

## **NOTE TO USERS**

**The original document received by UMI contains pages with slanted print. Pages were microfilmed as received.**

**This reproduction is the best copy available**

**UMI**



THE UNIVERSITY OF CALGARY

CLAY-CATALYZED THIOMETHYLATION OF THIOPHENES  
AND PREPARATION OF SOME TETRATHIAFULVALENE  
DERIVATIVES

by

ALEXIY PRIMAK

A THESIS

SUBMITTED TO THE FACULTY OF GRADUATE STUDIES  
IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE  
DEGREE OF DOCTOR OF PHILOSOPHY

DEPARTMENT OF CHEMISTRY

CALGARY, ALBERTA

AUGUST, 1998

© Alexiy Primak 1998



National Library  
of Canada

Acquisitions and  
Bibliographic Services

395 Wellington Street  
Ottawa ON K1A 0N4  
Canada

Bibliothèque nationale  
du Canada

Acquisitions et  
services bibliographiques

395, rue Wellington  
Ottawa ON K1A 0N4  
Canada

*Your file    Votre référence*

*Our file    Notre référence*

The author has granted a non-exclusive licence allowing the National Library of Canada to reproduce, loan, distribute or sell copies of this thesis in microform, paper or electronic formats.

The author retains ownership of the copyright in this thesis. Neither the thesis nor substantial extracts from it may be printed or otherwise reproduced without the author's permission.

L'auteur a accordé une licence non exclusive permettant à la Bibliothèque nationale du Canada de reproduire, prêter, distribuer ou vendre des copies de cette thèse sous la forme de microfiche/film, de reproduction sur papier ou sur format électronique.

L'auteur conserve la propriété du droit d'auteur qui protège cette thèse. Ni la thèse ni des extraits substantiels de celle-ci ne doivent être imprimés ou autrement reproduits sans son autorisation.

0-612-34694-3

## ABSTRACT

The initial objective of this study was to investigate the clay-catalyzed reaction of dimethyldisulfide with heteroaromatic as well as some olefinic compounds. Olefins react readily under these conditions resulting in the addition of the disulfide molecule across the olefin  $\pi$ -bond. In this manner, the adducts of dimethyldisulfide and cyclohexene were prepared in good yield. The more easily polymerized olefins indene and acenaphthylene also reacted with dimethyldisulfide to give the adducts in good yield. These results demonstrate the mildness of the procedure and its applicability towards acid-sensitive compounds.

In the case of heteroaromatic compounds, it was found that thiophene and its alkyl derivatives are the only such compounds that may be exhaustively thiomethylated by this method (although much more forcing conditions had to be employed). In the case of thiophene, good yields of 2,3,4,5-*tetrakis*(methylthio)thiophene were obtained only when the reaction was performed in a sealed system at 150°C and with an overpressure of air.

Once the products in these reactions were isolated and identified, it was decided to employ these compounds as intermediates in the synthesis of various thiophene-based tetrathiafulvalene derivatives. In order to achieve this, metal-amine reductions were carried out on these compounds to generate their corresponding polythiols. The reduction proceeded well with 3,4-*bis*(methylthio)-2,5-dimethylthiophene, but was much more difficult to achieve in the case of *tetrakis*(methylthio)thiophene. The demethylation of this molecule was always accompanied by a de-thiomethylation side-reaction which could not be prevented although a number of various different conditions

were employed. Complete de-methylation was achieved when HMPA (heated to 105°C) was used as the solvent to produce a mixture consisting of roughly equal amounts of 2,3,4,5-thiophenetetrathiolate and 2,3,5-thiophenetrithiolate.

By using the above mentioned methods, the 1,3-dithiole-2-thione derivatives of benzo[*b*]thiophene and 2,5-dimethylthiophene were prepared in good yield and these were readily converted into their TTF-derivatives by standard phosphite coupling methods. Systems based on benzo[*b*]thiophene and DMIT were successfully coupled to produce the mixed TTFs in good yields. On the other hand, the 2,5-dimethylthiophene derivatives proved somewhat more difficult to prepare although eventually conditions were optimized to obtain the parent compound as well as the mixed derivatives in modest yields.

## **ACKNOWLEDGEMENTS**

I would like to acknowledge and express my gratitude to the following people:

My parents Yuri and Olga; my sister Olga and my grandma for all their love, advice and support.

My supervisor Dr. Peter D. Clark, for his advice, guidance and above all his support throughout these years.

My friends and colleagues with whom I have shared office and laboratory facilities during my studies. In particular, Dr. Andrew Kirk, Dr. Hong Yao, Dr. Shaun Mesher, Dr. Nick Irvine, Dr. Martin Kirk, James Yee and Kathy Almond.

To Alberta Sulphur Research Ltd. (ASRL) for the use of their facilities and instrumentation as well as to its staff for all the advice they have given me throughout these years. In particular, a special thanks to Diane Jorgensen for all her help in administrative matters, Krys Ciesluk for all her help with the formatting of this dissertation, Ed Fitzpatrick for his help and advice regarding the use of the high pressure equipment, and Kevin Lesage for his help in the use of GC and GC-MS analysis and the various other instruments I've used throughout my time in ASRL.

Greta Prihodko for her kindness and help with administrative matters.

Dr. Raghav Yamdagni, Dr. Qiao Wu and Dorothy Fox for their technical assistance.

Dr. Massod Parvez for performing X-ray crystallographic analyses.

The Department of Chemistry at The University of Calgary for the research facilities and Graduate Teaching Assistanship (GAT).

The Natural Science and Engineering Research Council of Canada and Alberta Sulphur Research Ltd. for funding of this research project.



## TABLE OF CONTENTS

APPROVAL PAGE .....	ii
ABSTRACT.....	iii
ACKNOWLEDGEMENTS .....	v
TABLE OF CONTENTS .....	vii
LIST OF FIGURES .....	xii
LIST OF SCHEMES .....	xiii
LIST OF TABLES .....	xviii
ABBREVIATIONS.....	xix

## CHAPTER 1 CLAYS, SULFIDES, AND TETRATHIAFULVALENES

1.0	OVERALL OBJECTIVES .....	1
1.1	CLAY CATALYSTS .....	2
1.1.0	INTRODUCTION.....	2
1.1.1	INTERNAL STRUCTURE OF MONTMORILLONITE CLAYS...	3
1.1.2	A MODIFIED MONTMORILLONITE: “K10” .....	4
1.1.3	CLAYZIC .....	7
1.1.4	CLAYS IN ORGANIC REACTIONS .....	11
	A. BASE-CATALYZED REACTIONS .....	11
	B. CARBONYL PROTECTION AND DEPROTECTION .....	11
	C. NITRATIONS .....	15
	D. OXIDATIONS .....	15
	E. CARBON-CARBON BOND FORMATION REACTIONS.....	18
1.2	THIOLS, SULFIDES, AND DISULFIDES.....	22
1.2.0	INTRODUCTION.....	22
1.2.1	PREPARATION OF ARYL THIOLS OR SULFIDES .....	23
1.3	TETRATHIAFULVALENES.....	29
1.3.0	INTRODUCTION.....	29

1.3.1	PREVIOUS SYNTHESIS OF TTF DERIVATIVES AND THEIR PRECURSORS.....	31
1.3.2	CONDUCTIVITY OF TTF DERIVATIVES .....	42
1.3.3	OXIDATION METHODS AND CRYSTAL GROWING .....	47
1.3.4	MEASUREMENT OF CONDUCTIVITY .....	48

## CHAPTER 2 CLAY-CATALYZED THIOMETHYLATION OF AROMATIC COMPOUNDS

2.0	INTRODUCTION.....	50
2.0.0	BACKGROUND .....	51
2.1	THIOPHENES.....	54
2.1.0	BACKGROUND .....	54
2.1.1	THIOMETHYLATION OF THIOPHENE .....	54
	A. REACTIONS IN NITROMETHANE.....	54
	B. OTHER SOLVENTS AND CATALYSTS .....	56
	C. REACTIONS IN CHLOROBENZENE.....	63
	D. CLAYMAN.....	68
	E. OTHER DISULFIDES.....	71
2.1.2	THIOMETHYLATION OF 2,5-DIMETHYLTHIOPHENE.....	72
2.1.3	DIBROMOTHIOPHENES .....	73
2.1.4	THIOALKYLATIONS OF THIOPHENE BY STANDARD HOMOGENEOUS METHODS .....	75
2.2	THIOMETHYLATION OF OTHER AROMATICS AND HETEROAROMATICS .....	77
2.2.0	BACKGROUND .....	77
2.2.1	NAPHTHALENE AND PHENANTHRENE .....	77
2.2.2	FURAN, PYRROLE AND INDOLE.....	78
2.3	CONCLUDING REMARKS .....	80

## CHAPTER 3 CLAY-CATALYZED THIOMETHYLATION OF ALKENES

3.0	INTRODUCTION.....	82
3.0.0	BACKGROUND .....	82
3.1	CYCLOHEXENE .....	86

3.1.0	BACKGROUND .....	86
3.1.1	KINETIC EXPERIMENTS.....	88
3.1.2	CLAYMAN.....	90
3.2	INDENE, ACENAPHTHYLENE AND 1,4-DIHYDRONAPHTHALENE ..	92
3.2.0	BACKGROUND .....	92
3.2.1	THIOMETHYLATION RESULTS.....	92
3.2.2	DEHYDROGENATION RESULTS.....	95
	A. INDENE ADDUCT .....	95
	B. ACENAPHTHYLENE ADDUCT .....	96
	C. 1,4-DIHYDRONAPHTHALENE ADDUCT .....	96
3.3	CONCLUDING REMARKS .....	97

## CHAPTER 4 METAL-AMINE REDUCTIONS OF SULFIDES

4.0	INTRODUCTION.....	99
4.0.1	BACKGROUND .....	99
4.0.1	PREVIOUS SYNTHESSES OF POLYTHIOLS .....	100
4.1	RESULTS AND DISCUSSION .....	106
4.1.0	INTRODUCTION.....	106
4.1.1	2,5-DIMETHYLTHIOPHENE-3,4-DITHIOL .....	106
4.1.2	2,3,4,5-THIOPHENETETRATHIOL .....	108
	A. REDUCTIONS IN LIQUID AMMONIA.....	109
	B. REDUCTIONS IN PYRIDINE.....	112
	C. REDUCTIONS IN HMPA.....	114
	D. ISOLATION OF THIOLS .....	116
4.1.3	1,2-INDANDITHIOL AND 1,2-ACENAPHENEDITHIOL .....	120
4.2	CONCLUDING REMARKS .....	123

## CHAPTER 5 SYNTHESIS OF TETRATHIAFULVALENE DERIVATIVES

5.0	INTRODUCTION.....	126
5.1	COMPOUNDS BASED ON THIOPHENE.....	128
5.1.0	BACKGROUND .....	128
5.1.1	RESULTS .....	128

<b>5.2</b>	<b>COMPOUNDS BASED ON 2,5-DIMETHYLTHIOPHENE .....</b>	<b>131</b>
5.2.0	BACKGROUND .....	131
5.2.1	4,6-DIMETHYLTHIENO[3,4- <i>d</i> ]-1,3-DITHIOLE-2-THIONE AND ITS TTF .....	132
5.2.2	OTHER DERIVATIVES .....	135
<b>5.3</b>	<b>CONCLUDING REMARKS .....</b>	<b>141</b>

## CHAPTER 6 EXPERIMENTAL SECTION

<b>6.0</b>	<b>GENERAL COMMENTS.....</b>	<b>142</b>
	<i>Preparation of the clayzic catalyst .....</i>	<i>143</i>
	<i>Preparation of other clay catalysts.....</i>	<i>143</i>
<b>6.1</b>	<b>REACTIONS PERTAINING TO CHAPTER 2.....</b>	<b>144</b>
6.1.1	REACTIONS UNDER HIGH AIR PRESSURE .....	144
	<i>2,3,4,5-Tetrakis(methylthio)thiophene.....</i>	<i>145</i>
	<i>2,3,5-Tris(methylthio)thiophene. ....</i>	<i>145</i>
	<i>2,5-Bis(methylthio)thiophene. ....</i>	<i>146</i>
	<i>2,5-Bis(methanesulfonyl)thiophene .....</i>	<i>146</i>
6.1.2	REACTIONS AT ATMOSPHERIC PRESSURE.....	148
	<i>Reactions with Thiophene .....</i>	<i>148</i>
	<i>2,5-Dimethyl-3,4-bis(methylthio)thiophene. ....</i>	<i>148</i>
	<i>1,4-Bis(methylthio)naphthalene. ....</i>	<i>149</i>
	<i>Preparation in the presence of clayzic.....</i>	<i>149</i>
	<i>Preparation in the presence of clayman: .....</i>	<i>150</i>
	<i>2,3-Bis(methylthio)benzo[<i>b</i>]thiophene .....</i>	<i>150</i>
<b>2.2</b>	<b>REACTIONS PERTAINING TO CHAPTER 3.....</b>	<b>151</b>
	<i>1,2-Bis(methylthio)indan .....</i>	<i>151</i>
	<i>Preparation in the presence of clayzic.....</i>	<i>151</i>
	<i>Preparation in the presence of K10 .....</i>	<i>152</i>
	<i>1,2-Bis(methylthio)acenaphthene. ....</i>	<i>152</i>
	<i>1,2-bis(methylthio)acenaphthylene.....</i>	<i>153</i>
	<i>2,3-Bis(methylthio)-1,2,3,4-tetrahydronaphthalene. ....</i>	<i>154</i>
<b>6.3</b>	<b>REACTIONS PERTAINING TO CHAPTERS 4 AND 5.....</b>	<b>155</b>

<i>4,6-Dimethylthieno[3,4-d]-1,3-dithiole-2-thione</i> .....	155
<i>Benzothieno[2,3-d]-1,3-dithiole-2-thione</i> .....	157
<i>Bis(tetraethylammonium)bis(1,3-dithiole-2-thione-4,5-dithiolato)zincate</i> .....	158
<i>4,5-Ethylenedithia-1,3-dithiole-2-thione</i> .....	159
<i>4,5-Bis(methylthio)-1,3-dithiole-2-thione</i> .....	160
<i>General procedure for the transchalcogenation of 1,3-dithioles-2-thiones</i> .....	160
<i>4,6-Dimethylthieno[3,4-d]-1,3-dithiole-2-one</i> .....	161
<i>Benzothieno[2,3-d]-1,3-dithiole-2-one</i> .....	161
<i>4,5-Ethylenedithia-1,3-dithiole-2-one</i> .....	162
<i>4,5-Bis(methylthio)-1,3-dithiole-2-one</i> .....	163
<i>(4,6-Dimethylthieno[3,4-d]-1,3-dithiole-2-ylidene)-4,6-dimethylthieno[3,4-d]-1,3-dithiole</i> .....	163
<i>General procedure for the preparation of mixed TTF's</i> .....	164
<i>(4,6-Dimethylthieno[3,4-d]-1,3-dithiole-2-ylidene)-4,5-ethylenedithia-1,3-dithiole</i> .....	164
<i>(4,6-Dimethylthieno[3,4-d]-1,3-dithiole-2-ylidene)-4,5-bis(methylthio)-1,3-dithiole</i> .....	165
<i>(Benzothieno[2,3-d]-1,3-dithiole-2-ylidene)-4,5-ethylenedithio-1,3-dithiole</i> .....	166
<i>(Benzothieno[2,3-d]-1,3-dithiole-2-ylidene)-4,5-bis(methylthio)-1,3-dithiole</i> .....	166
<i>Thiophthalic anhydride</i> .....	167

<b>REFERENCES</b> .....	<b>168</b>
-------------------------	------------

<b>APPENDIX X-RAY STRUCTURE REPORT FOR 1,2-BIS(METHYLTHIO)-INDAN</b> .....	<b>176</b>
--	------------

## LIST OF FIGURES

<b>Figure 1-1:</b> Metasilicate structures found in clays .....	3
<b>Figure 1-2:</b> General crystal structure of clays .....	4
<b>Figure 1-3:</b> Effect of acid treatment on montmorillonite clays.....	5
<b>Figure 1-4:</b> Structure of clayzic .....	8
<b>Figure 1-5:</b> Parent molecule .....	29
<b>Figure 1-6:</b> The first organic superconductors .....	30
<b>Figure 1-7:</b> 1,3-Dithioles.....	31
<b>Figure 1-8:</b> Simple band-theory analysis for conductivity in organic metals .....	43
<b>Figure 1-9:</b> Schematic representation of band states .....	44
<b>Figure 1-10:</b> Effect of crystal lattice on conductivity .....	45
<b>Figure 2-1:</b> Compounds observed by GC-MS during the thiomethylation of thiophene .....	57
<b>Figure 2-2:</b> Structure of the main thiomethylated products isolated from the reaction mixture.....	59
<b>Figure 2-3:</b> Schematic representation of the autoclave used.....	65
<b>Figure 3-1:</b> Kinetic data obtained for the clayzic-catalyzed thiomethylation of cyclohexene .....	88
<b>Figure 3-2:</b> 1,3-dithiol-2-thione derivatives that could be prepared from indene, acenaphthylene and 1,4-dihydronaphthalene .....	92
<b>Figure 3-3:</b> ORTEP diagram of <i>trans</i> -1,2-bis(methanesulfonyl)indan .....	94
<b>Figure 4-1:</b> Solid-state <sup>13</sup> C-NMR spectrum of the unknown solid .....	117
<b>Figure 5-1:</b> Space-filling model of BEDT-TTF .....	126
<b>Figure 5-2:</b> 1,3-dithiole-2-thiones from benzenhexathiolate and thiophene- tetrathiolate .....	127

## LIST OF SCHEMES

<b>Scheme 1-1:</b> Selectivity in the clayzic-catalyzed benzylation of benzene .....	10
<b>Scheme 1-2:</b> Some reactions catalyzed by KF-alumina .....	12
<b>Scheme 1-3:</b> K10/Fe <sup>3+</sup> catalyzed thioacetalization of benzaldehyde .....	12
<b>Scheme 1-4:</b> Mont./Ce <sup>3+</sup> catalyzed ketalization .....	13
<b>Scheme 1-5:</b> Deprotection of ketones with K10.....	14
<b>Scheme 1-6:</b> Mild dethioketalization with clayfen.....	14
<b>Scheme 1-7:</b> Nitration of phenol with claycop.....	15
<b>Scheme 1-8:</b> Oxidation alcohols with modified silica.....	16
<b>Scheme 1-9:</b> Oxidation of alcohols with clayfen .....	16
<b>Scheme 1-10:</b> Oxidation of cyclohexane catalyzed by Mn <sup>2+</sup> -TSM.....	17
<b>Scheme 1-11:</b> Coupling of thiols with K10.....	18
<b>Scheme 1-12:</b> Coupling of 2-naphthols catalyzed by Cu <sup>2+</sup> -exchanged montmorillonite.	19
<b>Scheme 1-13:</b> Synthesis of $\alpha$ -tocopherol .....	19
<b>Scheme 1-14:</b> Alkylation of aromatics with carbonyl compounds .....	20
<b>Scheme 1-15:</b> Diene self-condensation catalyzed by K10/Fe <sup>3+</sup> .....	21
<b>Scheme 1-16:</b> Diels-Alder reaction with furan.....	21
<b>Scheme 1-17:</b> Displacement of fluoride ion from an activated fluoroaromatic .....	23
<b>Scheme 1-18:</b> Synthesis of <i>tetrakis</i> (isopropylthio)benzene .....	24
<b>Scheme 1-19:</b> Synthesis of aryl thiolates by reaction with excess methane thiolate.....	24
<b>Scheme 1-20:</b> Selective removal of various alkyl groups on aryl ethers or thioethers ....	25
<b>Scheme 1-21:</b> Preparation of <i>para</i> -toluenethiol .....	25

