(1)	5687(7)	-1610(6)	5840(7)	112(2)
F(1)	13719(5)	-961(4)	3035(4)	126(2)
F(2)	12460(7)	-1947(4)	1762(5)	152(2)
F(3)	14409(9)	-1653(6)	1081(6)	192(3)
F(4)	15044(7)	-223(9)	1952(6)	200(3)
F(5)	12787(7)	-609(8)	-571(5)	210(4)
F(6)	13974(7)	692(5)	247(7)	176(3)
F(7)	11332(6)	1052(5)	49(4)	143(2)
S(1)	10478(2)	-860(1)	2668(2)	83(1)

Table A3: Bond lengths [Å] and angles [°] for 4.45.

C(1)-N(1)	1.137(9)
C(1)-C(2)	1.441(12)
C(2)-C(7)	1.361(10)
C(2)-C(3)	1.366(10)
C(3)-C(4)	1.344(10)
C(3)-H(3)	0.9300
C(4)-C(5)	1.375(10)
C(4)-H(4)	0.9300
C(5)-C(6)	1.387(9)
C(5)-C(8)	1.464(9)
C(6)-C(7)	1.389(10)
C(6)-H(6)	0.9300
C(7)-H(7)	0.9300
C(8)-C(9)	1.331(9)
C(8)-S(1)	1.715(7)
C(9)-C(10)	1.407(11)
C(9)-H(9)	0.9300
C(10)-C(11)	1.379(9)
C(10)-C(12)	1.520(10)
C(11)-C(13)	1.438(9)
C(11)-S(1)	1.730(7)
C(12)-H(12A)	0.9600
C(12)-H(12B)	0.9600
C(12)-H(12C)	0.9600
C(13)-C(17)	1.319(10)
C(13)-C(14)	1.486(10)
C(14)-F(2)	1.334(9)
C(14)-F(1)	1.343(9)
C(14)-C(15)	1.540(13)
C(15)-F(3)	1.229(11)
C(15)-F(4)	1.452(13)
C(15)-C(16)	1.463(13)
C(16)-F(6)	1.328(10)
C(16)-F(5)	1.347(10)
C(16)-C(17)	1.470(12)
C(17)-F(7)	1.323(9)

N(1)-C(1)-C(2)	179.5(9)
C(7)-C(2)-C(3)	119.5(7)
C(7)-C(2)-C(1)	119.4(7)
C(3)-C(2)-C(1)	121.0(7)
C(4)-C(3)-C(2)	120.8(7)
C(4)-C(3)-H(3)	119.6
C(2)-C(3)-H(3)	119.6
C(3)-C(4)-C(5)	122.0(7)
C(3)-C(4)-H(4)	119.0
C(5)-C(4)-H(4)	119.0
C(4)-C(5)-C(6)	117.1(7)

C(4)-C(5)-C(8)	123.0(6)
C(6)-C(5)-C(8)	119.9(6)
C(5)-C(6)-C(7)	120.8(7)
C(5)-C(6)-H(6)	119.6
C(7)-C(6)-H(6)	119.6
C(2)-C(7)-C(6)	119.6(7)
C(2)-C(7)-H(7)	120.2
C(6)-C(7)-H(7)	120.2
C(9)-C(8)-C(5)	128.8(6)
C(9)-C(8)-S(1)	110.4(6)
C(5)-C(8)-S(1)	120.7(5)
C(8)-C(9)-C(10)	115.7(6)
C(8)-C(9)-H(9)	122.1
C(10)-C(9)-H(9)	122.1
C(11)-C(10)-C(9)	111.1(6)
C(11)-C(10)-C(12)	125.8(7)
C(9)-C(10)-C(12)	123.0(7)
C(10)-C(11)-C(13)	129.4(6)
C(10)-C(11)-S(1)	110.5(5)
C(13)-C(11)-S(1)	120.1(5)
C(10)-C(12)-H(12A)	109.5
C(10)-C(12)-H(12B)	109.5
H(12A)-C(12)-H(12B)	109.5
C(10)-C(12)-H(12C)	109.5
H(12A)-C(12)-H(12C)	109.5
H(12B)-C(12)-H(12C)	109.5
C(17)-C(13)-C(11)	129.0(7)
C(17)-C(13)-C(14)	106.8(7)
C(11)-C(13)-C(14)	124.1(6)
F(2)-C(14)-F(1)	104.2(7)
F(2)-C(14)-C(13)	112.7(8)
F(1)-C(14)-C(13)	112.7(6)
F(2)-C(14)-C(15)	110.2(7)
F(1)-C(14)-C(15)	111.4(8)
C(13)-C(14)-C(15)	105.8(7)
F(3)-C(15)-F(4)	102.6(10)
F(3)-C(15)-C(16)	121.3(9)
F(4)-C(15)-C(16)	101.2(9)
F(3)-C(15)-C(14)	116.7(9)
F(4)-C(15)-C(14)	107.3(8)
C(16)-C(15)-C(14)	105.8(9)
F(6)-C(16)-F(5)	104.0(8)
F(6)-C(16)-C(15)	115.5(9)
F(5)-C(16)-C(15)	107.7(9)
F(6)-C(16)-C(17)	113.1(8)
F(5)-C(16)-C(17)	112.6(8)
C(15)-C(16)-C(17)	104.1(8)
C(13)-C(17)-F(7)	125.6(9)
C(13)-C(17)-C(16)	115.9(8)
F(7)-C(17)-C(16)	118.4(8)

C(8)-S(1)-C(11)	92.2(3)

Symmetry transformations used to generate equivalent atoms:

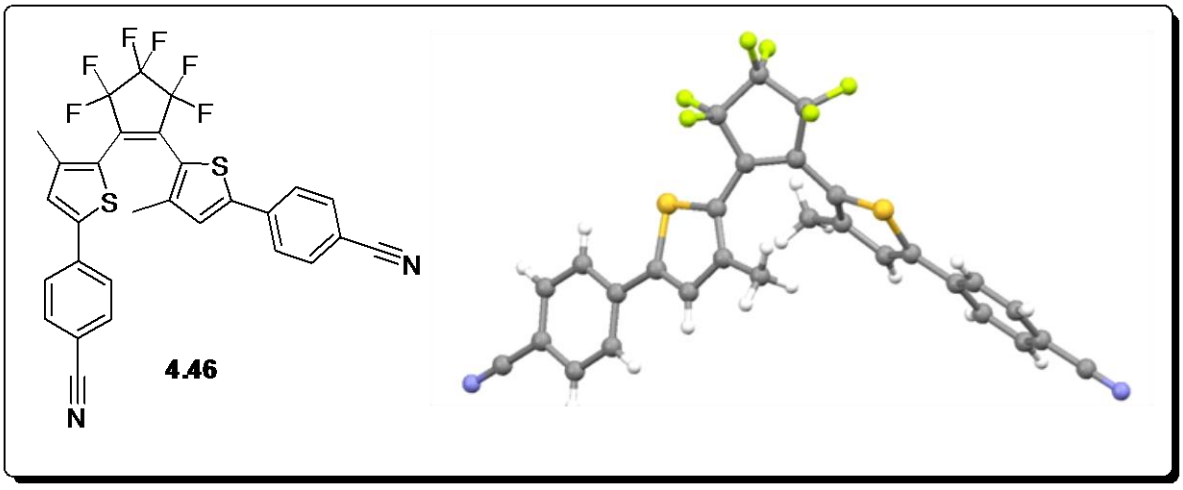
Table A4: Anisotropic displacement parameters ($Å^2 x\ 10^3$)for 4.45. The anisotropic displacement factor exponent takes the form: $-2\pi^2$ [h2a*$^2U^{11}$ + ... + 2 h k a* b* U^{12}]

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C(1)	76(5)	73(5)	109(6)	-3(4)	36(5)	1(4)
C(2)	68(4)	64(5)	88(5)	-5(3)	27(4)	-6(3)
C(3)	125(6)	66(5)	130(6)	2(4)	70(6)	2(5)
C(4)	120(6)	66(5)	130(6)	-10(4)	74(6)	4(4)
C(5)	67(4)	55(4)	76(4)	-4(3)	19(3)	-2(3)
C(6)	87(5)	63(5)	137(7)	18(4)	47(5)	7(4)
C(7)	85(5)	72(6)	139(7)	6(5)	54(5)	11(4)
C(8)	71(4)	61(4)	71(4)	-4(3)	19(3)	0(3)
C(9)	80(4)	61(5)	104(5)	-9(4)	36(4)	5(3)
C(10)	88(5)	63(5)	82(4)	-1(4)	23(4)	-7(4)
C(11)	82(4)	70(5)	75(4)	-4(3)	28(4)	-8(4)
C(12)	139(7)	79(6)	150(7)	17(5)	71(6)	-7(5)
C(13)	87(5)	81(5)	61(4)	2(3)	26(4)	-5(4)
C(14)	127(7)	86(6)	101(6)	2(4)	61(6)	15(5)
C(15)	169(10)	104(7)	135(9)	10(6)	91(8)	21(7)
C(16)	134(8)	118(8)	96(7)	-8(6)	55(6)	-6(6)
C(17)	111(6)	108(6)	83(5)	13(5)	29(5)	19(5)
N(1)	106(5)	92(5)	157(7)	10(4)	70(5)	-5(4)
F(1)	139(4)	146(4)	93(4)	19(3)	44(3)	44(3)
F(2)	207(6)	82(4)	197(6)	-6(3)	110(5)	-5(4)
F(3)	280(9)	149(6)	227(7)	50(5)	186(7)	81(6)
F(4)	123(5)	324(11)	146(5)	-9(6)	44(4)	-23(6)
F(5)	173(6)	353(11)	94(4)	-67(5)	40(4)	36(6)
F(6)	182(6)	134(5)	268(9)	27(5)	148(6)	-13(4)
F(7)	160(5)	174(5)	92(3)	41(3)	44(3)	40(4)
S(1)	104(2)	67(1)	88(2)	-2(1)	46(1)	3(1)

Table A5: Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^{2}x 10^3) for 4.45.

	x	y	z	U(eq)
H(3)	7937	-2421	4723	121
H(4)	9242	-1883	3831	117
H(6)	7963	1094	3777	113
H(7)	6650	539	4716	114
H(9)	9353	1602	2991	97
H(12A)	11896	2149	1922	177
H(12B)	11001	2728	2449	177
H(12C)	10411	2387	1201	177

Table A6: Crystal data and structure refinement for 4.46.



Identification code	4.46	
Empirical formula	$C_{29.50}$ $H_{16.50}$ $Cl_{1.50}$ F_6 N_2 S_2	
Formula weight	630.24	
Temperature	293(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	C2/c	
Unit cell dimensions	a = 18.4237(4) Å	α = 90°.
	b = 15.7594(6) Å	β = 113.280(2)°.
	c = 20.9299(7) Å	γ = 90°.
Volume	5582.2(3) Å^3	
Z	8	
Density (calculated)	1.500 Mg/m^3	

Absorption coefficient	0.398 mm^{-1}
F(000)	2552
Crystal size	? x ? x ? mm^3
Theta range for data collection	2.79 to 27.44°.
Index ranges	-23<=h<=23, -18<=k<=20, -27<=l<=27
Reflections collected	10636
Independent reflections	6329 [R(int) = 0.0423]
Completeness to theta = 27.44°	99.4 %
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	6329 / 782 / 509
Goodness-of-fit on F^2	1.046
Final R indices [I>2sigma(I)]	R1 = 0.0658, wR2 = 0.1389
R indices (all data)	R1 = 0.1053, wR2 = 0.1608
Largest diff. peak and hole	0.260 and -0.390 e.$Å^{-3}$

Table A7: Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for 4.46. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
C(1)	3329(2)	12411(2)	-422(2)	51(1)
C(2)	3946(2)	11825(2)	-11(2)	45(1)
C(3)	3842(2)	11334(2)	490(2)	57(1)
C(4)	4418(2)	10764(2)	874(2)	56(1)
C(5)	5113(1)	10683(2)	766(1)	39(1)
C(6)	5210(2)	11185(2)	257(1)	44(1)
C(7)	4638(2)	11755(2)	-128(2)	46(1)
C(8)	5731(1)	10084(2)	1177(1)	37(1)
C(9)	6481(1)	10002(2)	1202(1)	36(1)
C(10)	6944(1)	9371(2)	1671(1)	36(1)
C(11)	7776(2)	9167(2)	1770(2)	46(1)
C(12)	6525(1)	8969(2)	1999(1)	38(1)
C(13)	6803(2)	8294(2)	2521(1)	41(1)
C(14)	6331(4)	7513(4)	2523(4)	49(2)
C(15)	6927(4)	6864(3)	2962(3)	43(2)
C(16)	7601(3)	7418(4)	3459(4)	47(2)
C(17)	7490(2)	8253(2)	3090(1)	42(1)
F(1)	5925(3)	7240(2)	1872(2)	68(1)
F(2)	5789(2)	7683(2)	2786(3)	70(1)
F(3)	7181(2)	6402(2)	2561(2)	62(1)
F(4)	6628(2)	6334(3)	3290(2)	69(1)
F(5)	8304(2)	7038(2)	3589(3)	66(1)
F(6)	7555(5)	7465(6)	4081(3)	71(2)
C(13A)	6803(2)	8294(2)	2521(1)	41(1)
C(14A)	6315(6)	7490(7)	2331(7)	45(4)
C(15A)	6693(8)	6959(8)	2989(7)	67(5)

C(16A)	7531(8)	7328(7)	3340(8)	57(5)
C(17A)	7490(2)	8253(2)	3090(1)	42(1)
F(1A)	6321(6)	7074(5)	1771(4)	74(2)
F(2A)	5530(4)	7583(5)	2194(6)	86(3)
F(3A)	6727(6)	6133(5)	2874(6)	118(5)
F(4A)	6312(5)	7065(7)	3409(4)	111(4)
F(5A)	8070(6)	6908(5)	3171(5)	80(2)
F(6A)	7805(11)	7344(14)	4037(8)	100(6)
C(18)	8079(2)	8910(2)	3391(1)	40(1)
C(19)	7954(2)	9757(2)	3470(1)	40(1)
C(20)	7165(2)	10172(2)	3304(1)	46(1)
C(21)	8670(2)	10204(2)	3770(1)	43(1)
C(22)	9331(2)	9722(2)	3914(1)	45(1)
C(23)	10164(2)	9987(2)	4218(1)	45(1)
C(24)	10359(2)	10848(2)	4325(2)	57(1)
C(25)	11129(2)	11126(2)	4611(2)	55(1)
C(26)	11738(2)	10531(2)	4798(1)	51(1)
C(27)	11559(2)	9675(2)	4697(2)	56(1)
C(28)	10785(2)	9404(2)	4412(2)	52(1)
C(29)	12554(2)	10802(2)	5095(2)	58(1)
N(1)	2841(2)	12866(2)	-737(2)	66(1)
N(2)	13206(2)	11008(2)	5326(2)	71(1)
S(1)	5573(1)	9361(1)	1730(1)	42(1)
S(2)	9077(1)	8675(1)	3695(1)	49(1)
C(30)	4989(5)	12494(5)	2282(4)	56(3)
Cl(1)	4286(5)	11920(5)	2464(5)	81(2)
Cl(2)	5059(6)	13543(2)	2594(6)	81(3)
Cl(3)	5925(5)	12034(6)	2695(7)	96(4)
C(30A)	5104(8)	12081(8)	2273(8)	62(7)
Cl(1A)	4641(6)	11228(7)	2485(4)	108(4)
Cl(2A)	4438(6)	12929(9)	1955(6)	120(5)
Cl(3A)	5922(6)	12389(8)	3014(6)	80(4)

Table A8: Bond lengths [Å] and angles [°] for 4.46.