<b>Scheme 1-22:</b> The use of palladium chemistry in the synthesis of aromatic thiols .....	26
<b>Scheme 1-23:</b> Thiol formation from 1,3-dithiol-2-thiones.....	27
<b>Scheme 1-24:</b> Synthesis of 3,4-thiophenedithiol.....	27
<b>Scheme 1-25:</b> Synthesis of alkylthio-substituted thiophenes by reaction of cyclopropenyl cations .....	28
<b>Scheme 1-26:</b> Thiocyanates as intermediates in the synthesis of aromatic sulfides .....	28
<b>Scheme 1-27:</b> Original large-scale synthesis of tetrathiafulvalene .....	32
<b>Scheme 1-28:</b> Bryce's improved large-scale synthesis of tetrathiafulvalene.....	33
<b>Scheme 1-29:</b> Preparation $(Et_4N)_2[Zn(DMIT)_2]$ .....	34
<b>Scheme 1-30:</b> Introduction of spacer molecules between the 1,3-dithiole units .....	35
<b>Scheme 1-31:</b> Wittig chemistry in the synthesis of TTF derivatives .....	36
<b>Scheme 1-32:</b> Mechanism of the phosphite coupling reaction.....	36
<b>Scheme 1-33:</b> Synthesis of a pyrrole-based TTF synthesis through phosphite- mediated coupling.....	37
<b>Scheme 1-34:</b> Synthesis of a furan-based TTF through phosphite-mediated coupling....	37
<b>Scheme 1-35:</b> Introduction of spacer molecules by the phosphite coupling reaction .....	38
<b>Scheme 1-36:</b> Proposed mechanism for the formation of phosphonate esters .....	38
<b>Scheme 1-37:</b> Reaction of $CS_2$ with triple bonds .....	39
<b>Scheme 1-38:</b> Preparation of 1,3-dithiol-2-thiones from the thermolysis of thiadiazoles	39
<b>Scheme 1-39:</b> Trapping of $CS_2$ /phosphine adducts with C-C multiple bonds .....	40
<b>Scheme 1-40:</b> Synthesis of TTF derivatives from a tetrahaloethylene.....	40
<b>Scheme 1-41:</b> Synthesis of a stacked TTF molecule.....	41
<b>Scheme 1-42:</b> A two-dimensional tetrathiafulvalene .....	42
<b>Scheme 2-1:</b> Mukaiyama's mixed aromatic sulfide synthesis .....	51





<b>Scheme 3-8:</b> Dehydrogenation of 1,2- <i>bis</i> (methylthio)acenaphthene .....	96
<b>Scheme 3-9:</b> Dehydrogenation of 2,3- <i>bis</i> (methylthio)tetralin with DDQ .....	97
<b>Scheme 4-1:</b> General mechanism for the dissolving metal reduction of sulfides .....	100
<b>Scheme 4-2:</b> HMPA reduction of <i>hexakis</i> (isopropylbenzene) .....	101
<b>Scheme 4-3:</b> Preference towards the reduction of thioethers vs. ethers .....	102
<b>Scheme 4-4:</b> Concentration effects on the reduction of <i>tetrakis</i> (ethylthio)benzene .....	103
<b>Scheme 4-5:</b> Synthesis of tetrathia-s-indacenedithione .....	104
<b>Scheme 4-6:</b> Improved synthesis of benzenhexathiolate .....	104
<b>Scheme 4-7:</b> Reduction of 2,5-dimethyl-3,4- <i>bis</i> (methylthio)thiophene in liquid ammonia .....	107
<b>Scheme 4-8:</b> Reduction of 2,5-dimethyl-3,4- <i>bis</i> (methylthio)thiophene in pyridine .....	108
<b>Scheme 4-9:</b> Products observed after 2,3,4,5- <i>tetrakis</i> (methylthio)thiophene is reduced and quenched with bromoethane .....	110
<b>Scheme 4-10:</b> The autothiylation of 2-thiophenethiol .....	118
<b>Scheme 4-11:</b> Proposed mechanism for the initial step in the polymerization of 2,3,4,5-thiophenetetrathiol .....	120
<b>Scheme 4-12:</b> Reduction of 1,2- <i>bis</i> (methylthio)indan .....	121
<b>Scheme 4-13:</b> Proposed mechanism for the formation of indene in the reduction of 1,2- <i>bis</i> (methylthio)indan .....	121
<b>Scheme 4-14:</b> Reduction of 1,2- <i>bis</i> (methylthio)acenaphthene .....	123
<b>Scheme 5-1:</b> Attempted synthesis of the <i>bis</i> (1,3-dithiole-2-thione) from thiophenetetrathiol .....	129
<b>Scheme 5-2:</b> Reaction of the reduction products with alkyl dihalides .....	130
<b>Scheme 5-3:</b> Original synthesis of the TTF-derivative based on 2,5-dimethylthiophene .....	131
<b>Scheme 5-4:</b> Preparation of 4,6-dimethylthieno-[3,4- <i>d</i> ]-1,3-dithiole-2-thione .....	133

<b>Scheme 5-5:</b> Variation in the preparation of 4,6-dimethylthieno[3,4- <i>d</i> ]-1,3-dithiole-2-thione.....	133
<b>Scheme 5-6:</b> Synthesis of the 2,5-dimethylthiophene-based TTF.....	134
<b>Scheme 5-7:</b> Preparation of ethylenedithio and <i>bis</i> (methylthio) derivatives of DMIT ..	135
<b>Scheme 5-8:</b> Preparation of benzothieno[2,3- <i>d</i> ]-1,3-dithiole-2-thione (BTT) .....	138
<b>Scheme 5-9:</b> Coupling of BTT with the other dithioles available.....	138
<b>Scheme 5-10:</b> Preparation of thiophthalic anhydride .....	139
<b>Scheme 5-11:</b> Couplings with thiophthalic anhydride .....	140
<b>Scheme 5-12:</b> Attempts to prepare spacer-based TTF's.....	140

## LIST OF TABLES

<b>Table 2-1:</b> Thiomethylations of thiophene under varying conditions .....	57
<b>Table 2-2:</b> Thiomethylations of thiophene in chlorobenzene .....	64
<b>Table 2-3:</b> Thiomethylations of thiophene performed under pressure .....	67
<b>Table 2-4:</b> Thioalkylations of thiophene with various disulfides.....	72
<b>Table 3-1:</b> Selected bond lengths for <i>trans</i> -1,2- <i>bis</i> (methylthio)indan .....	94
<b>Table 4-1:</b> Reductions of 2,3,4,5- <i>tetrakis</i> (methylthio)thiophene in liquid ammonia with 8 equivalents of metal .....	111
<b>Table 4-2:</b> Reductions of 2,3,4,5- <i>tetrakis</i> (methylthio)thiophene in pyridine at 105°C.....	113
<b>Table 4-3:</b> Reductions of 2,3,4,5- <i>tetrakis</i> (methylthio)thiophene in HMPA at 105°C ...	114
<b>Table 4-4:</b> Reduction of 1,2- <i>bis</i> (methylthio)indan.....	122
<b>Table 5-1:</b> Coupling of ET with DMT .....	136
<b>Table 5-2:</b> Coupling of BMT with DMT .....	136

## ABBREVIATIONS

°C	degrees Celsius
Ac	acetyl
Ar	aryl
b.p.	boiling point
BMT	4,5- <i>bis</i> (methylthio)-1,3-dithiole-2-thione
Bn	benzyl
BT	benzo[ <i>b</i> ]thiophene
BTT	benzo[ <i>b</i> ]thieno[2,3- <i>d</i> ]-1,3-dithiole-2-thione
Bu	butyl
cat.	catalytic
$\delta$	chemical shift in parts per million
d	doublet (NMR)
DCE	1,2-dichloroethane
DDQ	2,3-dichloro-5,6-dicyano-1,4-benzoquinone
DMDS	dimethyldisulfide
DMF	N,N-dimethylformamide
DMIT	4,5-dithiolato-1,3-dithiole-2-thione
EDTA	ethylenediaminetetraacetate
eq.	equivalent(s)
ET	4,5-ethylenedithia-1,3-dithiole-2-thione

Et	ethyl
g	grams
GC	gas chromatography
h	hour
HMPA	hexamethylphosphorictriamide
HOMO	highest occupied molecular orbital
Hz	hertz
i	iso
IR	infrared spectroscopy
L	litre
LDA	lithium diisopropylamide
LUMO	lowest unoccupied molecular orbital
<i>m</i>	<i>meta</i>
M	moles per litre
m	multiplet (NMR); minute(s)
m.p.	melting point
<i>m/z</i>	mass to charge ratio (in mass spectrometry)
$M^+$	molecular ion
Me	methyl
mol	mole(s)
mont.	montmorillonite clay
MS	mass spectrometry
NBS	N-bromosuccinimide

NMR	nuclear magnetic resonance
<i>p</i>	<i>para</i>
Pa	pascals
Ph	phenyl
Pr	propyl
psi	pounds per square inch
qt.	quaternary (NMR)
s	singlet (NMR); second(s)
<i>t</i>	<i>tert</i>
T <sub>c</sub>	critical temperature for superconductivity
TCNQ	tetracyanoquinodimethane
Tf	trifluoromethanesulfonyl
TFA	trifluoroacetic acid
THF	tetrahydrofuran
TMS	tetramethylsilane
Tol	tolyl
Ts	toluenesulfonyl
TTF	tetrathiafulvalene

## **CHAPTER 1**

### **CLAYS, SULFIDES, AND TETRATHIAFULVALENES**

#### **1.0 OVERALL OBJECTIVES**

The primary goal of this work was to investigate the substitution or addition of thioalkyl groups into aromatic and/or olefinic bonds by means of montmorillonite-K10 clay-supported reagents and alkyl disulfides. These reactions have been performed with varying degrees of success in the past with standard Lewis-acids but never with clay-supported reagents. Some effort was devoted to determine the importance of the clay support and the influence of the type and amount of active phase dispersed on the support on reaction rates.

A second goal of this work was to make use of these sulfur compounds in the synthesis of derivatives of tetrathiafulvalenes, whose interesting electrical properties make them excellent candidates for high-tech electronic applications.



## 1.1 CLAY CATALYSTS

### 1.1.0 INTRODUCTION

The usefulness of supported reagents in organic synthesis has been known for some 25 years.<sup>1</sup> Industry has employed heterogeneous catalysts for many decades, but it has only recently turned its attention to supported reagents as a means of large-scale synthesis. As will be seen later, some "so-called" supported reagents act in a catalytic fashion. Thus,  $\text{AlCl}_3$ , which is used in a 1:1 molar ratio for Friedel-Crafts alkylations, may be used catalytically when used in a supported form.

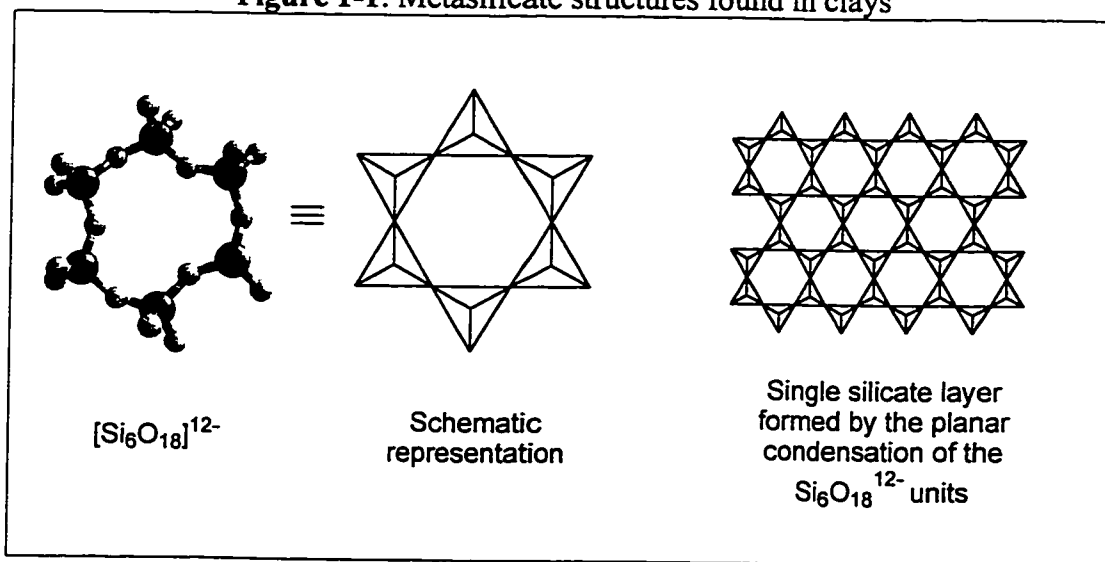
Sulfuric acid, hydrofluoric acid, aluminium chloride, titanium tetrachloride, amongst other materials, have been used for many years, both in academia and industry, with a great deal of success. These are all acids which are readily available, highly reactive, and, perhaps just as importantly, relatively inexpensive. So one might ask what possible reason could there be for finding replacements for these compounds? The answer becomes a little clearer when product isolation procedures are taken into account. The use of these acids generates large amounts of aqueous acidic waste which must be neutralized or otherwise disposed of. Although this is a trivial problem in the average organic chemistry laboratory where reactions in the kilogram scale are rarely performed, in industry by-product and spent reagent disposal is entirely another matter. The waste generated from a reaction which employs a few hundred kilograms of, for example,  $\text{AlCl}_3$  as catalyst is no longer acceptable in a world which is becoming increasingly environmentally conscious.

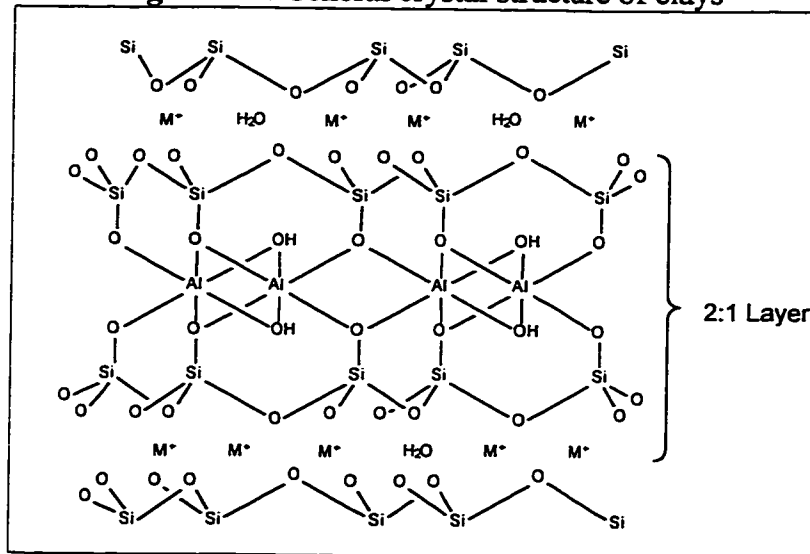
With this in mind, clay-based catalysts have become particularly attractive because the disposal problems associated with traditional catalysts are virtually eliminated taking with them a potential source of pollution.

### 1.1.1 INTERNAL STRUCTURE OF MONTMORILLONITE CLAYS

Clays belong to the family of the silicate minerals.<sup>2</sup> More specifically, clays are aluminosilicate minerals consisting of layers of octahedral  $\text{AlO}_6$  units sandwiched between two layers of tetrahedral  $\text{SiO}_4$  units. The silicon units are arranged in a 6T network which means that the repeat distance consists of six tetrahedra as shown in **Figure 1-1**. In this arrangement, three of the four oxygen atoms are shared between the silicon atoms leaving the remaining apical oxygen to be shared with the octahedral  $\text{AlO}_6$  units. This “sandwich” is known as a 2:1 clay layer (**Figure 1-2**).

**Figure 1-1: Metasilicate structures found in clays**



**Figure 1-2: General crystal structure of clays**

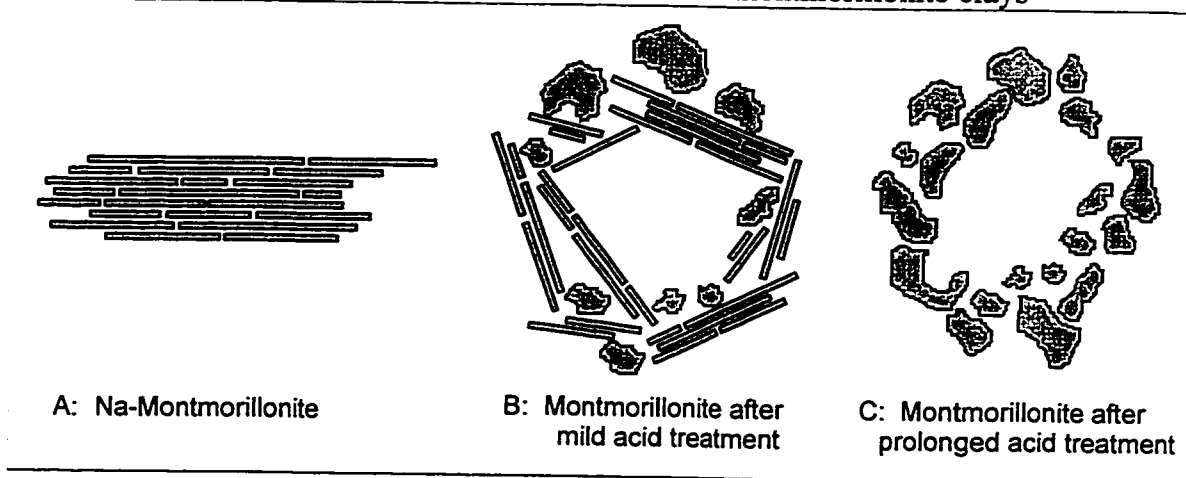
There are many varieties of clays and these differ, for the most part, by the types of atoms that may replace either the silicon or aluminium atoms and by the species that reside in the interlayer regions.<sup>2</sup> The clay used in this study, montmorillonite, is a clay where some of the aluminium(III) atoms have been replaced by iron(II) or magnesium(II). This has the effect of generating an overall negative charge on the clay sheet which then must be counterbalanced by cations such as Na<sup>+</sup>, K<sup>+</sup>, Mg<sup>2+</sup>, or Ca<sup>2+</sup> (shown as M<sup>+</sup> in **Figure 1-2**). These cations are bound in the interlayer regions, along with water molecules, by weak electrostatic forces and can therefore be subject to cation exchange reactions.

### 1.1.2 A MODIFIED MONTMORILLONITE: “K10”

Ordinary montmorillonite possesses little catalytic activity because the closely stacked arrangement of the clay sheets (**Figure 1-3A**) prevents any organic molecule

from penetrating the interlayer regions. Any reactivity is, therefore, limited to the external surfaces of the sheets. There are ways, however, of getting around this problem. One possible solution deals very directly with the problem, so to speak, and simply involves propping the layers apart by introducing large organic or inorganic cationic species, known as pillars, between the clay sheets.<sup>3</sup> The second method, although at first glance seems less elegant, involves disrupting the arrangement of the sheets to such a degree so as to increase the number of surfaces available for reactions to occur.<sup>4,5</sup> This involves treating the clay for a few hours with aqueous acid to partly dissolve the silica/alumina framework. K10 is a commercially available montmorillonite that has been acid-treated in this manner.