C(1)-N(1)	1.135(4)
C(1)-C(2)	1.453(4)
C(2)-C(3)	1.377(4)
C(2)-C(7)	1.395(4)
C(3)-C(4)	1.381(4)
C(4)-C(5)	1.392(4)
C(5)-C(6)	1.392(4)
C(5)-C(8)	1.468(3)
C(6)-C(7)	1.377(4)
C(8)-C(9)	1.367(3)
C(8)-S(1)	1.730(3)
C(9)-C(10)	1.421(3)
C(10)-C(12)	1.374(4)
C(10)-C(11)	1.499(3)
C(12)-C(13)	1.464(4)
C(12)-S(1)	1.731(2)
C(13)-C(17)	1.354(4)
C(13)-C(14)	1.509(7)
C(14)-F(1)	1.339(6)
C(14)-F(2)	1.345(6)
C(14)-C(15)	1.517(8)
C(15)-F(3)	1.329(6)
C(15)-F(4)	1.330(6)
C(15)-C(16)	1.537(8)
C(16)-F(6)	1.341(7)
C(16)-F(5)	1.354(5)
C(16)-C(17)	1.498(7)
C(17)-C(18)	1.451(4)
C(14A)-F(1A)	1.347(14)
C(14A)-F(2A)	1.367(12)
C(14A)-C(15A)	1.526(13)
C(15A)-F(3A)	1.330(13)
C(15A)-F(4A)	1.336(13)
C(15A)-C(16A)	1.538(13)
C(16A)-F(6A)	1.341(13)
C(16A)-F(5A)	1.352(13)
C(18)-C(19)	1.376(4)
C(18)-S(2)	1.732(3)
C(19)-C(21)	1.406(4)
C(19)-C(20)	1.504(4)
C(21)-C(22)	1.365(4)
C(22)-C(23)	1.470(4)
C(22)-S(2)	1.726(3)
C(23)-C(28)	1.397(4)
C(23)-C(24)	1.399(4)
C(24)-C(25)	1.375(4)
C(25)-C(26)	1.395(4)
C(26)-C(27)	1.385(5)

C(26)-C(29)	1.445(4)
C(27)-C(28)	1.379(4)
C(29)-N(2)	1.151(4)
C(30)-Cl(1)	1.741(7)
C(30)-Cl(3)	1.751(7)
C(30)-Cl(2)	1.763(8)
Cl(1)-Cl(3)#1	0.44(2)
Cl(1)-C(30)#1	1.524(12)
Cl(2)-Cl(2)#1	0.37(2)
Cl(2)-C(30)#1	1.681(9)
Cl(3)-Cl(1)#1	0.44(2)
Cl(3)-C(30)#1	1.851(13)
C(30A)-Cl(1A)	1.741(11)
C(30A)-Cl(3A)	1.751(11)
C(30A)-Cl(2A)	1.757(12)
Cl(1A)-Cl(1A)#1	1.30(2)
Cl(1A)-C(30A)#1	1.448(14)
Cl(1A)-Cl(3A)#1	2.159(17)
Cl(2A)-Cl(3A)#1	1.10(2)
Cl(2A)-C(30A)#1	2.007(16)
Cl(2A)-Cl(2A)#1	2.40(2)
Cl(3A)-Cl(2A)#1	1.10(2)
Cl(3A)-C(30A)#1	1.809(18)
Cl(3A)-Cl(1A)#1	2.159(17)
N(1)-C(1)-C(2)	179.0(4)
C(3)-C(2)-C(7)	120.1(2)
C(3)-C(2)-C(1)	119.7(3)
C(7)-C(2)-C(1)	120.2(3)
C(2)-C(3)-C(4)	120.2(3)
C(3)-C(4)-C(5)	120.7(3)
C(4)-C(5)-C(6)	118.4(2)
C(4)-C(5)-C(8)	120.9(3)
C(6)-C(5)-C(8)	120.7(2)
C(7)-C(6)-C(5)	121.2(3)
C(6)-C(7)-C(2)	119.4(3)
C(9)-C(8)-C(5)	128.3(2)
C(9)-C(8)-S(1)	110.31(19)
C(5)-C(8)-S(1)	121.34(19)
C(8)-C(9)-C(10)	114.5(2)
C(12)-C(10)-C(9)	111.4(2)
C(12)-C(10)-C(11)	125.3(2)
C(9)-C(10)-C(11)	123.3(2)
C(10)-C(12)-C(13)	127.5(2)
C(10)-C(12)-S(1)	111.73(19)
C(13)-C(12)-S(1)	120.8(2)
C(17)-C(13)-C(12)	128.4(2)
C(17)-C(13)-C(14)	107.3(3)
C(12)-C(13)-C(14)	124.2(3)
F(1)-C(14)-F(2)	105.9(5)
F(1)-C(14)-C(13)	110.5(5)

F(2)-C(14)-C(13)	111.1(5)
F(1)-C(14)-C(15)	112.3(6)
F(2)-C(14)-C(15)	111.3(6)
C(13)-C(14)-C(15)	105.8(5)
F(3)-C(15)-F(4)	107.7(5)
F(3)-C(15)-C(14)	109.8(5)
F(4)-C(15)-C(14)	112.8(6)
F(3)-C(15)-C(16)	110.3(5)
F(4)-C(15)-C(16)	113.3(5)
C(14)-C(15)-C(16)	103.0(5)
F(6)-C(16)-F(5)	104.5(5)
F(6)-C(16)-C(17)	113.8(6)
F(5)-C(16)-C(17)	114.7(5)
F(6)-C(16)-C(15)	110.2(6)
F(5)-C(16)-C(15)	109.8(6)
C(17)-C(16)-C(15)	104.0(4)
C(13)-C(17)-C(18)	128.8(2)
C(13)-C(17)-C(16)	112.6(3)
C(18)-C(17)-C(16)	118.5(3)
F(1A)-C(14A)-F(2A)	104.0(10)
F(1A)-C(14A)-C(15A)	111.2(10)
F(2A)-C(14A)-C(15A)	108.4(11)
F(3A)-C(15A)-F(4A)	108.4(11)
F(3A)-C(15A)-C(14A)	114.3(11)
F(4A)-C(15A)-C(14A)	110.8(11)
F(3A)-C(15A)-C(16A)	110.3(11)
F(4A)-C(15A)-C(16A)	109.2(10)
C(14A)-C(15A)-C(16A)	103.7(9)
F(6A)-C(16A)-F(5A)	107.1(12)
F(6A)-C(16A)-C(15A)	113.6(13)
F(5A)-C(16A)-C(15A)	113.1(12)
C(19)-C(18)-C(17)	127.8(2)
C(19)-C(18)-S(2)	111.5(2)
C(17)-C(18)-S(2)	120.7(2)
C(18)-C(19)-C(21)	111.6(2)
C(18)-C(19)-C(20)	125.9(2)
C(21)-C(19)-C(20)	122.4(2)
C(22)-C(21)-C(19)	114.7(3)
C(21)-C(22)-C(23)	128.7(3)
C(21)-C(22)-S(2)	110.4(2)
C(23)-C(22)-S(2)	120.9(2)
C(28)-C(23)-C(24)	117.6(3)
C(28)-C(23)-C(22)	122.2(3)
C(24)-C(23)-C(22)	120.2(3)
C(25)-C(24)-C(23)	122.2(3)
C(24)-C(25)-C(26)	119.1(3)
C(27)-C(26)-C(25)	119.7(3)
C(27)-C(26)-C(29)	119.8(3)
C(25)-C(26)-C(29)	120.5(3)
C(28)-C(27)-C(26)	120.7(3)