**Figure 1-3: Effect of acid treatment on montmorillonite clays**



Acid treatment causes two important structural changes to occur in the clay which dramatically increase the clay's catalytic activity. First of all, flocculation of the clay occurs due to coulombic attraction of protonated hydroxyl sites on the edges of a sheet and the negatively charged surface of neighbouring sheets. This flocculation has

sometimes been described as resulting in a “house of cards” structure. Second, many of the 2:1 layers are completely destroyed, through leaching of the aluminium from the octahedral sites, resulting in silicate sheets and amorphous silica being interspersed throughout the “house of cards” (**Figure 1-3B**). The formation of this type of structure explains the three basic changes in the physical properties of the clay:

- i.* A five-fold increase in the measured surface area. This results from the extensive disruption of the ordered and compact lamellar structure of the clay thus exposing many of the “internal” sheets.
- ii.* A six-fold increase in the cumulative pore volume in the clay. The gigantic number of cavities which result from the “house of cards” form the extensive micro-, meso-, and macropore networks of the acid-treated clay. Catalytic activity is believed to take place in the mesopores and in K10 these range, on average, from 5 to 10 nm but may be as large as 20 nm.
- iii.* A roughly 50% decrease in the cation exchange capacity of the clay. This is hardly surprising. Most of the cation exchange sites reside in the interlamellar regions and therefore it is to be expected that any disruption in this area would adversely affect this property.

The active sites of clays have been examined by studying the IR spectrum of pyridine molecules adsorbed on the clay. Pyridine is an excellent molecule for this kind of study because its IR absorption bands are very sensitive to its environment and this can be exploited in order to determine whether the pyridine is free, is bound to either Brønsted or Lewis acid sites, or is hydrogen-bonded. Benzonitrile is another common

test molecule, but unlike pyridine it is unaffected by Brønsted acids interacting only with Lewis acid sites.

Clark and Brown<sup>4,6</sup> have recorded the IR spectra of pyridine adsorbed on K10 and have observed absorption bands at 1637 and 1537  $\text{cm}^{-1}$  which are indicative of the presence of the pyridinium ion. IR studies with benzonitrile do not show significant changes in the absorption bands. These observations suggest that the active sites in K10, for the most part, are Brønsted-acid sites

However, if K10 is thermally activated prior to adsorption of pyridine, the pyridinium ion absorption bands disappear. Since thermal activation of the clay has, as a general rule, the effect of removing any water molecules physisorbed on the clay, this observation indicates that the water molecules are essential for the Brønsted sites. It has been previously theorized that the Brønsted activity of K10 was due to the polarization of these water molecules by Lewis acidic cations in the clay, but since there is no IR evidence for Lewis bound pyridine molecules, this is unlikely and therefore the exact role that water plays in the Brønsted activity of K10 is not yet well understood.

### 1.1.3 CLAYZIC

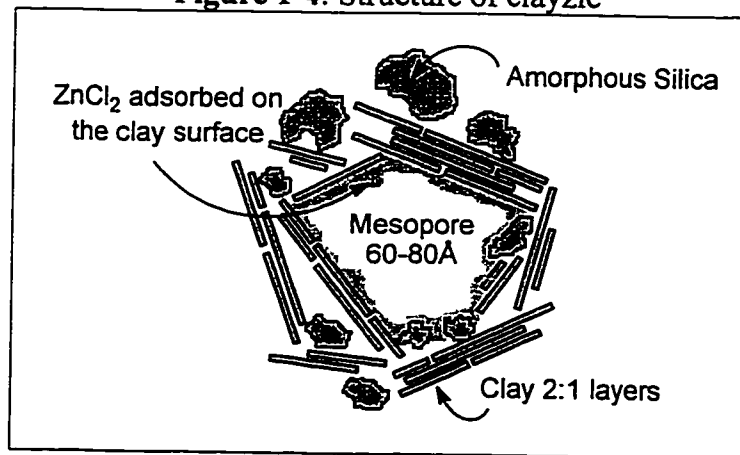
There are two common methods that are used to increase the catalytic activity of K10 and both involve the use of various metal salts in an attempt to create Lewis acid sites in the clay. The first method simply involves washing the clay with a solution of the desired metal salt in order to promote cation exchange.<sup>7</sup> The second method involves

mixing the clay with a metal salt solution followed by evaporation of the solvent after a set time thus essentially impregnating the clay with large amounts of the salt.<sup>8,9</sup>

Cation exchanged clays do indeed show an increase in activity and have found some use in organic synthesis (**Chap. 1.1.3**),<sup>7</sup> but it is the impregnated clays which have proven to be the most active supported catalysts. In particular, K10 impregnated with zinc chloride, termed clayzic, has been found to be a highly active and yet at the same time a fairly selective Friedel-Crafts catalyst. In addition to this, when the clayzic is calcined (typically at 250°C overnight), the rate increase in Friedel-Crafts reactions is dramatic.

In order to test and compare the activity of various catalysts, the benzene-benzyl chloride reaction has become a favourite in this field of study.<sup>6</sup> Clayzic shows an activity several orders in magnitude higher than the best ion-exchanged materials with selectivity towards mono-alkylation at 100% and conversion being greater than 80%.

**Figure 1-4: Structure of clayzic**



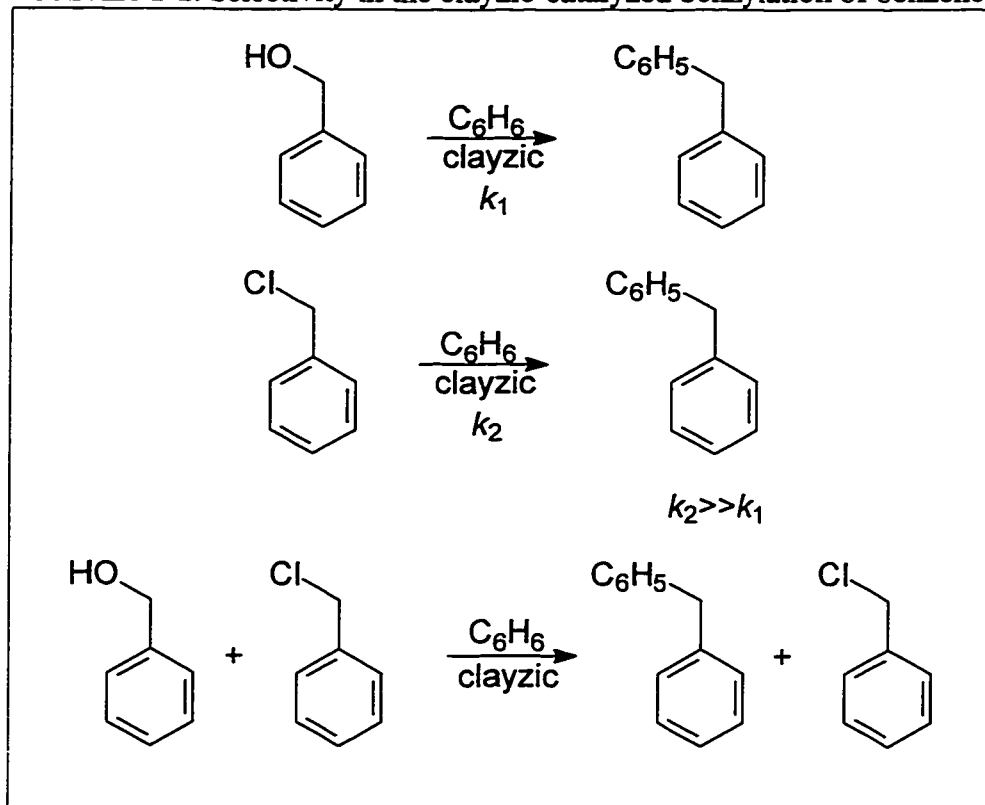
It is proposed that the structure of clayzic differs from that of K10 only in that the surfaces of the clay are coated with a layer of zinc chloride (**Figure 1-4**). Therefore, as

might be expected, pyridine adsorption studies<sup>4,5</sup> of this catalyst differ from that of ordinary K10 in that one now observes absorption bands due to Lewis-bound pyridine molecules in addition to those due to the pyridinium ion (which disappear when the catalyst is calcined). One important thing to note is that the positions of the IR bands indicate, even when the clay is thermally activated, that the zinc chloride in clayzic is not a much stronger Lewis acid than ordinary zinc chloride. Clark suggests,<sup>4</sup> therefore, that the catalytic activity of clayzic is not due to the presence of a somehow stronger Lewis acidic zinc species but rather due to the presence of regions where the local concentration of the Lewis acid is very high.

Another question that arises from these studies is whether the zinc exists as zinc chloride or whether it is somehow co-ordinated to the clay (perhaps *via* the oxygen atoms). Some recent work provided evidence for the existence of zinc chloride in clayzic.<sup>10</sup> Raman spectroscopy was used on clayzic as well as on bulk and on  $\text{SOCl}_2$ -dried zinc chloride to detect the Zn-Cl stretch in the samples. This led to the conclusion that Zn(II) was present as thoroughly dehydrated zinc chloride.

The theory that the catalytic sites in clayzic consist of regions of high concentration of zinc chloride (making these highly polar) has been given strength by competitive studies performed with the Friedel-Crafts benzylation of benzene.<sup>6</sup> Benzene reacts with both benzyl alcohol and benzyl chloride in the presence of clayzic to form diphenylmethane. As one would expect, the rate of reaction with benzyl chloride is much greater than that with benzyl alcohol. However, when the reaction is performed in the



**Scheme 1-1:** Selectivity in the clayzic-catalyzed benzylation of benzene

presence of both benzyl chloride and benzyl alcohol (**Scheme 1-1**), one observes that the benzyl alcohol, albeit slowly, reacts first. Once the supply of benzyl alcohol in the reaction has been exhausted, then benzyl chloride begins to react. This is explained by the fact that benzyl alcohol is the more polar of the two species and so it is preferentially attracted to the very polar active sites in the clay.

Another interesting observation that is consistent with this theory is that the rate of benzylation of anisole is much slower than that of benzene.<sup>10</sup> Once again this may be explained by invoking the presence of highly polar sites in the clay. Because the anisole molecule is more polar than benzyl chloride, it is more strongly adsorbed onto the catalyst. It therefore competes with the benzyl chloride for the active sites resulting in an overall reduction in the rate of reaction.

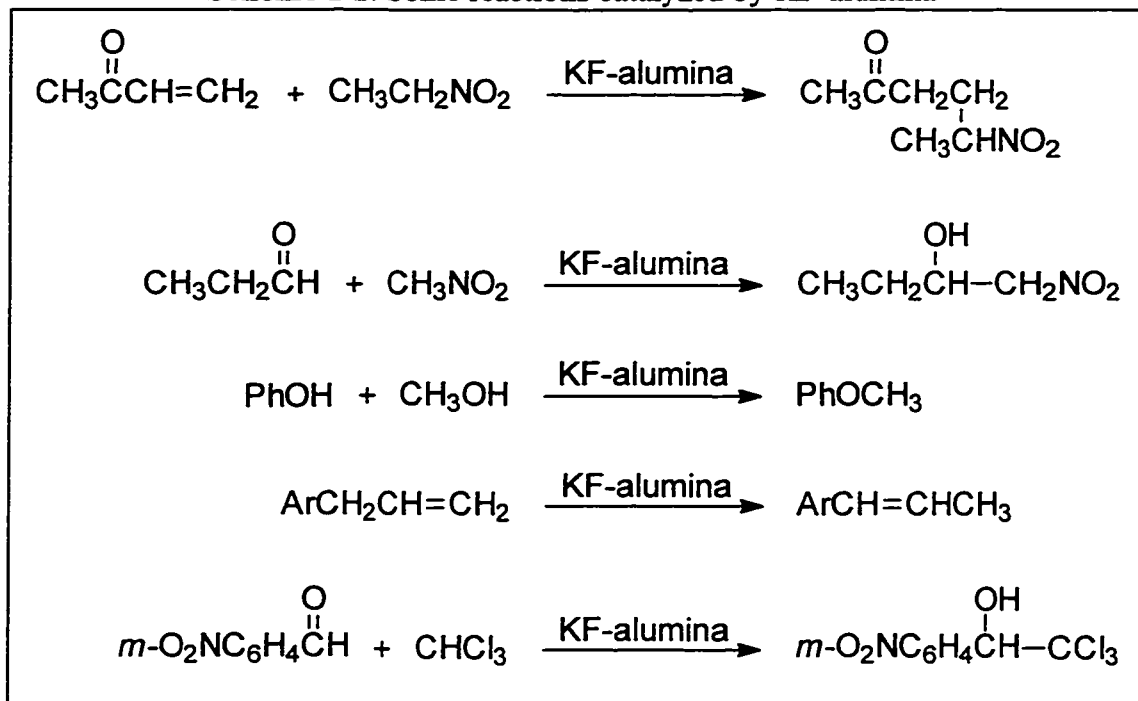
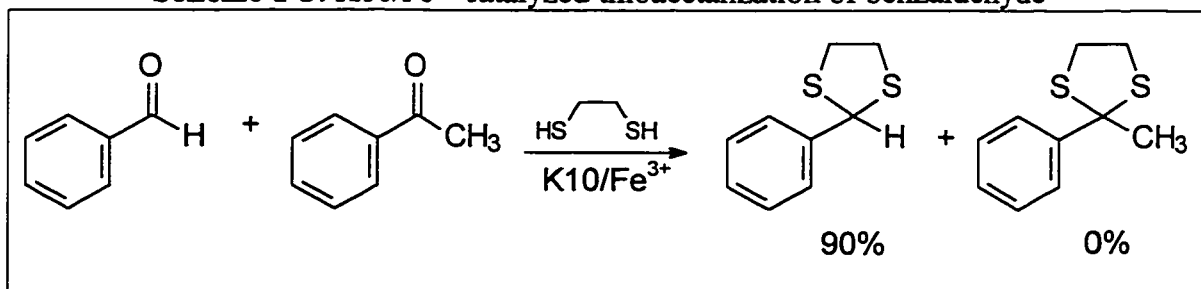
#### 1.1.4 CLAYS IN ORGANIC REACTIONS

##### A. BASE-CATALYZED REACTIONS

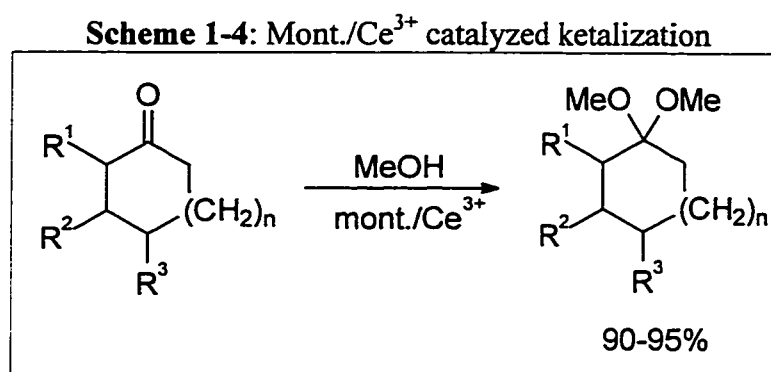
For many decades the organic reactions which employed clays were limited to petrochemistry and, in particular, to the cracking of crude oil. Even in this area, however, clays have lost their appeal and were replaced with more active solid acids such as zeolites and the new MCM catalysts.<sup>11</sup> Within the last decade, supported catalysts were given a second chance in academic research primarily due to ease of separation from products and subsequent recycling. One of the first truly catalytic supported reagents was KF/alumina,<sup>9</sup> which may be employed as a base catalyst in a variety of organic reactions such as the Aldol and Knoevenagel condensations as well as in alkylations and Michael reactions (**Scheme 1-2**). In contrast to bases such as hydrides, amides and alkoxides, KF/alumina is not destroyed in reactions that produce water although its activity can be reduced in some cases.

##### B. CARBONYL PROTECTION AND DEPROTECTION

The use of the thioacetal or thioketal functionality as a means of protecting the carbonyl group has always played an important role in organic synthesis. Fe<sup>3+</sup>-exchanged K10 has been found to be an excellent catalyst for this purpose with the added bonus of selectively catalyzing the reaction in favour of aldehydes (**Scheme 1-3**).<sup>12</sup>

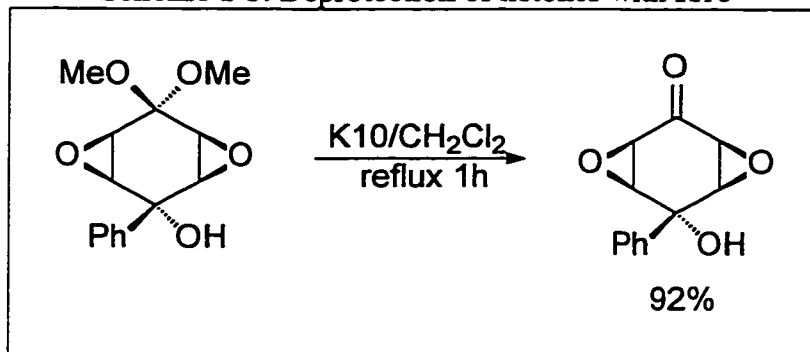
**Scheme 1-2:** Some reactions catalyzed by KF-alumina<sup>9</sup>**Scheme 1-3:** K10/Fe<sup>3+</sup> catalyzed thioacetalization of benzaldehyde<sup>12</sup>

This reaction, however, gives disappointingly low yields when clays (as well as resins and zeolites) are used in conjunction with alcohols. Uemura and co-workers<sup>13</sup> tested the commonly used  $\text{Zn}^{2+}$ ,  $\text{Fe}^{3+}$ ,  $\text{Na}^{+}$ -exchanged montmorillonites as well as  $\text{Ce}^{3+}$ -exchanged montmorillonite and found that only with the latter were they able to prepare the ketal in good yield (**Scheme 1-4**).

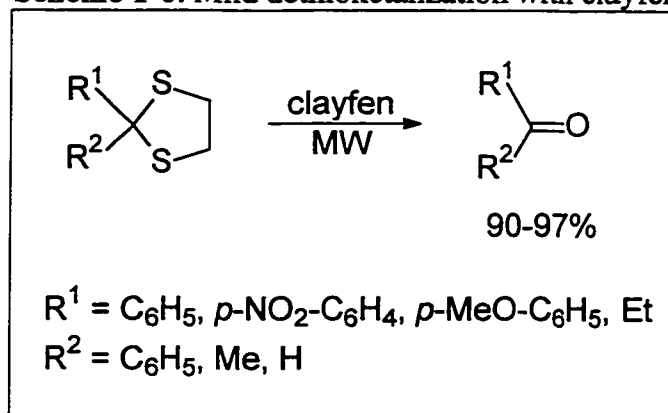


The reverse reaction, as might be expected, is also possible as shown by Taylor.<sup>14</sup> In this case, there is enough water present in the clay to completely convert the ketal back to the ketone under very mild conditions. Usually stirring at room temperature for a couple of hours is sufficient to effect the transformation, but, as in the example below (**Scheme 1-5**), mild heating may sometimes be necessary. Filtration and evaporation of the solvent was all the workup required in many instances to obtain a pure sample of the product.

Under normal conditions, the deprotection of a thioketal usually requires the use of heavy metal salts, but one may also use a less toxic catalyst such as K10 impregnated with ferric nitrate, "clayfen", to perform this reaction. Initially,<sup>15</sup> the use of clayfen in this reaction was found to require large amounts of solvent and several hours (3-6 h) for

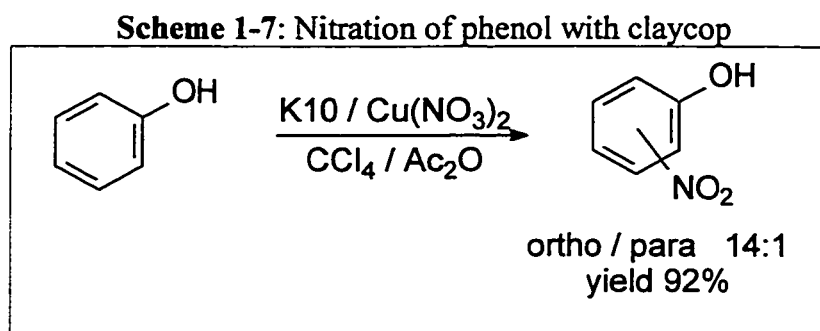
**Scheme 1-5:** Deprotection of ketones with K10

completion.<sup>16</sup> Recently, however, Varma<sup>17</sup> has found that by simply mixing the ketal and the clay and irradiating the dry mixture in an ordinary household microwave oven, the reaction was completed within minutes and with excellent yields (**Scheme 1-6**). Again, the workup is simple and involves washing the clay with dichloromethane. The dithiol produced in this reaction is so strongly bound to the clay that a base-extraction of the washings need not be performed.

**Scheme 1-6:** Mild dethioketalization with clayfen

### C. NITRATIONS

This reaction has been studied extensively by Laszlo and co-workers.<sup>18</sup> They found that “claycop”, which is cupric nitrate impregnated on K10, is a fairly mild nitrating agent for highly activated aromatic compounds (**Scheme 1-7**). By adding some fuming nitric acid, Laszlo also found that he was able to nitrate less reactive species such as aryl halides.

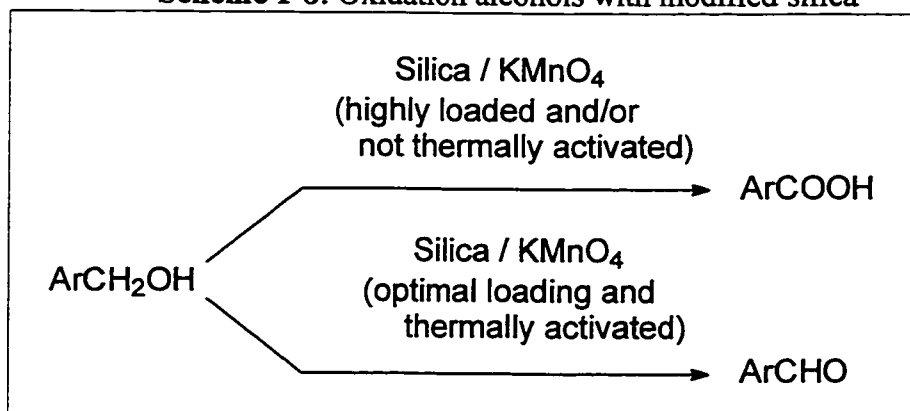


### D. OXIDATIONS

One of the earlier solid oxidants was found to be  $\text{KMnO}_4$  on silica. This reagent, although it is a stoichiometric reagent rather than a catalyst, has been found to be fairly selective depending on the way it is prepared. Clark<sup>9</sup> has discovered that by preparing the reagent with an optimal loading of  $\text{KMnO}_4$  and thermally activating it, benzyl alcohol may be oxidized to benzaldehyde. On the other hand, by preparing a highly loaded or unactivated reagent, the reaction proceeded all the way to benzoic acid (**Scheme 1-8**).

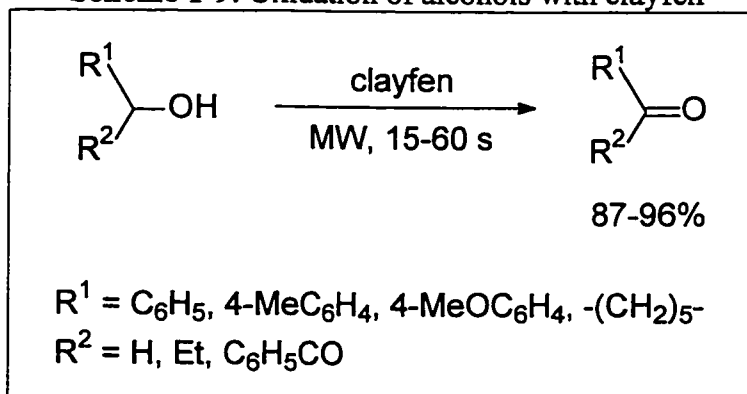
Treating alumina with  $\text{KMnO}_4$  or  $\text{K}_2\text{Cr}_2\text{O}_7$  under carefully controlled conditions produces a truly catalytic reagent capable of oxidizing alkylaromatics under normal pressure using atmospheric oxygen as the oxidant.<sup>19</sup>

**Scheme 1-8:** Oxidation alcohols with modified silica

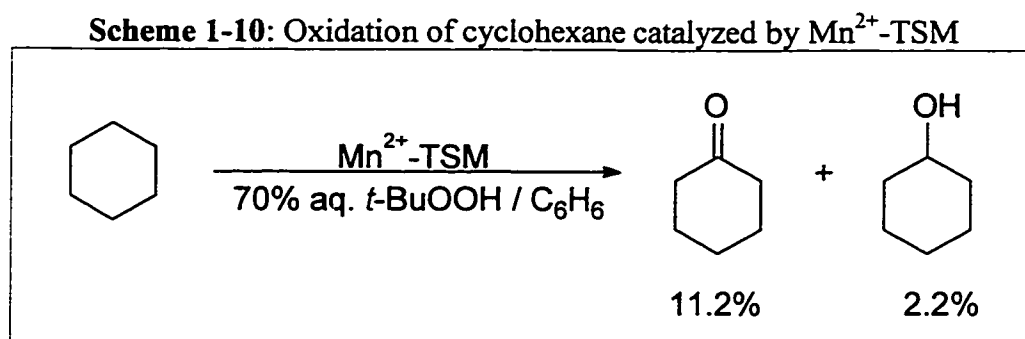


As well as performing dethioacetalizations, clayfen may be used to oxidize alcohols to aldehydes or ketones. Varma reports that in addition to the shorter reaction times, by performing the reaction in a standard household microwave oven under solvent-free conditions, the amount of catalyst required is half of that which is needed under standard heterogeneous conditions (**Scheme 1-9**).<sup>20</sup>

**Scheme 1-9:** Oxidation of alcohols with clayfen

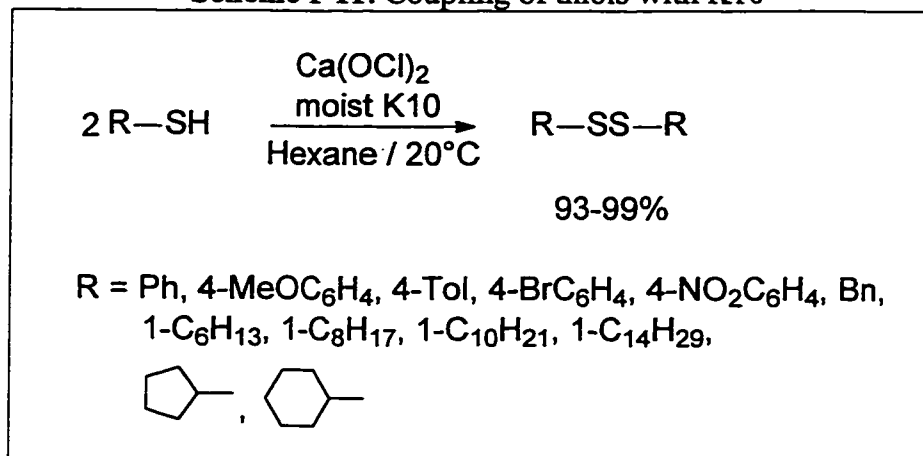


The oxidation of alkanes to alcohols or ketones is of great industrial importance. Uemura and co-workers have achieved moderate success employing a  $\text{Mn}^{2+}$ -exchanged fluorotetrasilicic mica ( $\text{Mn}^{2+}$ -TSM) as catalyst and *tert*-butylhydroperoxide as the oxidizing agent (**Scheme 1-10**).<sup>21</sup> A similar reaction is observed with  $\text{Mn}^{2+}$ -montmorillonite although the yields are even lower.



The oxidation of thiols to disulfides is a very well known reaction. This conversion may be performed with a large variety of oxidizing agents, but a review of the literature shows that not all of the existing methods may be applicable for all thiols. Morimoto<sup>22</sup> claims that by employing  $\text{Ca}(\text{OCl})_2$  in conjunction with moist K10, one may obtain excellent yields of disulfides for a large variety of thiols. More importantly, this method improves upon existing clay-based reagents for the formation of disulfides in that thiols bearing electron-withdrawing groups may be oxidized as efficiently as electron-rich thiols (**Scheme 1-11**).



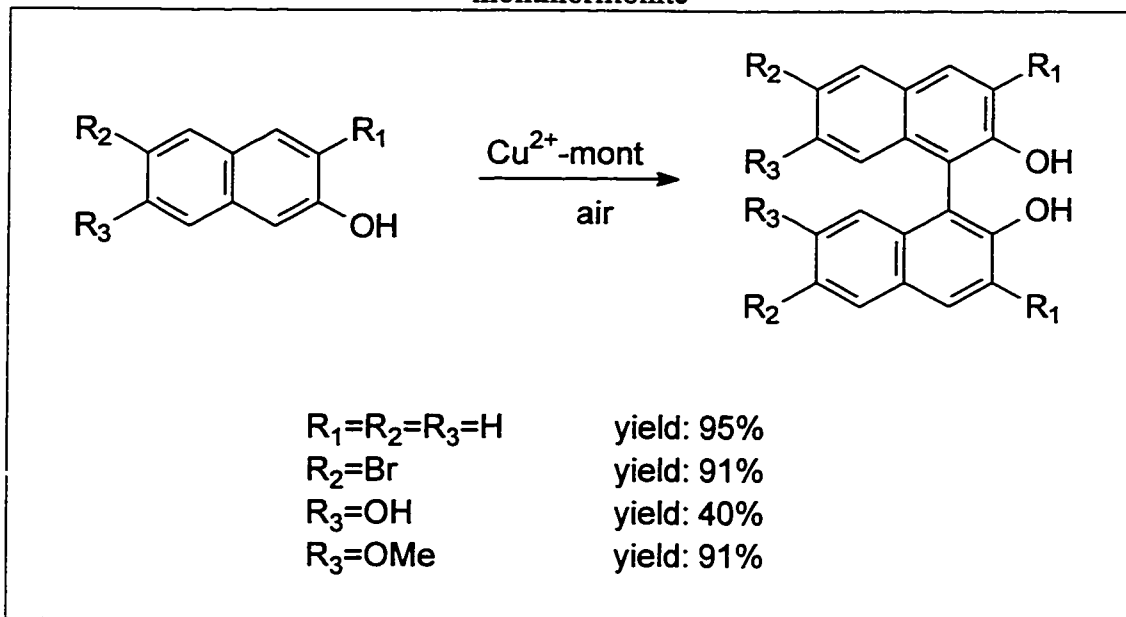
**Scheme 1-11: Coupling of thiols with K10**

## E. CARBON-CARBON BOND FORMATION REACTIONS

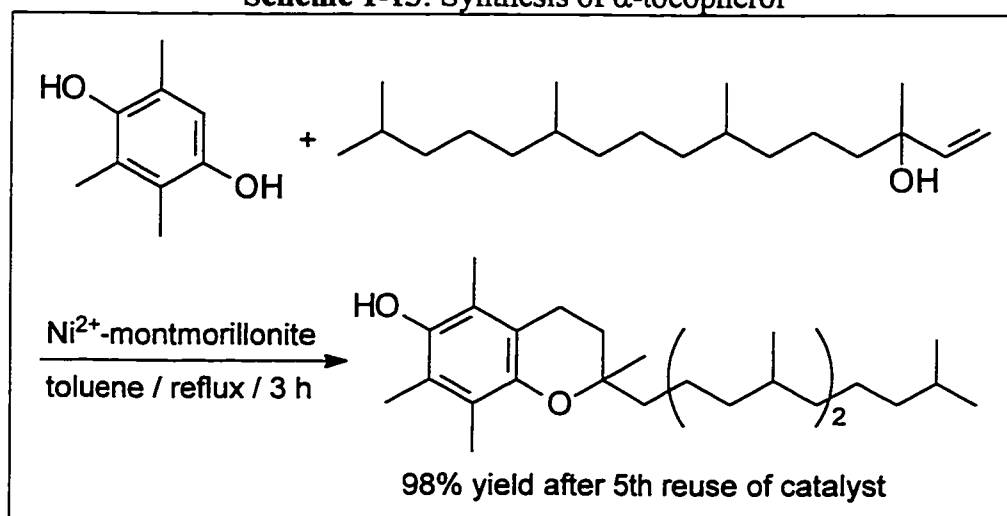
The best-known clay-catalyzed reaction for C-C bond formation is the Friedel-Crafts alkylation or acetylation.<sup>9,23,24</sup> This, however, does not mean that other such reactions have been ignored in clay research. Kantam and Santhi have employed Cu<sup>2+</sup>-montmorillonite to oxidatively couple 2-naphthols in their synthesis of various binaphthols. In addition to good yields and ease of workup, the copper-exchanged clay may be re-used without any significant loss of activity (**Scheme 1-12**).<sup>25</sup>

Yamamoto has studied the clay-catalyzed condensation of hydroquinone with allylic alcohols and subsequently used it to synthesize  $\alpha$ -tocopherol (better known as Vitamin E, **Scheme 1-13**).<sup>26</sup> Most metals he used worked equally well to promote the condensation with the exception of La-mont, Sm-mont and Na-mont. Re-use of the catalyst, as demonstrated in a series of five consecutive reactions with Ni-mont, suggests that this type of reaction system would be commercially viable.

**Scheme 1-12:** Coupling of 2-naphthols catalyzed by  $\text{Cu}^{2+}$ -exchanged montmorillonite

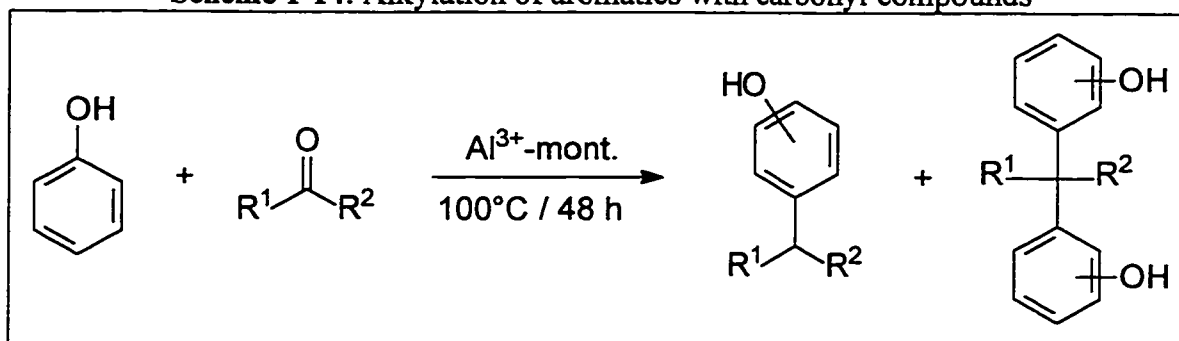


**Scheme 1-13:** Synthesis of  $\alpha$ -tocopherol



The aromatic alkylation with aldehydes and ketones is less well studied than its counterpart with alkyl halides, alcohols or alkenes. This is primarily due to low yields resulting from the formation of polymeric by-products.  $\text{Al}^{3+}$ -exchanged montmorillonite catalyzes this reaction to give the alkylation products in moderate yield (**Scheme 1-14**).<sup>27</sup> When the carbonyl is an aldehyde, the product distribution favours the *bis*(hydroxyphenyl) products while ketones favour the *mono*(hydroxyphenyl) products.

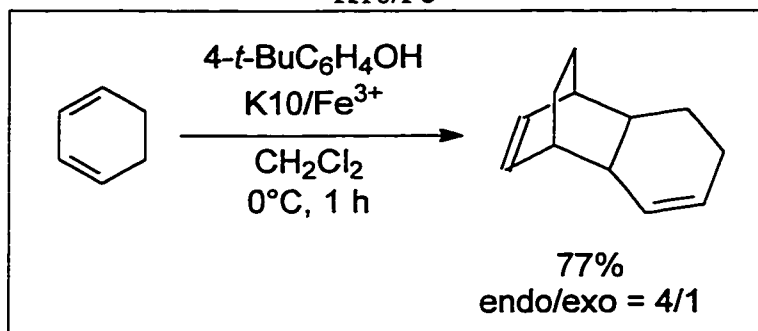
**Scheme 1-14:** Alkylation of aromatics with carbonyl compounds



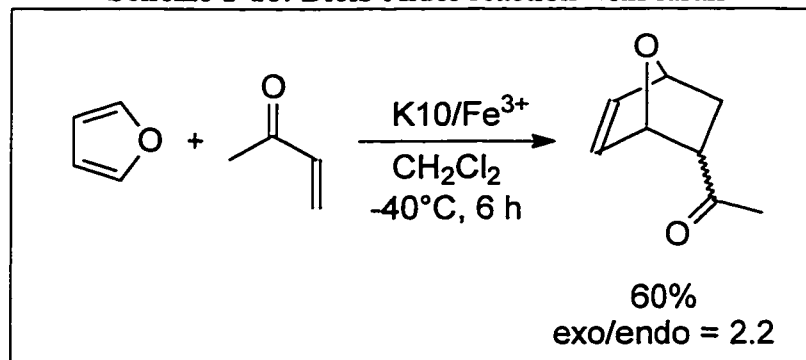
Clay-based Lewis acids may also be used as catalysts in Diels-Alder reactions. The reactions proceed under very mild conditions (-24 °C) and, as is usually the case, the workup simply involves filtration and removal of the solvent. Laszlo has used the oxidizing properties of  $\text{Fe}^{3+}$ -exchanged K10 to oxidize 4-*tert*-butylphenol to its radical cation and used this species to catalyze the Diels-Alder reaction of unactivated systems (**Scheme 1-15**).<sup>28</sup>

The Diels-Alder reaction with furans may also be carried out with the same clay-based catalyst. Although the yield is not quantitative, some stereoselectivity is observed (**Scheme 1-16**).<sup>29</sup>

**Scheme 1-15:** Diene self-condensation catalyzed by K10/Fe<sup>3+</sup>



**Scheme 1-16:** Diels-Alder reaction with furan



## 1.2 THIOLS, SULFIDES, AND DISULFIDES

### 1.2.0 INTRODUCTION

Thiols and their derivatives play a very important role in living systems as well as in many areas of industry and science. This is due, in part, to the relative high lability of the S-H and S-C bonds that permit them to undergo electrophilic or nucleophilic-type reactions depending on the conditions employed.