C(27)-C(28)-C(23)	120.7(3)
N(2)-C(29)-C(26)	179.0(4)
C(8)-S(1)-C(12)	92.02(12)
C(22)-S(2)-C(18)	91.78(13)
Cl(1)-C(30)-Cl(3)	110.4(5)
Cl(1)-C(30)-Cl(2)	111.0(5)
Cl(3)-C(30)-Cl(2)	107.0(6)
Cl(3)#1-Cl(1)-C(30)#1	114.3(17)
Cl(3)#1-Cl(1)-C(30)	98(2)
C(30)#1-Cl(1)-C(30)	31.0(6)
Cl(2)#1-Cl(2)-C(30)#1	96.9(7)
Cl(2)#1-Cl(2)-C(30)	71.1(6)
C(30)#1-Cl(2)-C(30)	30.1(6)
Cl(1)#1-Cl(3)-C(30)	52.5(14)
Cl(1)#1-Cl(3)-C(30)#1	68.8(18)
C(30)-Cl(3)-C(30)#1	28.7(5)
Cl(1A)-C(30A)-Cl(3A)	109.0(8)
Cl(1A)-C(30A)-Cl(2A)	110.2(9)
Cl(3A)-C(30A)-Cl(2A)	110.7(10)
Cl(1A)#1-Cl(1A)-C(30A)	#178.4(8)
Cl(1A)#1-Cl(1A)-C(30A)	54.6(7)
C(30A)#1-Cl(1A)-C(30A)	41.2(13)
Cl(1A)#1-Cl(1A)-Cl(3A)#1	108.0(6)
C(30A)#1-Cl(1A)-Cl(3A)#1	53.8(7)
C(30A)-Cl(1A)-Cl(3A)#1	54.0(7)
Cl(3A)#1-Cl(2A)-C(30A)	74.7(9)
Cl(3A)#1-Cl(2A)-C(30A)#1	60.5(6)
C(30A)-Cl(2A)-C(30A)#1	34.9(9)
Cl(3A)#1-Cl(2A)-Cl(2A)#1	105.0(9)
C(30A)-Cl(2A)-Cl(2A)#1	55.1(6)
C(30A)#1-Cl(2A)-Cl(2A)#1	45.9(6)
Cl(2A)#1-Cl(3A)-C(30A)	86.4(10)
Cl(2A)#1-Cl(3A)-C(30A)#1	69.6(8)
C(30A)-Cl(3A)-C(30A)#1	37.8(10)
Cl(2A)#1-Cl(3A)-Cl(1A)#1	120.0(8)
C(30A)-Cl(3A)-Cl(1A)#1	41.9(5)
C(30A)#1-Cl(3A)-Cl(1A)#1	51.1(5)

Table A9: Anisotropic displacement parameters ($Å^2 x\ 10^3$) for 4.46. The anisotropic displacement factor exponent takes the form: -2π [h2a*^{2}U^{11} + ... + 2 h k a* b* U^{12}]

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C(1)	40(2)	42(2)	59(2)	4(1)	8(1)	2(1)
C(2)	37(1)	35(1)	50(2)	0(1)	4(1)	1(1)

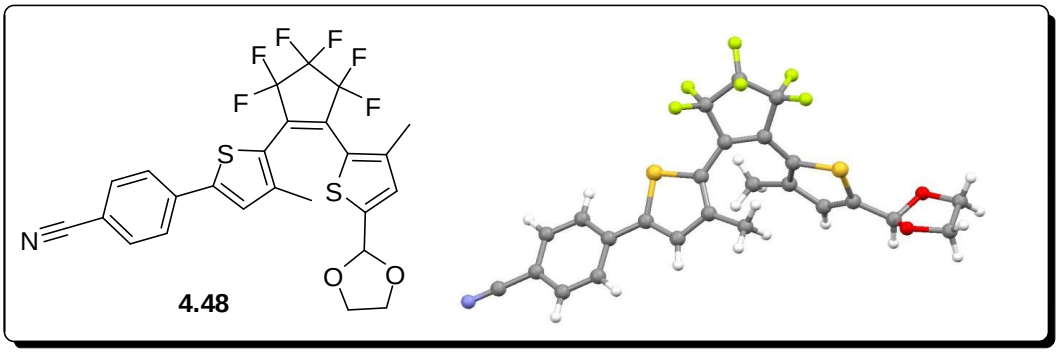
C(3)	35(1)	57(2)	75(2)	24(2)	18(1)	8(1)
C(4)	41(2)	58(2)	69(2)	24(2)	22(1)	10(1)
C(5)	33(1)	36(1)	40(2)	-3(1)	5(1)	-1(1)
C(6)	42(1)	40(2)	45(2)	2(1)	12(1)	4(1)
C(7)	44(2)	41(2)	47(2)	4(1)	11(1)	5(1)
C(8)	37(1)	33(1)	37(1)	0(1)	9(1)	-1(1)
C(9)	36(1)	34(1)	34(1)	0(1)	9(1)	-2(1)
C(10)	34(1)	34(1)	34(1)	-2(1)	8(1)	2(1)
C(11)	41(1)	51(2)	44(2)	6(1)	15(1)	4(1)
C(12)	36(1)	33(1)	41(2)	1(1)	12(1)	2(1)
C(13)	41(1)	34(1)	47(2)	4(1)	19(1)	4(1)
C(14)	46(4)	48(4)	47(4)	3(3)	11(3)	-2(3)
C(15)	51(3)	32(3)	46(3)	10(2)	19(2)	4(2)
C(16)	43(3)	41(4)	45(4)	-1(3)	5(3)	5(3)
C(17)	47(1)	35(1)	42(2)	5(1)	16(1)	8(1)
F(1)	68(3)	44(2)	60(3)	7(2)	-9(2)	-15(2)
F(2)	46(2)	65(2)	105(3)	20(2)	37(2)	3(1)
F(3)	68(2)	49(2)	58(2)	-9(1)	12(1)	7(1)
F(4)	74(2)	55(3)	71(3)	27(2)	21(2)	-9(2)
F(5)	50(2)	40(2)	89(3)	13(2)	7(2)	15(1)
F(6)	112(5)	55(3)	38(2)	11(2)	21(2)	-11(3)
C(13A)	41(1)	34(1)	47(2)	4(1)	19(1)	4(1)
C(14A)	37(7)	42(7)	54(8)	17(6)	18(6)	4(5)
C(15A)	78(9)	43(7)	77(9)	9(6)	28(7)	-3(6)
C(16A)	87(10)	23(6)	56(8)	17(6)	23(7)	16(6)
C(17A)	47(1)	35(1)	42(2)	5(1)	16(1)	8(1)
F(1A)	103(7)	46(4)	69(4)	-13(3)	31(5)	-24(4)
F(2A)	58(4)	68(4)	132(8)	33(5)	38(5)	0(3)
F(3A)	121(8)	40(4)	138(10)	23(6)	-7(8)	0(4)
F(4A)	110(6)	139(9)	95(6)	49(5)	50(5)	-15(5)
F(5A)	93(6)	47(4)	90(6)	15(4)	27(5)	26(4)
F(6A)	136(13)	70(7)	61(8)	28(6)	3(6)	10(8)
C(18)	45(1)	39(1)	32(1)	6(1)	11(1)	8(1)
C(19)	45(1)	42(1)	28(1)	4(1)	11(1)	5(1)
C(20)	49(2)	43(2)	42(2)	-2(1)	15(1)	7(1)
C(21)	49(2)	41(2)	35(1)	-2(1)	13(1)	2(1)
C(22)	49(2)	48(2)	33(1)	0(1)	11(1)	3(1)
C(23)	47(2)	51(2)	32(1)	2(1)	12(1)	5(1)
C(24)	51(2)	59(2)	50(2)	5(2)	11(1)	7(1)
C(25)	50(2)	59(2)	50(2)	2(2)	14(1)	-3(1)
C(26)	48(2)	72(2)	32(2)	4(1)	16(1)	-3(1)
C(27)	47(2)	77(2)	42(2)	7(2)	15(1)	10(2)
C(28)	55(2)	58(2)	42(2)	-1(1)	16(1)	7(1)
C(29)	55(2)	73(2)	49(2)	15(2)	24(2)	7(2)
N(1)	51(2)	54(2)	80(2)	15(2)	10(1)	11(1)
N(2)	50(2)	93(2)	69(2)	15(2)	23(1)	-2(2)
S(1)	36(1)	40(1)	49(1)	6(1)	14(1)	3(1)
S(2)	46(1)	45(1)	46(1)	2(1)	9(1)	10(1)
C(30)	46(5)	73(7)	56(7)	1(5)	27(6)	1(6)
Cl(1)	60(5)	107(5)	78(3)	-2(3)	31(3)	-31(3)

Cl(2)	105(4)	77(2)	92(7)	-31(4)	71(4)	-39(4)
Cl(3)	57(5)	89(5)	148(10)	64(6)	46(6)	27(3)
C(30A)	24(10)	74(15)	86(16)	14(13)	20(9)	14(11)
Cl(1A)	119(7)	109(7)	79(5)	-1(5)	23(6)	-66(6)
Cl(2A)	92(7)	160(11)	125(8)	59(8)	60(6)	63(7)
Cl(3A)	68(6)	83(8)	75(6)	1(5)	13(4)	-33(5)

Table A10: Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^{2}x 10^3) for 4.46.

	x	y	z	U(eq)
H(3)	3382	11387	571	69
H(4)	4341	10429	1207	67
H(6)	5669	11134	176	53
H(7)	4713	12091	-462	55
H(9)	6671	10332	934	43
H(11A)	8136	9496	2149	69
H(11B)	7851	9300	1353	69
H(11C)	7875	8574	1873	69
H(20A)	6968	10391	2838	68
H(20B)	7224	10629	3624	68
H(20C)	6800	9762	3344	68
H(21)	8691	10783	3862	51
H(24)	9953	11246	4200	68
H(25)	11241	11702	4677	66
H(27)	11966	9278	4824	67
H(28)	10675	8827	4348	63
H(30)	4845	12504	1779	67
H(30A)	5285	11903	1912	74

Table A11: Crystal data and structure refinement for 4.48.