There are literally hundreds, if not thousands, of methods for the preparation of thiols, sulfides and disulfides in the literature, a complete review of which is beyond this dissertation. Several excellent reviews, as well as books, have been published which deal with this subject very effectively.<sup>30,31,32</sup> However, when reading this material, one cannot help but notice that a large majority of syntheses fall into two major categories:

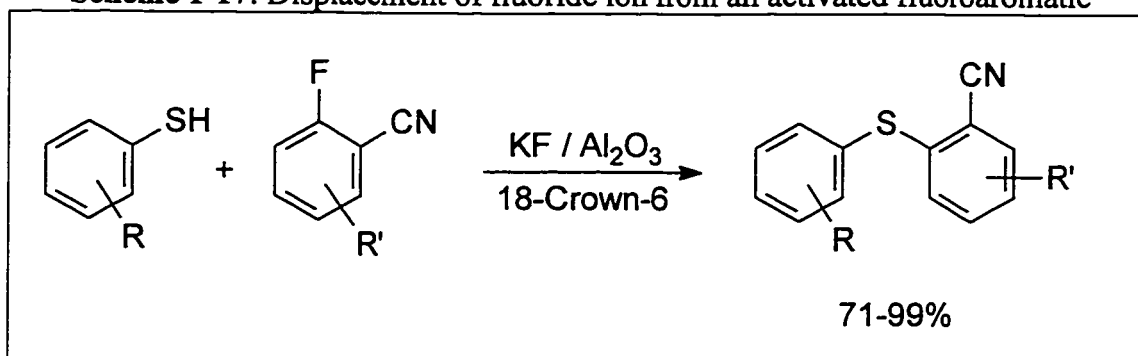
- i.* The reaction of various types of carbon nucleophiles with sulfur, disulfides, or sulfenyl halides, and
- ii.* The reaction of carbon-electrophiles with nucleophilic sulfur species.

One drawback in many of these methods, unfortunately, is that they were designed to introduce only one sulfur atom into the molecule. The interest in compounds such as tetrathiafulvalenes (**Chapter 1.3**), however, has sparked a greater demand for compounds having, at the very least, a 1,2-dithiol functionality. Abruptly, the large variety of organosulfur syntheses becomes rather inadequate and shrinks to a very few select methods.

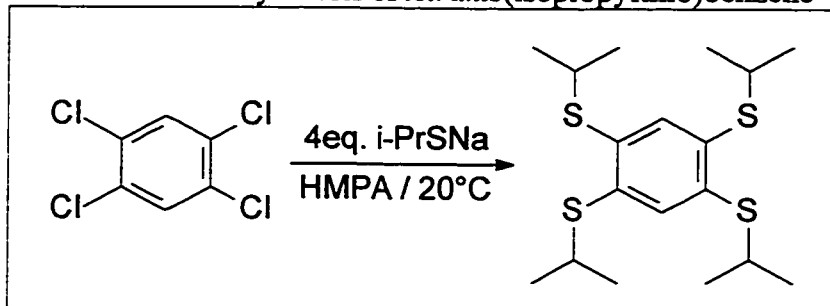
### 1.2.1 PREPARATION OF ARYL THIOLS OR SULFIDES

As mentioned previously, aryl sulfides are most commonly prepared by the reaction of aryl-lithium species with disulfides or sulfenyl halides but they may also be prepared by the reaction of thiolates with aryl halides in aprotic polar solvents such as DMF or HMPA. This reaction is most easily accomplished when the arene is activated as demonstrated in **Scheme 1-17**. Note also the use of KF/alumina as the base used in this example (see **Chapter 1.1.4A**).<sup>33</sup>

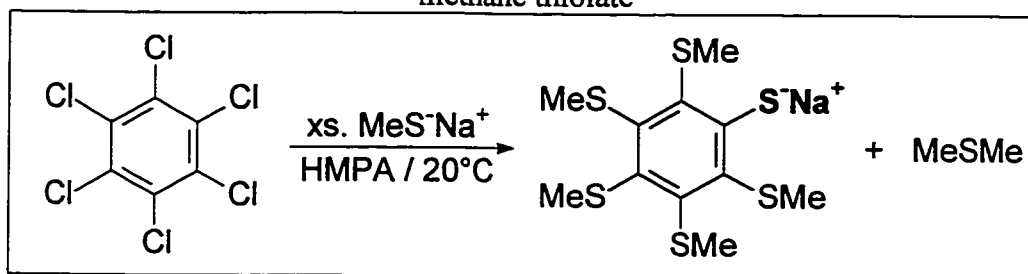
**Scheme 1-17:** Displacement of fluoride ion from an activated fluoroaromatic



Tiecco performed one of the most important series of studies on the synthesis of poly(alkylthio) aromatic compounds by this method.<sup>34</sup> These studies involved aromatic nucleophilic substitution of halides in polyhalobenzenes with alkyl thiolates in polar solvents such as DMF or HMPA followed by a metal/amine reduction to give the corresponding thiolates (for a discussion on these reductions see **Chapter 4**). The reactions proceed via a simple  $\text{S}_{\text{N}}\text{Ar}$  mechanism and do not stop until all halide atoms in the polyhalo-benzene have been replaced (**Scheme 1-18**).

**Scheme 1-18:** Synthesis of *tetrakis*(isopropylthio)benzene

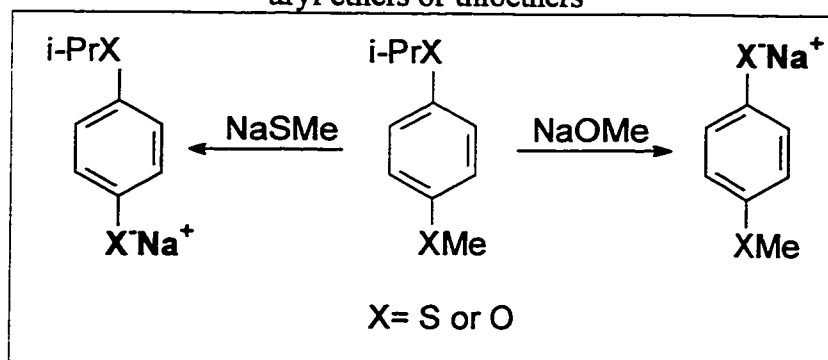
It was also discovered that when methane or ethanethiolates were used, the amount of thiolate had to be controlled carefully because, following the displacement of all the halides, an  $S_N2$  substitution occurred at a methyl (or ethyl) group displacing the corresponding aryl thiolate. This side-reaction, however, stops after only one thiolate has been displaced and so this particular method, although perhaps useful in other instances, is not suitable for the generation of arylpolythiolates (**Scheme 1-19**).

**Scheme 1-19:** Synthesis of aryl thiolates by reaction with excess methane thiolate

Tiecco also extended his studies to include compounds with both thioether and ether groups.<sup>35,36</sup> Depending on the type of alkyl group and the nucleophile used, he was able to selectively dealkylate specific groups (**Scheme 1-20**). By using the strongly nucleophilic methanethiolate, he was able to perform an  $S_N2$  reaction at a methyl group.

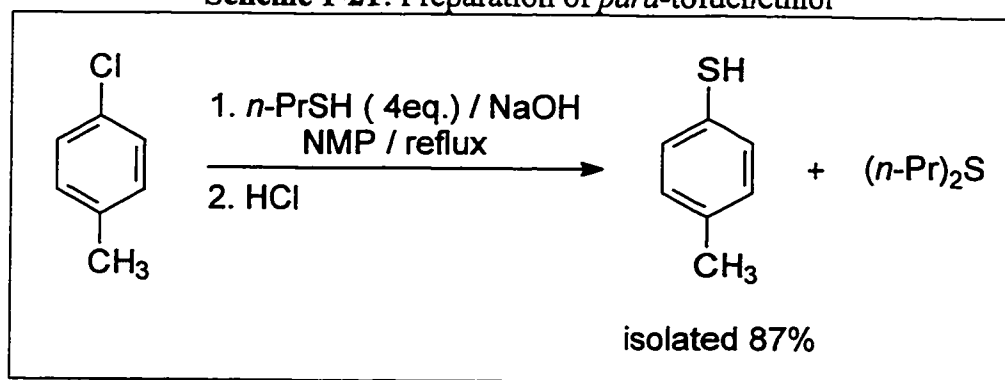
On the other hand, by using the strongly basic methoxide anion, elimination occurs at the isopropyl group generating propene and the thiolate (or phenolate).

**Scheme 1-20:** Selective removal of various alkyl groups on aryl ethers or thioethers



Ten years after Tiecco's work, the preparation of thiophenols from unactivated aryl chlorides was published by Shaw.<sup>37</sup> As would be expected, more forcing conditions are required for the reaction to proceed and Shaw solved this problem by using refluxing N-methyl-2-pyrrolidinone. By employing an excess of thiol, Shaw was able to directly obtain the aryl mercaptan in good yield (**Scheme 1-21**).

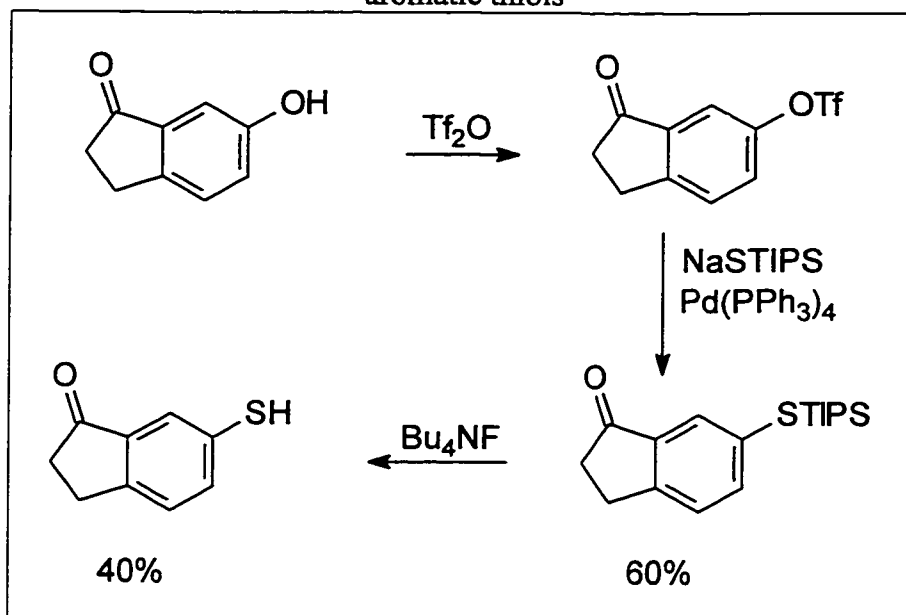
**Scheme 1-21:** Preparation of *para*-toluenethiol



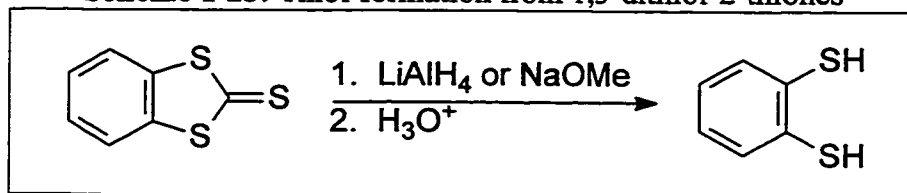


Aromatic thiols have also been prepared indirectly from phenols. The phenol is first converted into the triflate and then palladium chemistry is employed along with sodium triisopropylsilanethiolate (NaSTIPS). Simple deprotection of the resulting silylated thiol under standard conditions gives the desired compound (**Scheme 1-22**).<sup>38</sup> Although the yields in some cases are not very good, the availability of phenols makes this a convenient method for preparing a large variety of aromatic thiols.

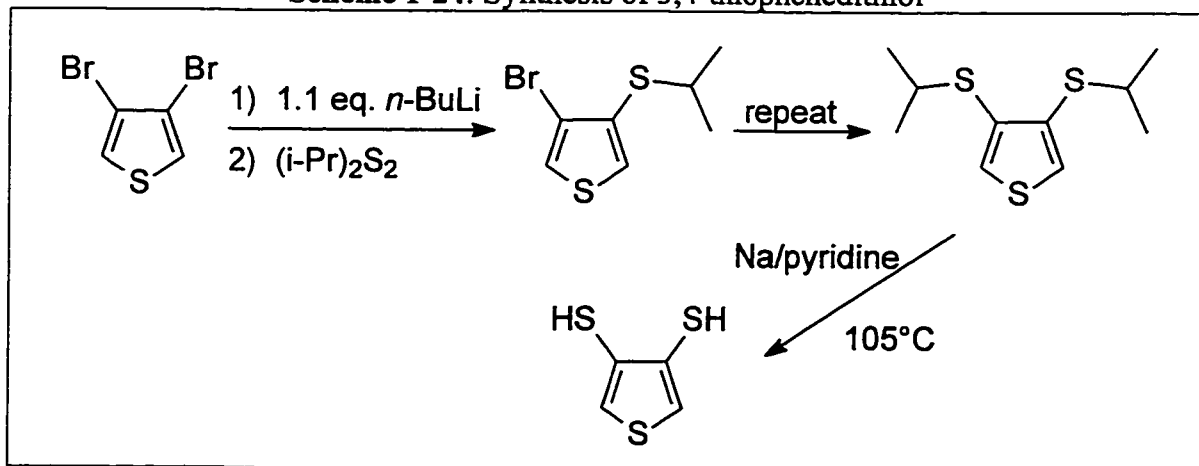
**Scheme 1-22:** The use of palladium chemistry in the synthesis of aromatic thiols



The preparation of aryl-1,2-dithiols may be accomplished by the reduction of benzo-1,3-dithiol-2-thiones (**Scheme 1-23**).<sup>39</sup> However, since such 1,3-dithioles-2-thiones are prepared from 1,2-dithiols (see **Chapter 1.3**), this method cannot be considered very useful unless the final product desired is not a tetrathiafulvalene or one of its derivatives.

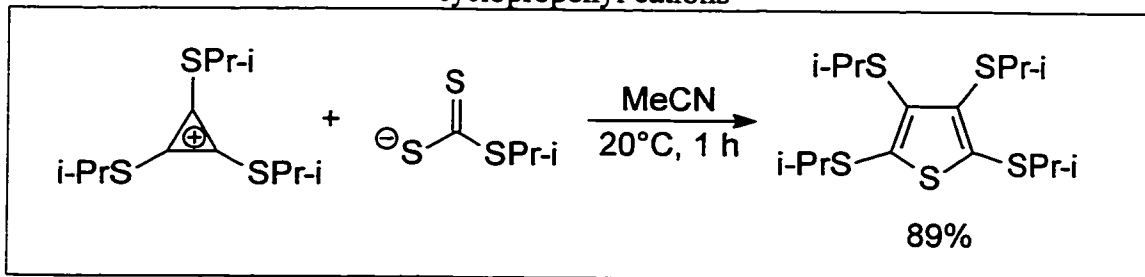
**Scheme 1-23:** Thiol formation from 1,3-dithiol-2-thiones

Some recent work by Reynolds describes the improved synthesis of 3,4-thiophenedithiol (**Scheme 1-24**).<sup>40</sup> He found, as others before him, that the reaction of the lithium species with elemental sulfur to be temperamental and he could never achieve yields close to those stated in the previous literature. Instead, he turned to generate the dithiol from *bis*(isopropylthio)thiophene. Reynolds performed a halogen-lithium exchange reaction on one of the bromines of 3,4-dibromothiophene and treated the resulting lithiothiophene species with isopropyl disulfide repeating the same process again for the second bromine. Reduction with sodium in pyridine (see **Chapter 4**) generated the dithiol.

**Scheme 1-24:** Synthesis of 3,4-thiophenedithiol

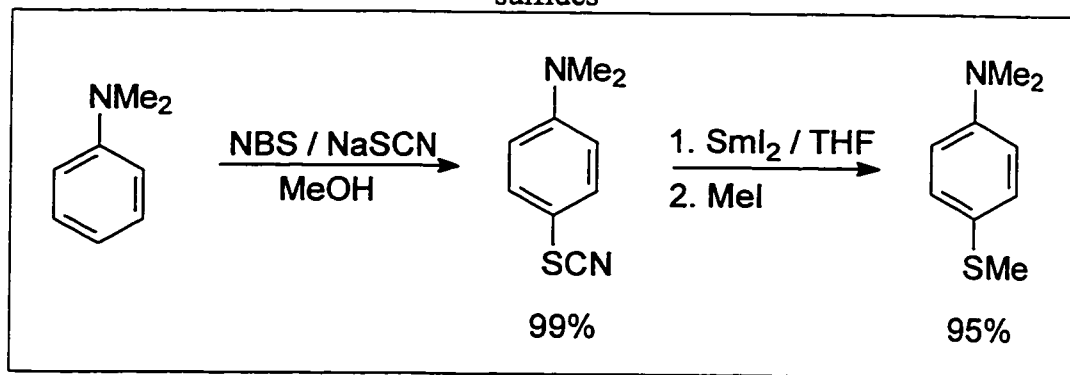
*Tetrakis(isopropylthio)thiophene* was recently prepared by Inoue,<sup>41</sup> albeit in microscale quantities, by the reaction of the cyclopropenyl cation and the carbon disulfide adduct of propane-2-thiol (**Scheme 1-25**).

**Scheme 1-25:** Synthesis of alkylthio-substituted thiophenes by reaction of cyclopropenyl cations



The reaction of various arylthiocyanates and samarium iodide followed by the appropriate electrophile is a very effective way to prepare a large variety of aryl sulfides and thioesters.<sup>42</sup> The thiocyanates are easily prepared under mild conditions by the reaction of N-thiocyanatosuccinimide with the aromatic substrate.<sup>43</sup> Both aromatic and heteroaromatic thiocyanates may be prepared with this procedure (**Scheme 1-26**).

**Scheme 1-26:** Thiocyanates as intermediates in the synthesis of aromatic sulfides

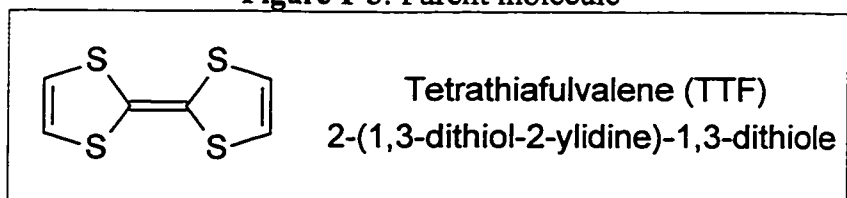


## 1.3 TETRATHIAFULVALENES

### 1.3.0 INTRODUCTION

The interest in the radical cation salts and charge transfer salts of tetrathiafulvalenes (TTF's) began in the early 1970's when it was first reported that the chloride salt of TTF possessed metallic conductivity.<sup>44</sup> The observed conductivity was modest, about  $0.2 (\Omega\text{cm})^{-1}$ , when compared to the conductivity metals such as copper, silver, or gold which exhibit conductivity of about  $10^6 (\Omega\text{cm})^{-1}$ . However, this level was enough to create world-wide interest in these compounds and some of the salts that were subsequently discovered possess conductivities that approach those found in metals.