Identification code	**4.48**	
Empirical formula	C_{25} H_{17} F_6 N O_2 S_2	
Formula weight	541.52	
Temperature	150(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P21/a	
Unit cell dimensions	a = 8.7227(3) Å	α = 90°.
	b = 12.4633(5) Å	β = 94.108(2)°.
	c = 21.7574(10) Å	γ = 90°.
Volume	2359.25(17) $Å^3$	
Z	4	
Density (calculated)	1.525 Mg/m^3	
Absorption coefficient	0.298 mm^{-1}	
F(000)	1104	
Crystal size	0.40 x 0.35 x 0.05 mm^3	
Theta range for data collection	2.49 to 20.82°.	
Index ranges	-8<=h<=8, -12<=k<=12, -21<=l<=21	
Reflections collected	4754	
Independent reflections	2457 [R(int) = 0.0424]	
Completeness to theta = 20.82°	99.2 %	
Max. and min. transmission	0.9853 and 0.8902	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2457 / 0 / 328	
Goodness-of-fit on F^2	1.130	
Final R indices [I>2sigma(I)]	R1 = 0.0869, wR2 = 0.2143	
R indices (all data)	R1 = 0.1004, wR2 = 0.2218	
Extinction coefficient	0.016(2)	
Largest diff. peak and hole	0.899 and -0.405 $e.Å^{-3}$	

Table A12: Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^{2}x 10^3) for 4.48. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
C(1)	8832(12)	6488(8)	-524(5)	50(3)
C(2)	7815(10)	6148(7)	-63(4)	41(2)
C(3)	7712(11)	5088(8)	93(4)	48(2)
C(4)	6765(11)	4770(8)	530(4)	49(3)
C(5)	5831(10)	5503(7)	822(4)	38(2)
C(6)	5994(12)	6578(8)	668(5)	55(3)
C(7)	6933(12)	6907(8)	235(5)	54(3)
C(8)	4753(10)	5140(7)	1261(4)	40(2)
C(9)	4625(10)	4142(7)	1525(4)	40(2)
C(10)	3454(10)	4054(7)	1930(4)	41(2)
C(11)	2658(10)	5000(7)	1971(4)	40(2)
C(12)	3085(11)	3021(7)	2244(4)	48(2)
C(13)	1335(9)	5226(6)	2320(4)	33(2)
C(14)	33(11)	5890(8)	2040(5)	51(3)
C(15)	-1280(11)	5695(8)	2448(5)	55(3)
C(16)	-557(10)	5244(9)	3037(5)	52(3)
C(17)	1080(9)	4965(7)	2902(4)	37(2)
C(18)	2162(9)	4515(7)	3374(4)	36(2)
C(19)	3661(10)	4779(7)	3519(4)	38(2)
C(20)	4335(11)	4126(8)	3996(4)	47(2)
C(21)	3369(11)	3421(7)	4224(4)	44(2)
C(22)	4542(11)	5657(8)	3214(4)	54(3)
C(23)	3695(11)	2659(8)	4747(4)	50(3)
C(24)	2700(14)	2175(12)	5653(6)	84(4)
C(25)	2900(15)	1236(11)	5249(5)	85(4)
N(1)	9617(12)	6753(7)	-895(4)	67(3)
O(1)	2948(9)	1678(6)	4639(3)	69(2)
O(2)	3138(10)	3072(6)	5295(3)	79(2)
F(1)	381(7)	6957(5)	2059(3)	81(2)
F(2)	-343(7)	5722(6)	1447(3)	84(2)
F(3)	-2252(9)	6457(7)	2486(3)	108(3)
F(4)	-2145(8)	4875(7)	2169(3)	102(3)
F(5)	-577(7)	5988(7)	3487(3)	101(3)
F(6)	-1324(6)	4412(6)	3238(3)	84(2)
S(1)	3373(3)	5988(2)	1507(1)	42(1)
S(2)	1576(3)	3484(2)	3848(1)	46(1)

Table A13: Bond lengths [Å] and angles [°] for 4.48.

C(1)-N(1)	1.144(12)
C(1)-C(2)	1.449(15)
C(2)-C(3)	1.368(13)
C(2)-C(7)	1.406(13)
C(3)-C(4)	1.363(13)
C(3)-H(3)	0.9500
C(4)-C(5)	1.406(12)
C(4)-H(4)	0.9500
C(5)-C(6)	1.391(13)
C(5)-C(8)	1.458(12)
C(6)-C(7)	1.356(13)
C(6)-H(6)	0.9500
C(7)-H(7)	0.9500
C(8)-C(9)	1.378(12)
C(8)-S(1)	1.717(9)
C(9)-C(10)	1.400(12)
C(9)-H(9)	0.9500
C(10)-C(11)	1.375(12)
C(10)-C(12)	1.504(12)
C(11)-C(13)	1.454(12)
C(11)-S(1)	1.735(9)
C(12)-H(12A)	0.9800
C(12)-H(12B)	0.9800
C(12)-H(12C)	0.9800
C(13)-C(17)	1.343(11)
C(13)-C(14)	1.498(12)
C(14)-F(2)	1.327(11)
C(14)-F(1)	1.364(11)
C(14)-C(15)	1.517(14)
C(15)-F(3)	1.280(11)
C(15)-F(4)	1.384(12)
C(15)-C(16)	1.498(14)
C(16)-F(6)	1.325(11)
C(16)-F(5)	1.350(11)
C(16)-C(17)	1.519(12)
C(17)-C(18)	1.455(12)
C(18)-C(19)	1.364(12)
C(18)-S(2)	1.746(8)
C(19)-C(20)	1.413(12)
C(19)-C(22)	1.517(12)
C(20)-C(21)	1.338(12)
C(20)-H(20)	0.9500
C(21)-C(23)	1.495(13)
C(21)-S(2)	1.714(9)
C(22)-H(22A)	0.9800
C(22)-H(22B)	0.9800
C(22)-H(22C)	0.9800
C(23)-O(1)	1.397(11)

C(23)-O(2)	1.417(11)
C(23)-H(23)	1.0000
C(24)-O(2)	1.429(14)
C(24)-C(25)	1.483(17)
C(24)-H(24A)	0.9900
C(24)-H(24B)	0.9900
C(25)-O(1)	1.440(12)
C(25)-H(25A)	0.9900
C(25)-H(25B)	0.9900

N(1)-C(1)-C(2)	178.9(11)
C(3)-C(2)-C(7)	119.1(9)
C(3)-C(2)-C(1)	120.6(9)
C(7)-C(2)-C(1)	120.3(8)
C(4)-C(3)-C(2)	120.6(9)
C(4)-C(3)-H(3)	119.7
C(2)-C(3)-H(3)	119.7
C(3)-C(4)-C(5)	121.8(9)
C(3)-C(4)-H(4)	119.1
C(5)-C(4)-H(4)	119.1
C(6)-C(5)-C(4)	116.3(8)
C(6)-C(5)-C(8)	122.6(8)
C(4)-C(5)-C(8)	121.0(8)
C(7)-C(6)-C(5)	122.5(9)
C(7)-C(6)-H(6)	118.8
C(5)-C(6)-H(6)	118.8
C(6)-C(7)-C(2)	119.6(9)
C(6)-C(7)-H(7)	120.2
C(2)-C(7)-H(7)	120.2
C(9)-C(8)-C(5)	128.9(8)
C(9)-C(8)-S(1)	110.2(7)
C(5)-C(8)-S(1)	120.8(7)
C(8)-C(9)-C(10)	114.7(8)
C(8)-C(9)-H(9)	122.7
C(10)-C(9)-H(9)	122.7
C(11)-C(10)-C(9)	111.6(8)
C(11)-C(10)-C(12)	125.4(8)
C(9)-C(10)-C(12)	122.9(8)
C(10)-C(11)-C(13)	128.6(8)
C(10)-C(11)-S(1)	111.5(7)
C(13)-C(11)-S(1)	119.9(6)
C(10)-C(12)-H(12A)	109.5
C(10)-C(12)-H(12B)	109.5
H(12A)-C(12)-H(12B)	109.5
C(10)-C(12)-H(12C)	109.5
H(12A)-C(12)-H(12C)	109.5
H(12B)-C(12)-H(12C)	109.5
C(17)-C(13)-C(11)	129.6(8)
C(17)-C(13)-C(14)	110.2(7)
C(11)-C(13)-C(14)	120.1(7)

F(2)-C(14)-F(1)	102.8(8)
F(2)-C(14)-C(13)	115.8(8)
F(1)-C(14)-C(13)	111.4(7)
F(2)-C(14)-C(15)	113.5(8)
F(1)-C(14)-C(15)	108.4(8)
C(13)-C(14)-C(15)	104.9(8)
F(3)-C(15)-F(4)	103.5(9)
F(3)-C(15)-C(16)	117.5(9)
F(4)-C(15)-C(16)	106.4(8)
F(3)-C(15)-C(14)	116.8(9)
F(4)-C(15)-C(14)	105.8(9)
C(16)-C(15)-C(14)	105.7(8)
F(6)-C(16)-F(5)	105.4(8)
F(6)-C(16)-C(15)	112.6(8)
F(5)-C(16)-C(15)	109.7(9)
F(6)-C(16)-C(17)	112.8(8)
F(5)-C(16)-C(17)	111.0(8)
C(15)-C(16)-C(17)	105.3(8)
C(13)-C(17)-C(18)	128.0(8)
C(13)-C(17)-C(16)	110.4(8)
C(18)-C(17)-C(16)	121.6(8)
C(19)-C(18)-C(17)	129.3(8)
C(19)-C(18)-S(2)	110.9(7)
C(17)-C(18)-S(2)	119.8(6)
C(18)-C(19)-C(20)	111.9(8)
C(18)-C(19)-C(22)	125.4(8)
C(20)-C(19)-C(22)	122.7(8)
C(21)-C(20)-C(19)	114.2(8)
C(21)-C(20)-H(20)	122.9
C(19)-C(20)-H(20)	122.9
C(20)-C(21)-C(23)	127.5(9)
C(20)-C(21)-S(2)	111.8(7)
C(23)-C(21)-S(2)	120.7(7)
C(19)-C(22)-H(22A)	109.5
C(19)-C(22)-H(22B)	109.5
H(22A)-C(22)-H(22B)	109.5
C(19)-C(22)-H(22C)	109.5
H(22A)-C(22)-H(22C)	109.5
H(22B)-C(22)-H(22C)	109.5
O(1)-C(23)-O(2)	106.0(8)
O(1)-C(23)-C(21)	111.5(7)
O(2)-C(23)-C(21)	110.6(8)
O(1)-C(23)-H(23)	109.5
O(2)-C(23)-H(23)	109.5
C(21)-C(23)-H(23)	109.5
O(2)-C(24)-C(25)	104.3(9)
O(2)-C(24)-H(24A)	110.9
C(25)-C(24)-H(24A)	110.9
O(2)-C(24)-H(24B)	110.9
C(25)-C(24)-H(24B)	110.9

H(24A)-C(24)-H(24B)	108.9
O(1)-C(25)-C(24)	104.9(10)
O(1)-C(25)-H(25A)	110.8
C(24)-C(25)-H(25A)	110.8
O(1)-C(25)-H(25B)	110.8
C(24)-C(25)-H(25B)	110.8
H(25A)-C(25)-H(25B)	108.8
C(23)-O(1)-C(25)	102.9(8)
C(23)-O(2)-C(24)	107.2(8)
C(8)-S(1)-C(11)	92.0(4)
C(21)-S(2)-C(18)	91.1(4)

Symmetry transformations used to generate equivalent atoms:

Table A14: Anisotropic displacement parameters ($Å^2$x 10^3)for 4.48. The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U^{11} + ... + 2 h k a^* b^* U^{12}]$

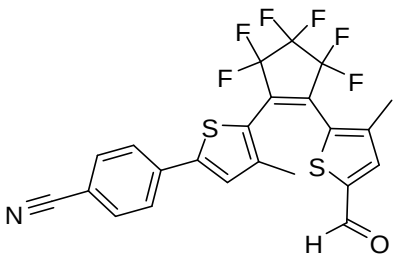
	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C(1)	59(7)	36(6)	54(7)	-1(5)	0(6)	5(5)
C(2)	49(6)	42(6)	32(5)	-1(5)	-7(5)	-4(5)
C(3)	60(6)	39(6)	46(6)	-1(5)	0(5)	6(5)
C(4)	68(7)	34(6)	44(6)	2(5)	6(6)	-4(5)
C(5)	41(5)	38(6)	35(5)	-4(4)	-4(5)	4(5)
C(6)	63(7)	38(6)	64(7)	-4(5)	7(6)	8(5)
C(7)	69(7)	33(6)	63(7)	6(5)	11(6)	2(5)
C(8)	40(5)	37(6)	44(5)	-3(5)	-2(5)	4(4)
C(9)	40(5)	39(6)	42(5)	-4(5)	4(5)	8(4)
C(10)	47(6)	31(5)	42(5)	-4(4)	-9(5)	5(5)
C(11)	48(6)	37(5)	32(5)	6(4)	-9(4)	-4(5)
C(12)	52(6)	42(6)	50(6)	5(5)	12(5)	-2(5)
C(13)	31(5)	26(5)	43(6)	2(4)	-2(4)	2(4)
C(14)	43(6)	48(7)	57(7)	-5(5)	-14(5)	4(5)
C(15)	38(6)	50(6)	77(8)	15(6)	3(6)	6(6)
C(16)	37(6)	62(7)	57(7)	2(6)	4(5)	0(5)
C(17)	33(5)	37(5)	40(6)	6(4)	-1(4)	-5(4)
C(18)	31(5)	41(5)	34(5)	-2(4)	1(4)	-7(4)
C(19)	33(5)	45(6)	37(5)	-7(5)	4(4)	-3(4)
C(20)	35(5)	61(6)	43(6)	-5(5)	0(5)	-10(5)
C(21)	45(6)	44(6)	42(5)	5(5)	-1(5)	10(5)
C(22)	45(6)	75(7)	42(6)	1(5)	-1(5)	-11(5)
C(23)	49(6)	64(7)	35(6)	6(5)	-4(5)	-5(5)
C(24)	63(7)	127(12)	61(8)	23(9)	10(6)	14(8)
C(25)	86(9)	94(10)	68(8)	41(8)	-30(7)	-29(8)
N(1)	85(7)	48(6)	69(6)	3(5)	19(6)	-7(5)
O(1)	79(5)	69(5)	56(5)	18(4)	-25(4)	-13(4)

O(2)	114(6)	78(5)	47(4)	12(4)	25(4)	32(5)
F(1)	62(4)	55(4)	126(6)	33(4)	12(4)	11(3)
F(2)	65(4)	132(6)	51(4)	4(4)	-16(3)	35(4)
F(3)	91(5)	128(7)	109(6)	51(5)	33(4)	62(5)
F(4)	79(5)	122(6)	97(5)	22(5)	-35(4)	-40(5)
F(5)	55(4)	167(7)	79(5)	-63(5)	-9(3)	31(4)
F(6)	40(3)	99(5)	114(5)	48(4)	11(3)	-6(4)
S(1)	49(2)	35(1)	42(1)	4(1)	3(1)	6(1)
S(2)	38(1)	54(2)	47(2)	11(1)	0(1)	-4(1)