**Figure 1-5: Parent molecule**

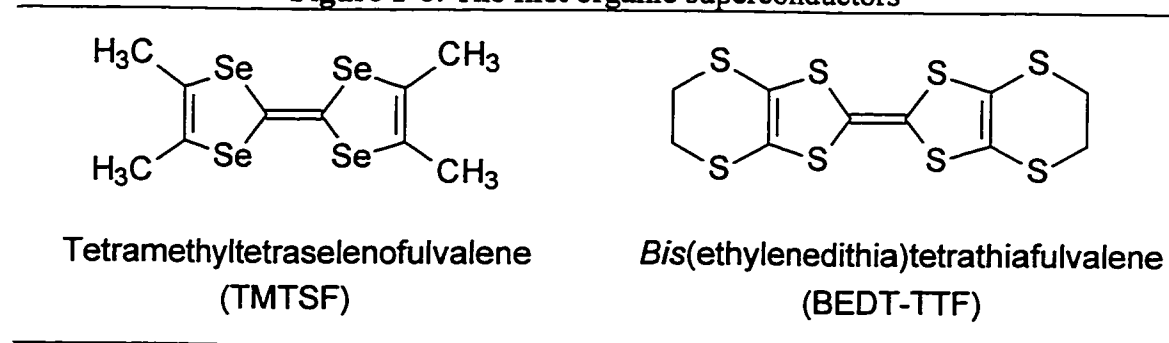


The reason for the interest in these and other conductive organic compounds (such as polythiophene and polypyrrole) stems from the fact that although their conductivity is not as high as that of metals (so far), the applications of these compounds in the area of electronics is immense. For example, the relative lightness of these materials could be exploited in places where weight is a major concern such as in aircraft or spacecraft. Also, the structure of these materials could potentially be controlled at the molecular

level making them an excellent choice in the areas of molecular electronic devices such as molecular switches, rectifiers, etc.

In 1980, it was reported that a selenium analogue of TTF, (tetramethyl-tetraselenofulvalene) $\text{PF}_6$ , exhibited superconductivity at low temperatures but under high pressure ( $T_c \sim 1.0\text{K}$  at 12kbar).<sup>45</sup> This was the first case where an organic compound exhibited the much-coveted property. Soon after,  $(\text{TMTSF})_2\text{ClO}_4$  was prepared and was found to be the first organic superconductor at ambient pressure ( $T_c \sim 1.2\text{K}$ ). A few years later, the first sulfur-based organic super-conductor,  $(\text{BEDT-TTF})_2\text{ReO}_4$ , was discovered.<sup>46</sup>

**Figure 1-6: The first organic superconductors**

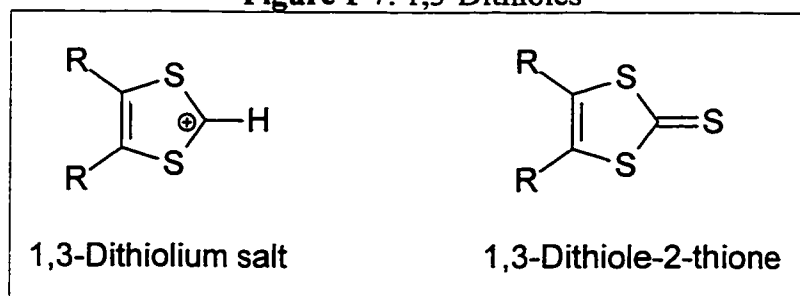


Current research in TTF derivatives and TTF-like molecules is focused mainly in the synthesis of novel compounds in the hopes of discovering materials with higher and higher conductivity's and, the "Holy-Grail" of materials science, a high-temperature superconductor. Research is also under way to better understand the role that the structures of these compounds play in the way these molecules interact with each other and how this ultimately affects the conductivity.

### 1.3.1 PREVIOUS SYNTHESSES OF TTF DERIVATIVES AND THEIR PRECURSORS

The most widely used routes towards the syntheses of TTF derivatives involve the coupling of 1,3-dithiolium salts or of 1,3-dithiole-2-thiones. Many of these syntheses, however, require the use of 1,2-dithiols, but unfortunately the syntheses for these, if they are not readily available, involve several steps.

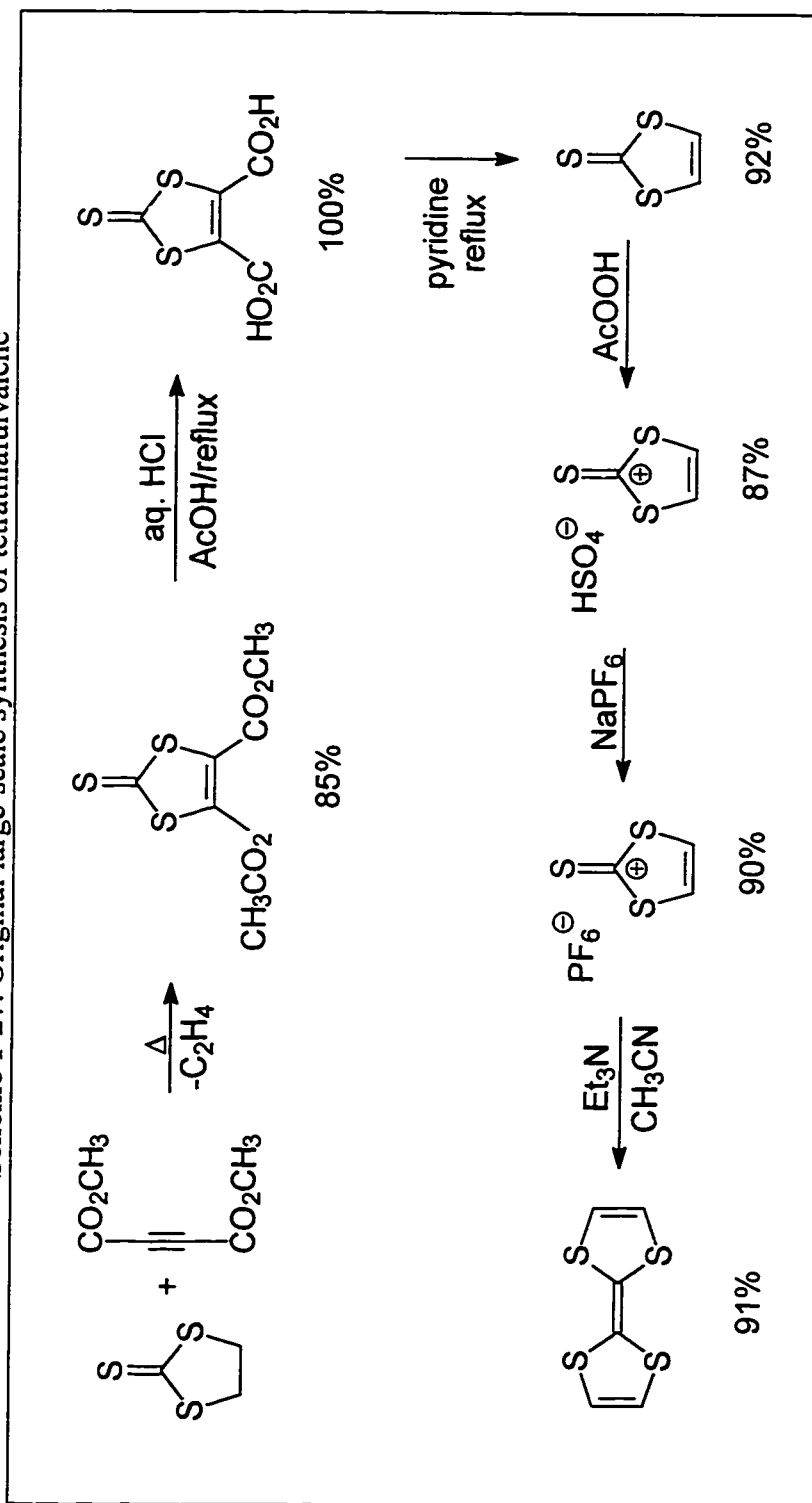
**Figure 1-7: 1,3-Dithioles**



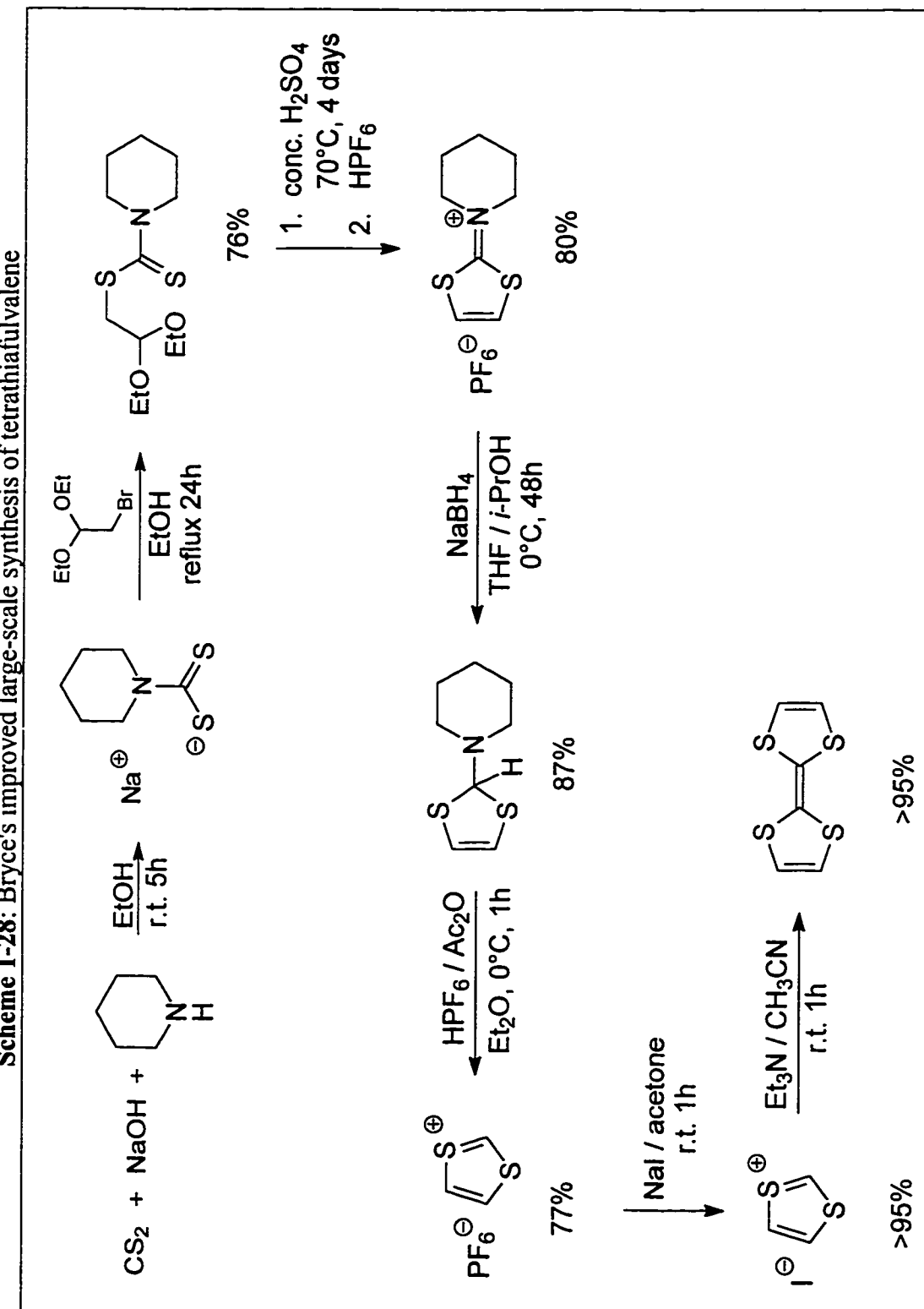
TTF itself was best synthesized according to the sequence outlined in **Scheme 1-27**. The overall yield of this six-step synthesis is a respectable 56% and is suitable for large-scales.<sup>47</sup>

Recently, Bryce and co-workers have published a new large-scale synthesis of TTF (**Scheme 1-28**).<sup>48</sup> Bryce claims that no chromatography is required at any stage and that *ca.* 20 g batches may be prepared at a time. The convenience of this scheme relies on the fact that it employs inexpensive and commonly available starting materials (unlike the starting material in the previous scheme). The overall yield is 37%.

**Scheme 1-27:** Original large-scale synthesis of tetrathiafulvalene

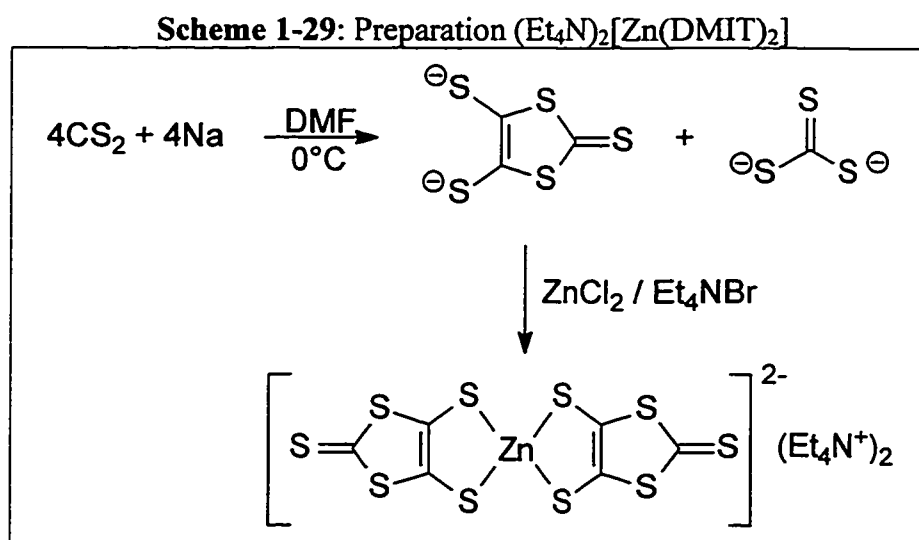


**Scheme 1-28:** Bryce's improved large-scale synthesis of tetrathiafulvalene



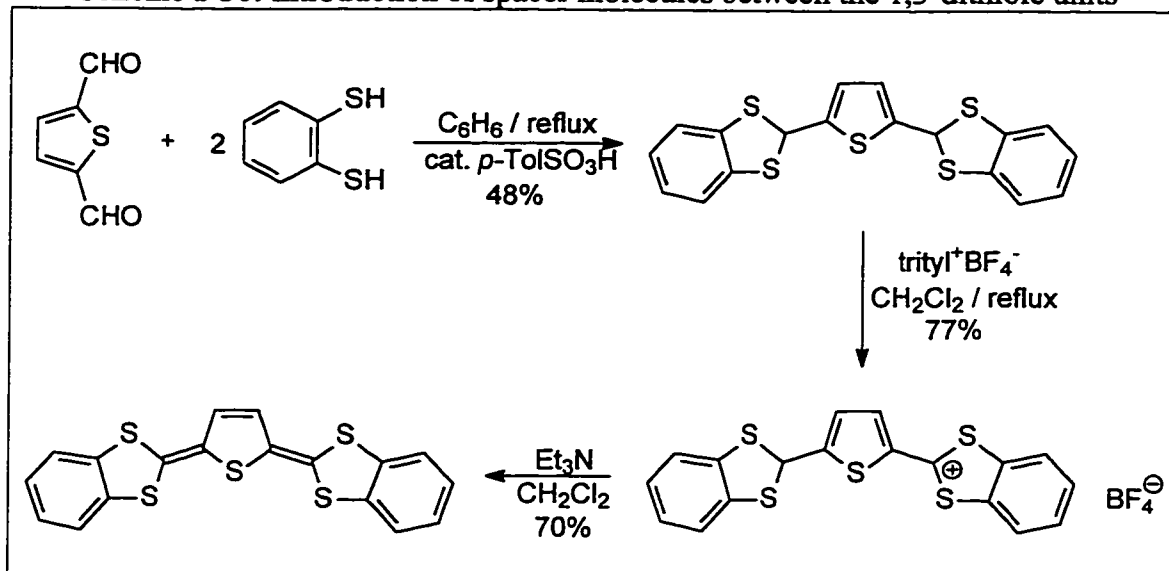


By far, the most widely used precursor for many TTF's is 4,5-dithiolato-1,3-dithiole-2-thione, also known as DMIT (an acronym for its archaic name, dimercapto-isotrithiole).<sup>49</sup> The parent DMIT is extremely unstable. When protonated, it undergoes immediate polymerization, while when deprotonated, its alkali metal salts are highly air sensitive. Therefore, for ease of separation from the reaction mixture as well as for handling and storage, the molecule is isolated as the tetraethylammonium salt of its zinc complex (Scheme 1-29).<sup>50</sup>



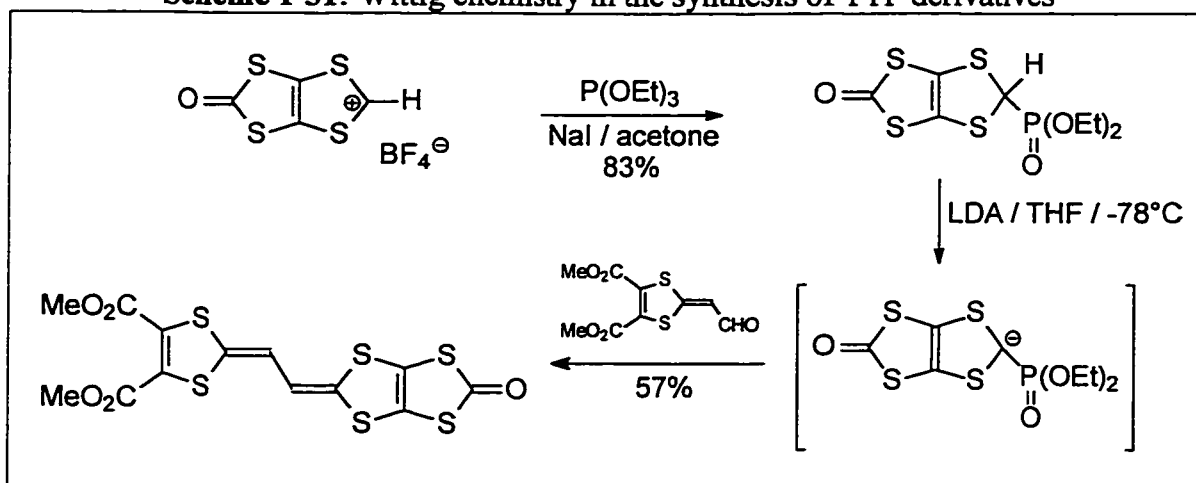
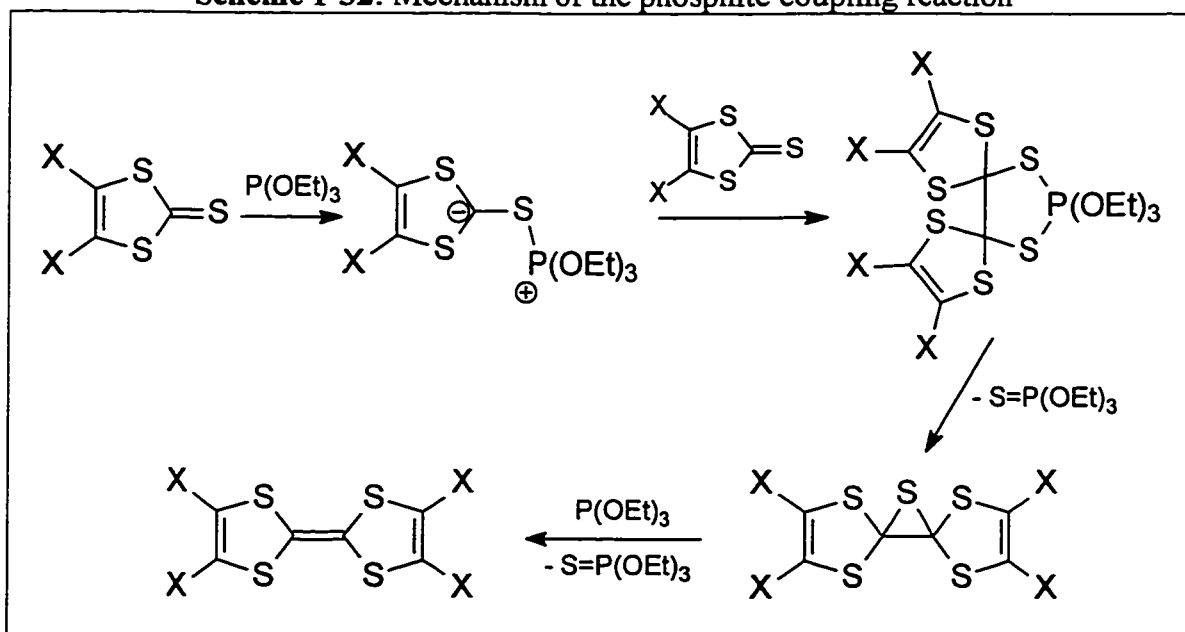
Most syntheses employing DMIT simply consist of reacting this compound with the appropriate electrophile. Becher has published a very useful review on the chemistry of this molecule, its synthesis, and its derivatization.<sup>51</sup>

TTF derivatives with spacers (extended conjugated  $\pi$ -systems between the dithiole rings) may also be prepared although a modification of the procedure is usually required. One of the more unconventional methods is shown in the synthesis below (Scheme 1-30) where a 1,3-dithiole precursor was never employed.<sup>52</sup>

**Scheme 1-30:** Introduction of spacer molecules between the 1,3-dithiole units

1,3-Dithiolium salts also react very easily with trialkyl phosphines or related compounds. Wittig-type chemistry can then be used with the resulting phosphonium salt or phosphonate ester for coupling to a suitable carbonyl compound.<sup>53</sup> This type of approach is particularly attractive for the synthesis of unsymmetrical TTF derivatives as well as spacer-based TTFs since there is nearly absolute control over which molecules are permitted to couple (**Scheme 1-31**).