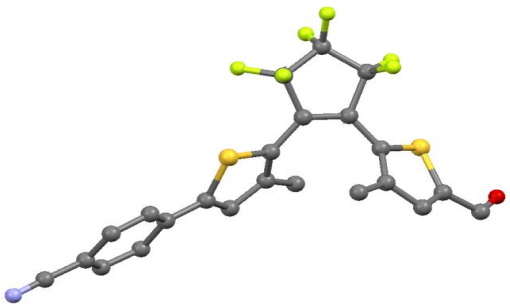
Table A15: Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^{2}x 10^3) for 4.48.

	x	y	z	U(eq)
H(3)	8306	4570	-105	58
H(4)	6735	4033	641	59
H(6)	5426	7101	873	66
H(7)	6996	7646	133	65
H(9)	5279	3560	1439	48
H(12A)	3681	2977	2643	71
H(12B)	3348	2414	1986	71
H(12C)	1985	2999	2309	71
H(20)	5385	4183	4142	56
H(22A)	5117	5345	2887	81
H(22B)	5258	5999	3522	81
H(22C)	3818	6194	3037	81
H(23)	4828	2536	4811	60
H(24A)	1618	2241	5758	100
H(24B)	3368	2115	6039	100
H(25A)	3866	852	5372	102
H(25B)	2028	731	5268	102

Table A16: Crystal data and structure refinement for 4.21.



4.21



Identification code	4.21	
Empirical formula	C_{23} H_{13} F_6 N O S_2	
Formula weight	497.46	
Temperature	293(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P21/a	
Unit cell dimensions	a = 8.6773(7) Å	α = 90°.
	b = 12.7605(11) Å	β = 98.733(4)°.
	c = 20.1076(11) Å	γ = 90°.
Volume	2200.6(3) $Å^3$	
Z	4	
Density (calculated)	1.501 Mg/m^3	
Absorption coefficient	0.309 mm^{-1}	
F(000)	1008	
Crystal size	? x? x ? mm^3	
Theta range for data collection	1.02 to 20.82°.	
Index ranges	-8<=h<=8, -12<=k<=12, -20<=l<=20	
Reflections collected	4474	
Independent reflections	2306 [R(int) = 0.1071]	
Completeness to theta = 20.82°	99.5 %	
Refinement method	Full-matrix-block least-squares on F^2	
Data / restraints / parameters	2306 / 217 / 363	
Goodness-of-fit on F^2	1.043	
Final R indices [I>2sigma(I)]	R1 = 0.1131, wR2 = 0.2766	
R indices (all data)	R1 = 0.1957, wR2 = 0.3313	
Extinction coefficient	0.008(3)	
Largest diff. peak and hole	0.539 and -0.534 $e.Å^{-3}$	

Table A17: Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^{2}x 10^3) for 4.21. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
C(1)	830(16)	1537(10)	-580(7)	72(4)
C(2)	2063(17)	1216(10)	-77(6)	67(4)
C(3)	2321(16)	149(10)	71(6)	70(4)
C(4)	3515(16)	-177(9)	562(6)	64(4)
C(5)	4570(15)	536(9)	901(6)	56(3)
C(6)	4306(17)	1567(10)	747(7)	80(4)
C(7)	3066(18)	1909(11)	274(7)	86(5)
C(8)	5862(16)	158(10)	1390(6)	66(4)
C(9)	6138(16)	-813(10)	1668(6)	68(4)
C(10)	7565(15)	-897(9)	2098(6)	57(3)
C(11)	8373(14)	16(9)	2167(5)	55(3)
C(12)	8088(18)	-1937(10)	2440(7)	86(5)
C(13)	9920(10)	221(8)	2549(5)	58(3)
C(14)	11102(9)	854(5)	2214(3)	92(8)
C(15)	12661(7)	578(6)	2653(4)	100(5)
C(16)	12269(9)	188(5)	3332(3)	83(6)
C(14A)	11102(9)	854(5)	2214(3)	92(7)
C(15A)	12448(9)	1025(5)	2797(4)	106(5)
C(16A)	12269(9)	188(5)	3332(3)	83(9)
C(17)	10514(10)	-61(8)	3177(5)	58(3)
C(18)	9744(15)	-523(10)	3686(6)	67(4)
C(19)	8368(15)	-196(11)	3881(6)	67(4)
C(20)	7991(17)	-795(11)	4419(6)	76(4)
C(21)	9032(17)	-1579(12)	4602(6)	79(4)
C(22)	7410(20)	719(12)	3597(8)	108(6)
C(23)	8934(18)	-2352(13)	5128(8)	100(5)
N(1)	-176(16)	1805(10)	-962(7)	97(4)
O(1)	9900	-3041	5258	133
F(1)	11009	668	1525	92
F(2)	10714	1931	2296	87
F(3)	13282	-236	2320	110
F(4)	13652	1456	2715	114
F(5)	13221	-620	3581	104
F(6)	12385	1057	3768	107
F(1A)	11709	107	1783	113
F(2A)	10721	1769	1858	108
F(3A)	13842	764	2540	98
F(4A)	12616	2027	3093	139
F(5A)	12951	-805	3201	87
F(6A)	12861	464	3996	79
S(1)	7412(4)	989(3)	1664(2)	69(1)
S(2)	10525(5)	-1570(3)	4154(2)	85(1)

Table A18: Bond lengths [Å] and angles [°] for 4.21.

C(1)-N(1)	1.125(17)
C(1)-C(2)	1.42(2)
C(2)-C(7)	1.361(18)
C(2)-C(3)	1.404(17)
C(3)-C(4)	1.383(17)
C(3)-H(3)	0.9300
C(4)-C(5)	1.394(17)
C(4)-H(4)	0.9300
C(5)-C(6)	1.362(18)
C(5)-C(8)	1.457(18)
C(6)-C(7)	1.393(19)
C(6)-H(6)	0.9300
C(7)-H(7)	0.9300
C(8)-C(9)	1.365(17)
C(8)-S(1)	1.735(14)
C(9)-C(10)	1.403(17)
C(9)-H(9)	0.9300
C(10)-C(11)	1.355(16)
C(10)-C(12)	1.532(17)
C(11)-C(13)	1.466(14)
C(11)-S(1)	1.733(13)
C(12)-H(12A)	0.9600
C(12)-H(12B)	0.9600
C(12)-H(12C)	0.9600
C(13)-C(17)	1.339(14)
C(13)-C(14)	1.5401(8)
C(14)-F(1)	1.396(6)
C(14)-F(2)	1.429(6)
C(14)-C(15)	1.5399(11)
C(15)-F(3)	1.388(7)
C(15)-F(4)	1.406(7)
C(15)-C(16)	1.5398(11)
C(16)-F(5)	1.368(6)
C(16)-F(6)	1.407(6)
C(16)-C(17)	1.5400(8)
C(15A)-F(4A)	1.408(7)
C(15A)-F(3A)	1.425(8)
C(17)-C(18)	1.432(15)
C(18)-C(19)	1.377(16)
C(18)-S(2)	1.713(13)
C(19)-C(20)	1.403(16)
C(19)-C(22)	1.494(18)
C(20)-C(21)	1.360(17)
C(20)-H(20)	0.9300
C(21)-C(23)	1.459(18)
C(21)-S(2)	1.686(14)
C(22)-H(22A)	0.9600