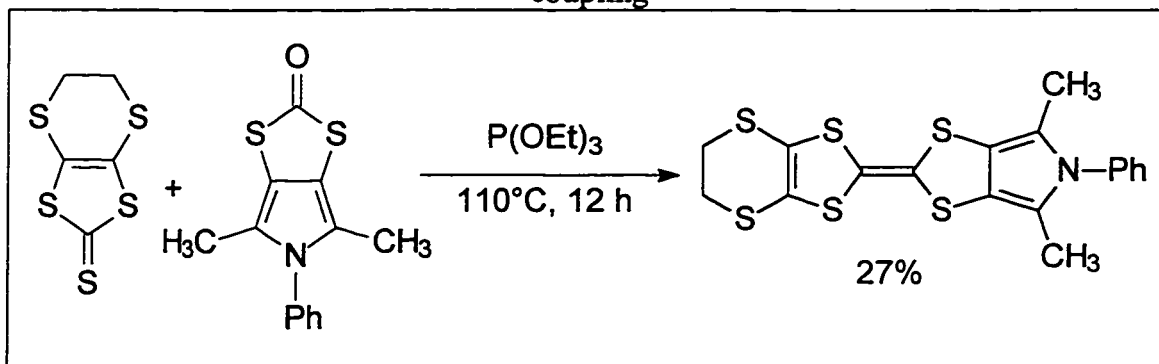
One of the most important and simplest methods of forming the TTF skeleton involves the coupling of a 1,3-dithiol-2-thione with a phosphine, phosphite (usually triethyl phosphite) or a phosphorus triamide. It has also been found that the yields usually improve when one of the dithiol-2-thiones is substituted by a dithiol-2-one. The phosphine (or phosphite) coupling reaction has been extensively studied and the mechanism illustrated in **Scheme 1-32** is proposed.<sup>54</sup>

**Scheme 1-31: Wittig chemistry in the synthesis of TTF derivatives****Scheme 1-32: Mechanism of the phosphite coupling reaction**

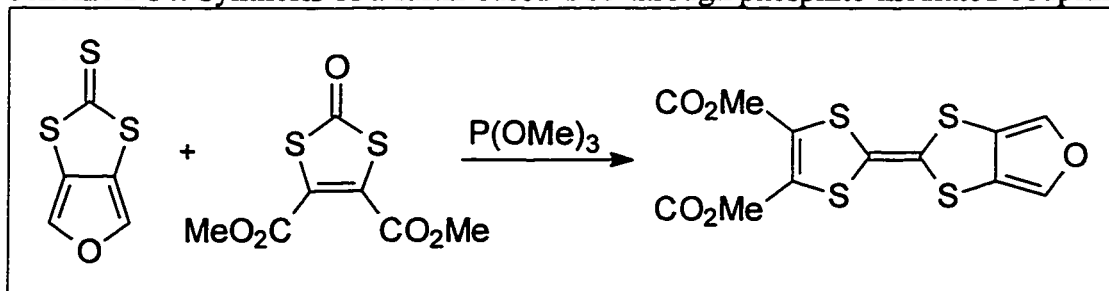
One drawback of the phosphite-mediated coupling is that the yields rarely go above 30% and it is not at all unusual to see publications where the yields reported are 10% or less. Nevertheless, owing to the simplicity of this method, most tetrathiafulvalene derivatives have been prepared this way.

Phosphite coupling has also been used to prepare unsymmetrical TTF derivatives and this is usually accomplished by using a mixture of the dithiole-2-thione and a dithiole-2-one as demonstrated by Cava's pyrrole derivatives (**Scheme 1-33**),<sup>55</sup> and Frère's furan derivatives (**Scheme 1-34**).<sup>56</sup>

**Scheme 1-33:** Synthesis of a pyrrole-based TTF synthesis through phosphite-mediated coupling

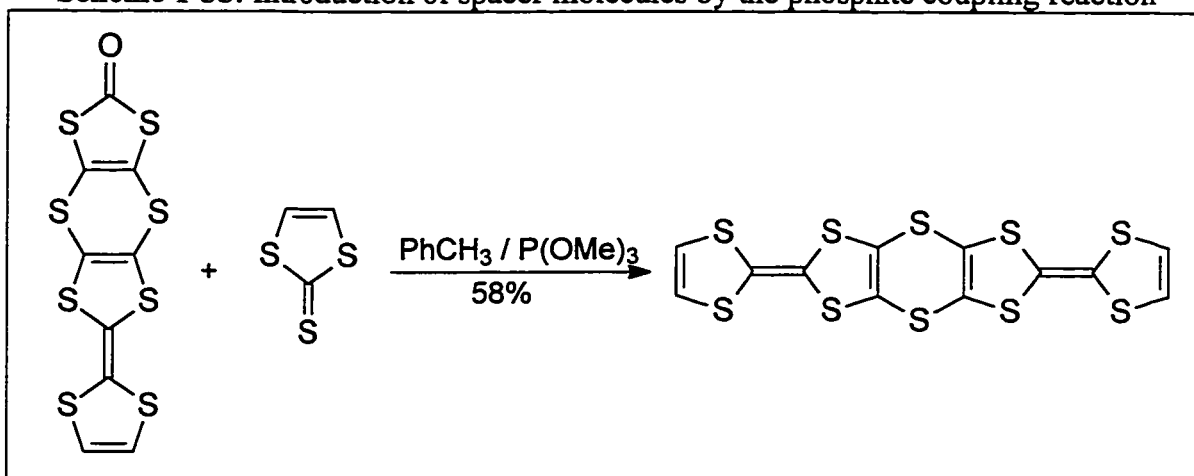


**Scheme 1-34:** Synthesis of a furan-based TTF through phosphite-mediated coupling

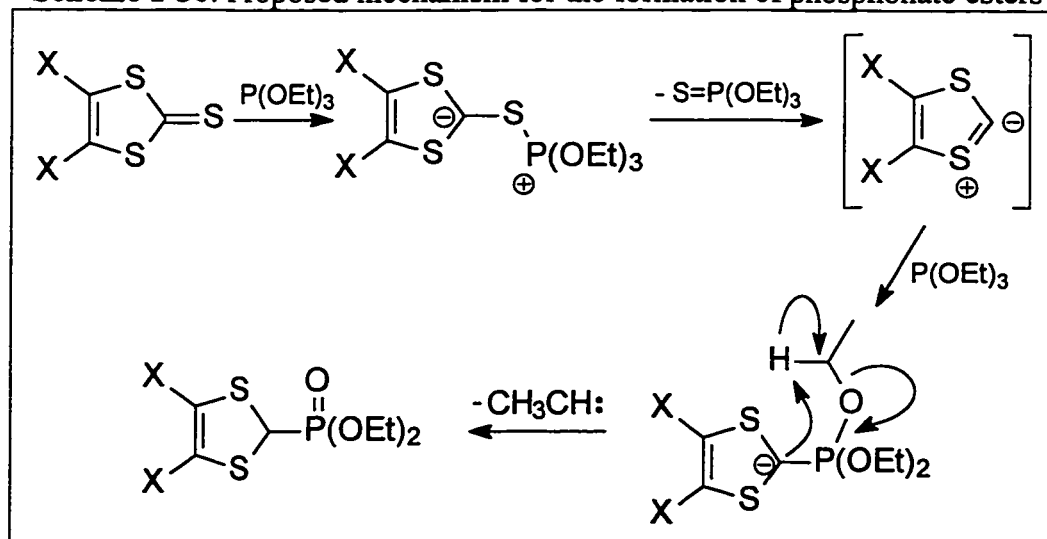


The introduction of spacer molecules between the dithiole units may also be performed with this approach (**Scheme 1-35**).<sup>57</sup> An interesting side-reaction that may occur in this case, especially with a large excess of phosphite, is the formation of phosphonate esters of the type shown in **Scheme 1-31**. This is the currently preferred method of preparing these compounds. The mechanism, however, is not completely understood, but the sequence of reactions in **Scheme 1-36** has been proposed.<sup>58</sup>

**Scheme 1-35:** Introduction of spacer molecules by the phosphite coupling reaction

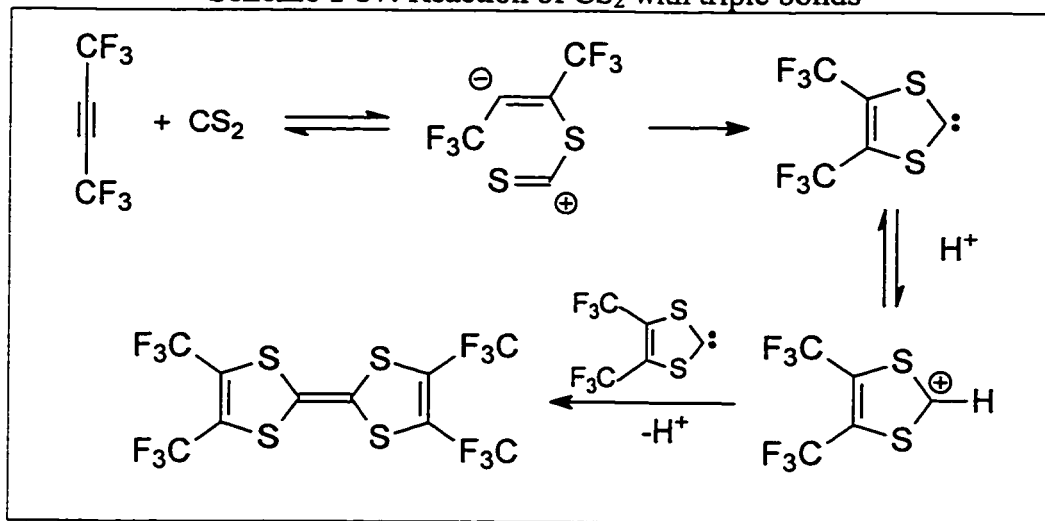


**Scheme 1-36:** Proposed mechanism for the formation of phosphonate esters



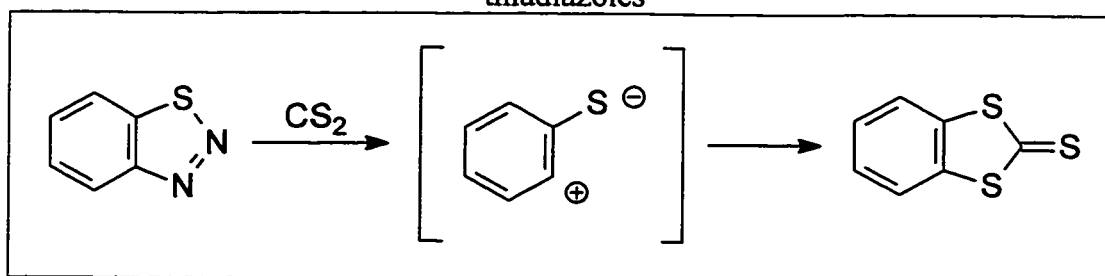
TTF derivatives may also be prepared by the reaction of acetylenes bearing electron-withdrawing groups with carbon disulfide. Hartzler studied this reaction with perfluoro-2-butyne and found that the reaction proceeds better in the presence of a strong acid. The following mechanism is postulated (**Scheme 1-37**).<sup>59,60</sup>

**Scheme 1-37:** Reaction of CS<sub>2</sub> with triple bonds



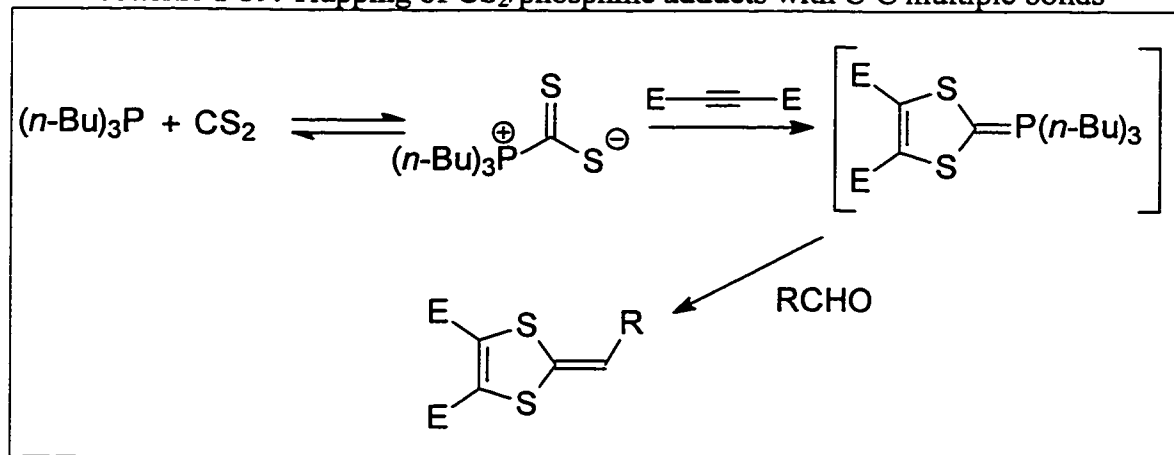
1,2,3-Thiadiazoles undergo thermolysis and the resulting dipoles can be trapped with carbon disulfide to form the 1,3-dithiol-2-thione (**Scheme 1-38**).<sup>61</sup> If carbon diselenide is used, the corresponding selenium derivative is formed.<sup>62</sup>

**Scheme 1-38:** Preparation of 1,3-dithiol-2-thiones from the thermolysis of thiadiazoles



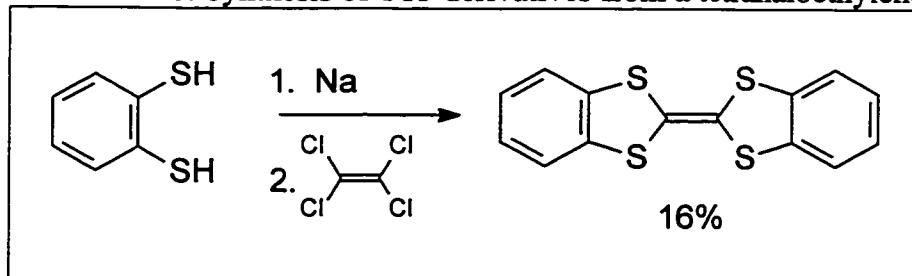
The adducts of carbon disulfide and trialkyl phosphines can also be used to form interesting dithiole derivatives. These 1,3-dipolar adducts react with electron deficient alkynes or alkenes to give 2-tri-*n*-alkylphosphonium-1,3-dithioles (**Scheme 1-39**).<sup>63</sup> Standard Wittig chemistry (see **Scheme 1-30**) may be used to form the conjugated dithiole system.