C(22)-H(22B)	0.9600
C(22)-H(22C)	0.9600
C(23)-O(1)	1.215(16)
C(23)-H(23)	0.9300
N(1)-C(1)-C(2)	177.6(17)
C(7)-C(2)-C(3)	116.8(14)
C(7)-C(2)-C(1)	122.4(13)
C(3)-C(2)-C(1)	120.7(14)
C(4)-C(3)-C(2)	121.4(13)
C(4)-C(3)-H(3)	119.3
C(2)-C(3)-H(3)	119.3
C(3)-C(4)-C(5)	121.2(12)
C(3)-C(4)-H(4)	119.4
C(5)-C(4)-H(4)	119.4
C(6)-C(5)-C(4)	116.4(12)
C(6)-C(5)-C(8)	124.0(13)
C(4)-C(5)-C(8)	119.7(12)
C(5)-C(6)-C(7)	122.9(13)
C(5)-C(6)-H(6)	118.5
C(7)-C(6)-H(6)	118.5
C(2)-C(7)-C(6)	121.1(13)
C(2)-C(7)-H(7)	119.4
C(6)-C(7)-H(7)	119.4
C(9)-C(8)-C(5)	130.2(13)
C(9)-C(8)-S(1)	110.2(11)
C(5)-C(8)-S(1)	119.5(10)
C(8)-C(9)-C(10)	113.9(13)
C(8)-C(9)-H(9)	123.1
C(10)-C(9)-H(9)	123.1
C(11)-C(10)-C(9)	113.1(12)
C(11)-C(10)-C(12)	125.8(13)
C(9)-C(10)-C(12)	121.1(13)
C(10)-C(11)-C(13)	128.7(11)
C(10)-C(11)-S(1)	111.1(10)
C(13)-C(11)-S(1)	120.0(8)
C(10)-C(12)-H(12A)	109.5
C(10)-C(12)-H(12B)	109.5
H(12A)-C(12)-H(12B)	109.5
C(10)-C(12)-H(12C)	109.5
H(12A)-C(12)-H(12C)	109.5
H(12B)-C(12)-H(12C)	109.5
C(17)-C(13)-C(11)	129.6(8)
C(17)-C(13)-C(14)	111.6(5)
C(11)-C(13)-C(14)	118.8(9)
F(1)-C(14)-F(2)	107.4(4)
F(1)-C(14)-C(15)	116.3(6)
F(2)-C(14)-C(15)	110.8(5)
F(1)-C(14)-C(13)	113.8(6)
F(2)-C(14)-C(13)	105.6(6)
C(15)-C(14)-C(13)	102.4(4)

F(3)-C(15)-F(4)	111.2(4)
F(3)-C(15)-C(16)	109.9(5)
F(4)-C(15)-C(16)	113.1(6)
F(3)-C(15)-C(14)	105.4(5)
F(4)-C(15)-C(14)	109.9(6)
C(16)-C(15)-C(14)	106.8(4)
F(5)-C(16)-F(6)	112.6(4)
F(5)-C(16)-C(15)	111.4(6)
F(6)-C(16)-C(15)	107.0(5)
F(5)-C(16)-C(17)	116.3(7)
F(6)-C(16)-C(17)	105.3(6)
C(15)-C(16)-C(17)	103.4(4)
F(4A)-C(15A)-F(3A)	109.0(4)
C(13)-C(17)-C(18)	129.1(8)
C(13)-C(17)-C(16)	111.3(5)
C(18)-C(17)-C(16)	119.7(9)
C(19)-C(18)-C(17)	126.7(11)
C(19)-C(18)-S(2)	111.6(10)
C(17)-C(18)-S(2)	121.7(9)
C(18)-C(19)-C(20)	111.5(12)
C(18)-C(19)-C(22)	125.7(12)
C(20)-C(19)-C(22)	122.7(12)
C(21)-C(20)-C(19)	112.8(12)
C(21)-C(20)-H(20)	123.6
C(19)-C(20)-H(20)	123.6
C(20)-C(21)-C(23)	125.8(13)
C(20)-C(21)-S(2)	112.5(10)
C(23)-C(21)-S(2)	121.7(12)
C(19)-C(22)-H(22A)	109.5
C(19)-C(22)-H(22B)	109.4
H(22A)-C(22)-H(22B)	109.5
C(19)-C(22)-H(22C)	109.5
H(22A)-C(22)-H(22C)	109.5
H(22B)-C(22)-H(22C)	109.5
O(1)-C(23)-C(21)	122.1(14)
O(1)-C(23)-H(23)	118.9
C(21)-C(23)-H(23)	119.0
C(11)-S(1)-C(8)	91.6(7)
C(21)-S(2)-C(18)	91.5(7)

Symmetry transformations used to generate equivalent atoms:

Table A19: Anisotropic displacement parameters ($Å^2 x\ 10^3$)for 4.21. The anisotropic displacement factor exponent takes the form: $-2\pi^2$ [h2a*$^2U^{11}$ + ... + 2 h k a* b* U^{12}]

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C(1)	67(11)	76(10)	73(10)	13(8)	10(9)	7(9)
C(2)	91(12)	44(9)	67(9)	0(8)	10(9)	11(9)
C(3)	82(11)	77(12)	54(8)	5(7)	19(8)	6(9)
C(4)	98(11)	34(8)	61(8)	1(7)	17(8)	3(8)
C(5)	66(10)	50(9)	54(8)	-7(7)	12(7)	-6(8)
C(6)	85(12)	55(11)	98(12)	-21(9)	4(10)	-13(9)
C(7)	105(14)	56(10)	95(11)	9(10)	12(11)	4(10)
C(8)	83(11)	65(10)	56(8)	-10(8)	26(8)	-1(9)
C(9)	72(11)	54(10)	80(10)	-10(8)	17(9)	-10(8)
C(10)	67(10)	44(9)	59(8)	2(7)	12(7)	1(8)
C(11)	67(10)	48(8)	53(7)	-13(6)	17(7)	-12(8)
C(12)	98(12)	61(10)	95(10)	18(8)	-1(9)	-25(9)
C(13)	51(9)	55(8)	75(9)	1(7)	33(8)	-19(7)
C(14)	63(15)	112(19)	99(17)	-51(14)	9(12)	-2(13)
C(15)	99(7)	96(7)	104(7)	2(6)	18(6)	-6(6)
C(16)	95(18)	56(14)	113(17)	6(12)	63(14)	3(12)
C(14A)	63(14)	112(12)	99(13)	-51(7)	9(7)	-2(7)
C(15A)	104(7)	106(8)	108(7)	4(7)	21(7)	-2(7)
C(16A)	95(12)	56(14)	113(12)	6(7)	63(8)	3(7)
C(17)	59(9)	54(8)	59(8)	1(7)	11(7)	3(7)
C(18)	60(9)	76(9)	65(8)	-5(7)	9(7)	15(8)
C(19)	65(10)	82(10)	59(8)	2(7)	28(7)	7(8)
C(20)	64(10)	99(11)	70(9)	0(8)	27(8)	1(9)
C(21)	76(11)	107(12)	56(8)	20(8)	21(8)	-1(9)
C(22)	124(15)	96(12)	114(12)	5(10)	48(11)	40(11)
C(23)	70(11)	124(14)	107(12)	29(11)	19(9)	-9(10)
N(1)	89(11)	92(10)	104(10)	26(8)	-3(9)	18(8)
O(1)	115	179	111	68	41	32
F(1)	92	92	92	0	14	0
F(2)	88	88	88	0	13	0
F(3)	110	110	110	0	17	0
F(4)	114	114	114	0	17	0
F(5)	104	104	104	0	16	0
F(6)	107	107	107	0	16	0
F(1A)	113	113	113	0	17	0
F(2A)	108	108	108	0	16	0
F(3A)	99	99	99	0	15	0
F(4A)	139	139	139	0	21	0
F(5A)	87	87	87	0	13	0
F(6A)	79	79	79	0	12	0
S(1)	79(3)	55(2)	71(2)	4(2)	12(2)	-9(2)

S(2)	66(3)	107(3)	84(3)	31(2)	17(2)	10(2)

Table A20: Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^{2}x 10^3) for 4.21.

	x	y	z	U(eq)
H(3)	1674	-349	-167	84
H(4)	3616	-886	668	77
H(6)	4984	2064	967	96
H(7)	2922	2623	198	103
H(9)	5442	-1368	1580	82
H(12A)	7307	-2462	2310	130
H(12B)	8231	-1849	2919	130
H(12C)	9054	-2153	2304	130
H(20)	7123	-671	4627	91
H(22A)	6513	785	3819	162
H(22B)	7084	613	3124	162
H(22C)	8026	1346	3665	162
H(23)	8107	-2317	5372	120