**Scheme 1-39:** Trapping of CS<sub>2</sub>/phosphine adducts with C-C multiple bonds



Another method for the synthesis of TTF derivatives, although not as widely used these days, involves the reaction between a 1,2-thiolate with a tetrahaloethylene. In fact, this reaction is one of the earliest known published syntheses of a TTF derivative.<sup>64</sup>

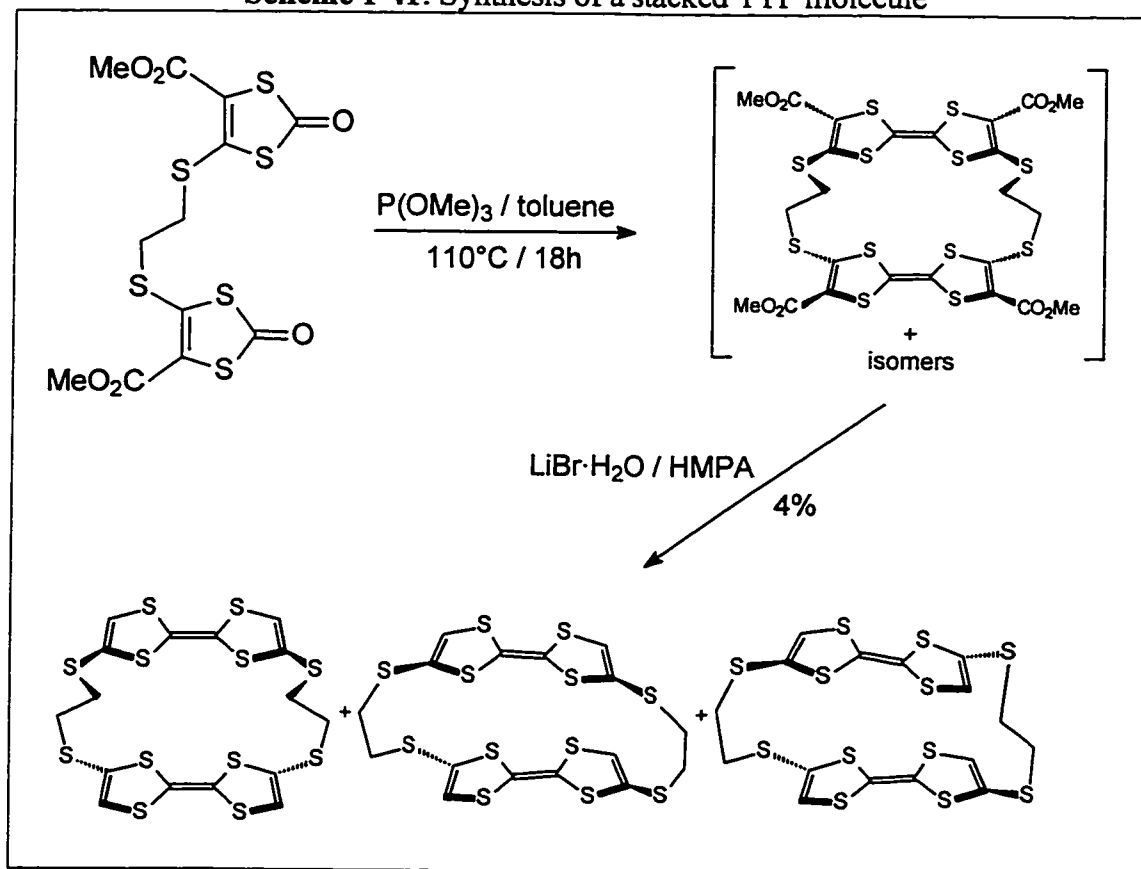
**Scheme 1-40:** Synthesis of TTF derivatives from a tetrahaloethylene



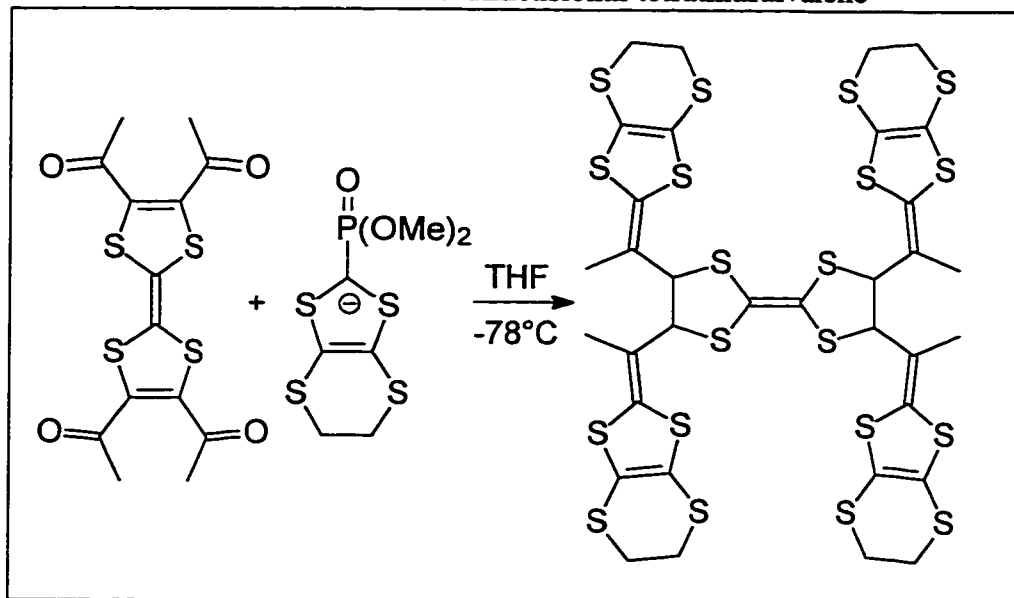
The variety possible with these compounds is limited only by one's imagination and this is confirmed time after time by the new articles that appear in the literature every few weeks. It is now possible to find not only structures where the TTF has been attached to a new kind of substituent, but also structures with multiple TTF centres arranged in two- and three-dimensional patterns (Scheme 1-41 and Scheme 1-42).<sup>65,66</sup>

The TTF skeleton in all of these syntheses, no matter how complex the final TTF, almost always begins with syntheses of the respective 1,3-dithiol-2-(thi)ones that are then coupled. In turn, the aromatic thiones are almost without exception synthesized from their corresponding 1,2-dithiols and therefore new methods for easily synthesizing these malodorous precursors is always in demand.

**Scheme 1-41:** Synthesis of a stacked TTF molecule





**Scheme 1-42: A two-dimensional tetrathiafulvalene**

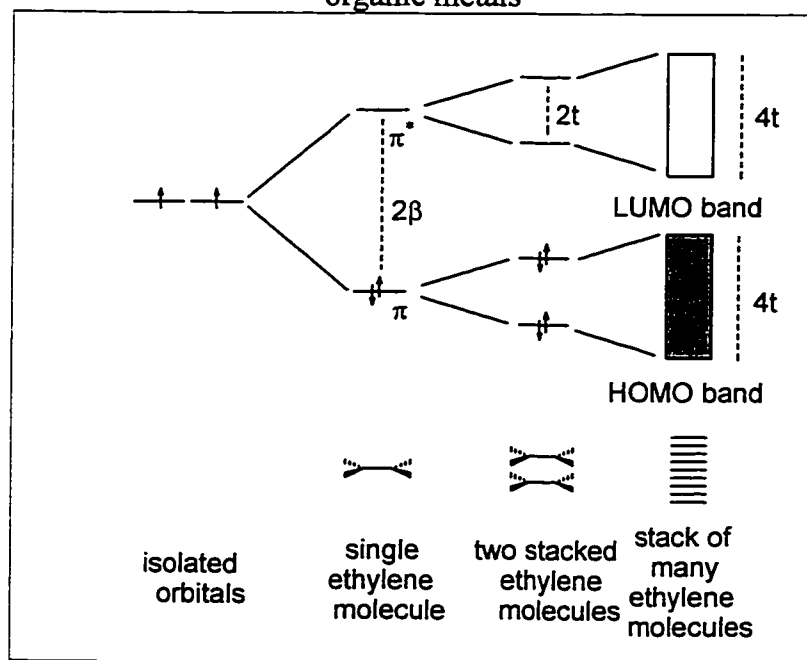
### 1.3.2 CONDUCTIVITY OF TTF DERIVATIVES <sup>67</sup>

The conductivity of the majority of organic compounds, including some TTF salts, is extremely low, between  $10^{-10}$  and  $10^{-15} (\Omega\text{cm})^{-1}$ , and this puts them in the realm of insulators. So what is so unusual about the salts of TTF compounds that allows them to conduct electricity so well? In order for conductivity to take place, several criteria have to be met, and indeed, when these are not met, conductivity does not take place even with TTF compounds.

First of all, the compounds must possess an extended  $\pi$ -system. The reason for this is that, in order for electron transfer to take place from one molecule to the next, the molecules must become stacked (as in the case of TTF or TCNQ) or aligned (as in the case of polythiophene, polypyrrole, etc.) so that the  $\pi$ -system of one molecule can interact with the  $\pi$ -systems of neighbouring molecules.

Second, as mentioned above, TTF molecules conduct electricity when their  $\pi$ -systems interact with each other and this requires a certain degree of planarity in the molecule in order to allow them to form segregated stacks (like a deck of playing cards) or planar sheets. In TTF-TCNQ, for example, the crystals are composed of two alternating stacks: one contains only TTF; the other only TCNQ. The interplanar distances between TCNQ molecules (0.317 nm) and TTF molecules (0.347 nm) allows for interactions between the  $\pi$ -orbitals of neighbouring molecules resulting in the formation of a band.

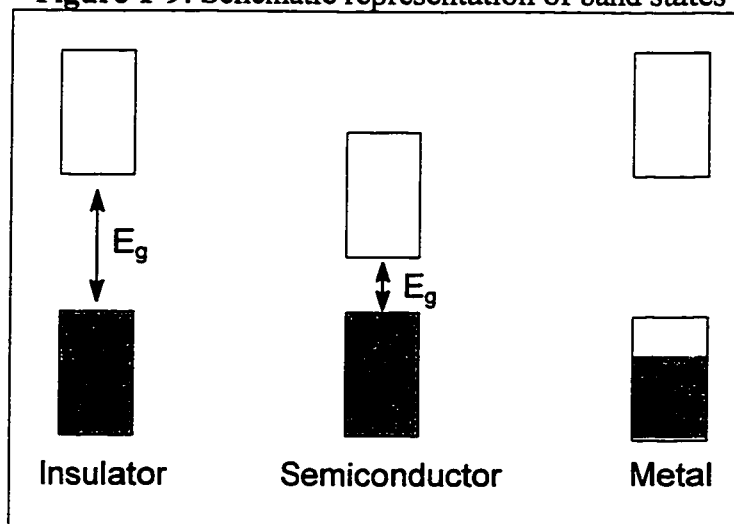
**Figure 1-8:** Simple band-theory analysis for conductivity in organic metals



So, what is a band? When a great number of atoms or molecules are brought together in a crystalline solid, their electronic states mix so as to form bands, each band consisting of electronic states whose energies form, for all intents and purposes, a

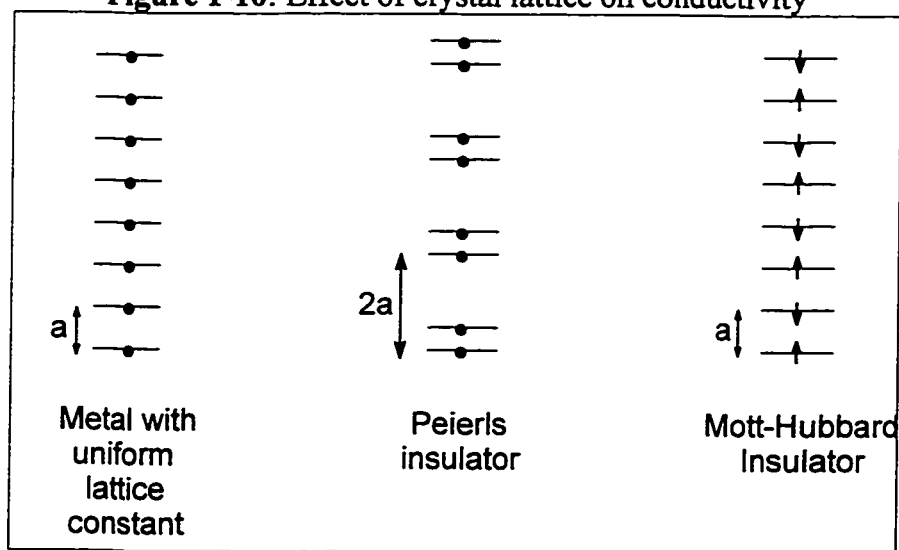
continuous range. A simple example, using ethylene molecules, is given in **Figure 1-8**. According to Hückel theory, if the two p-orbitals on ethylene are allowed to interact, two molecular orbitals,  $\pi$  and  $\pi^*$ , are formed with an energy separation of  $2\beta$ . If two ethylene molecules are stacked, one directly above the other, and the  $\pi$  and  $\pi^*$  orbitals allowed to interact, two sets of two molecular orbitals are formed, each set separated by an energy of  $2t$ , where  $t$  is the resonance or transfer integral. When  $n$  ethylene molecules interact in such a way,  $n$  number of states are formed from each of the  $\pi$  and  $\pi^*$  orbitals and into each of these bands  $2n$  electrons can be placed. The band arising from the p-orbital is called the HOMO band while the band arising from the  $\pi^*$ -orbital is called the LUMO band. The bands are filled in an analogous manner to the Aufbau principle for atoms: electrons are placed in the lowest energy states and then succeeding higher energy states are filled. The resulting filled band is called the valence band while the next higher empty band is called the conduction band. In the valence band, the highest occupied state is called the Fermi level.

**Figure 1-9:** Schematic representation of band states



The electrical properties of the compound arranged in such manner depend on the occupancy of these bands and on the size of the energy gap between them (Figure 1-9). If there is a large energy gap between the valence and conduction bands, then the material is an insulator. If the energy gap between the bands is small (but not infinitesimally small) then thermal excitation is enough to promote electrons from the Fermi level to the conduction band thus allowing for conduction to take place and the material is a semiconductor (this explains why the conductivity of semiconductors improves with increased temperature). If the valence band is only partially filled, then there is an infinitesimally small gap between the Fermi level and the conduction band and large numbers of electrons can move up to these infinitesimally higher levels resulting in metallic behaviour. The main obstacle, however, to conduction in metals (or for that matter organic metals) is high temperatures. As temperature increases, lattice vibrations increase thus scattering the electrons. This decreases the intermolecular orbital overlap between neighbours decreasing the conductivity.

**Figure 1-10: Effect of crystal lattice on conductivity**



Having achieved all this, there still exist a few obstacles to conduction in organic substances that may result in the conductivity being small or even non-existent. Electrical conduction involves moving electrons from one molecule to another, and since each molecule has one electron already, conduction must involve the pairing of two electrons. This results in a coulombic repulsion of the conduction electron spin-spin pairs and in order to reduce these repulsions, the electrons are redistributed into an antiferromagnetic spin state (the spins alternate). This material is called a Mott-Hubbard insulator (**Figure 1-10**). On the other hand, a different type of molecular rearrangement can take place in order to reduce the inherent instabilities of these one-electron systems. The molecules may dimerize to produce an energetically more favourable state (this type of distortion is analogous to the Jahn-Teller effect in molecules) and the resulting material is known as a Peierls-like insulator. As temperature increases, the electrons are thermally excited across the Peierls gap into states that are higher in energy than the empty states resulting from the undistorted crystal lattice. Therefore, at higher temperatures, the advantage of the distortion is reduced and so a transition is expected at a finite temperature from the insulating to the metallic lattice structure.

Superconductivity is one of the most interesting phenomena to have been discovered in the 20th century. When certain metals are cooled past a certain temperature, the critical temperature  $T_c$ , their electrical resistance goes down to zero and they cannot be penetrated by a magnetic field (the Meissner effect). Bardeen, Cooper, and Schrieffer provided the explanation for this phenomenon. For superconductors, at temperatures below their  $T_c$ , electrons form pairs as a result of an interaction between

conduction electrons and lattice vibrations (phonons). At higher temperatures, the thermal agitation of the electrons dissociates these pairs and superconductivity is lost.

The first superconducting organic metals discovered exhibited superconductivity at only very high pressures. The need for high pressure is because the superconducting state often competes with the spin-density-wave state (which results in a Mott-Hubbard insulator). Thus high pressures help to stabilize the metallic state down to the temperatures at which superconductivity takes place.

### **1.3.3 OXIDATION METHODS AND CRYSTAL GROWING <sup>68</sup>**

Most of the radical cation salts of TTF were first prepared by standard oxidation methods, and the first TTF-TCNQ complex was prepared by just mixing solutions of the two compounds. It was quickly realized, however, that the best conductivities were obtained in large crystals of very high purity. Magnetic impurities, for example, had to be rigorously excluded. Most of these compounds are highly insoluble and so the usual methods of growing crystals were not possible. Clearly, a new method had to be developed that took all of these items into account.

The most widely employed and probably the best method of both oxidizing the TTF and growing the very pure crystals required involves the use of an electro-crystallization apparatus. It consists of an H-cell of about a 15 mL capacity, the two halves of the cell being separated by a fine glass frit, and two platinum electrodes. The key factor for the growth of the high quality crystals required include the rigorous

purification of the solvents, special preparation of the electrodes, and thorough cleaning of the cell with aqua-regia prior to use.

Typically, a 5mL solution containing 5-10mg solution of the TTF is added to the cathode compartment, and a 10mL solution of 0.1 M  $\text{NBu}_4\text{X}$  (X being the desired anion) is added to the cathode compartment and then to the anode compartment as well in order to level both sides. If the supporting anions are air-sensitive, the cell must be set-up in a dry-box. The initial current density is held at about 0.5 to 1.0  $\mu\text{A cm}^{-2}$ , or just enough to initiate crystal growth. Crystals are collected when either depletion of the donor (the TTF) occurs or significant darkening of the solution appears. The time required for the electrocrystallization varies with the donor used and it can be as little as a few days to as much as several months.

#### 1.3.4 MEASUREMENT OF CONDUCTIVITY <sup>69</sup>

Once the TTF's and their radical cation salts have been prepared, the most interesting aspect of TTF research comes into play. The measurement of the conductivity reveals whether the various side-chains and functional groups that have been introduced into the TTF skeleton will have any effect (hopefully a positive one) on the electrical properties of these compounds. The measurement of these conductivities may be achieved in two ways depending on whether one is dealing with single crystals or with a powder.

Single crystals, by far, possess the highest conductivities, but as it was alluded to previously, the generation of these high-quality crystals is a rather challenging

accomplishment. Therefore, if circumstances do not permit the use of single crystals, the sample may be crushed to a fine powder and compressed in a special press as the measurements are taken. As the pressure within the cell increases, so does the conductivity until a maximum is reached.

Regardless of whether single crystals or powders are used to determine the conductivity of a particular TTF salt, the same method is used to measure it. Through the use of four electrodes, a constant current is applied to the sample while the voltage drop across a certain known distance is measured. The conductivity may be then calculated from the formula below:

$$\sigma = (I/V)(L/A)$$

In this equation, ( $I$ ) represents the applied current, ( $V$ ) is the measured voltage drop, ( $L$ ) is the distance across which the voltage drop was measured, and ( $A$ ) is the sample's cross-sectional area. It should be noted that when the conductivity of single crystals is being determined, measurements must be taken along all possible axes of the crystal because, unlike in metals, the conductivity of these compounds depends entirely on the arrangement of the individual molecules within the crystal. Therefore, it is entirely possible to measure very high conductivities along one axis of the crystal and nearly none along another axis perpendicular to the first.



## CHAPTER 2

### CLAY-CATALYZED THIOMETHYLATION OF AROMATIC COMPOUNDS

#### 2.0 INTRODUCTION

Recent research in our laboratories has examined the desulfurization of petroleum condensates and gasoline feedstocks. The current industry methods employed for hydrocarbon desulfurization usually involve the use of hydrogen gas at high temperatures, which makes this process rather expensive. Another unattractive feature of these processes is that, along with the desulfurized hydrocarbons, large quantities of hydrogen sulfide gas are produced.

But what if the sulfur-containing compounds (mostly thiols, disulfides, and thiophenes) could be removed by another, simpler method? Perhaps a simple distillation would be sufficient to achieve this. Unfortunately, due to the high volatility of some of these compounds and their distribution throughout the boiling range of the mixture, this is not the case. If distillation were to work, these compounds would have to be made heavier and less volatile. In other words, the hydrocarbon mixture would have to go through some kind of chemical process where new carbon-sulfur bonds would be formed.

Thinking along these lines, work was conducted with clay catalysts specifically designed to promote C-S and C-C bond formation and thus transfer the sulfur compounds from the lighter boiling fractions to the heavier ones. These experiments were, for the

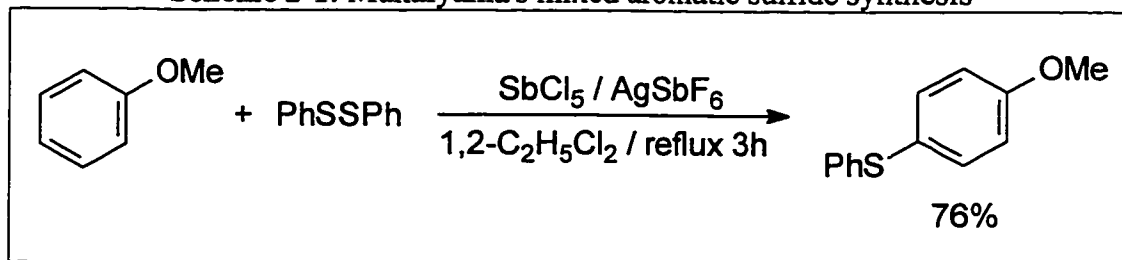
most part, successful and so a more in-depth study was required to investigate this new type of C-S bond forming reactions.

The initial model studies investigated the reaction of dimethyldisulfide (DMDS) and benzo[*b*]thiophene (BT) with clayzic as the catalyst. These reagents were refluxed under an inert atmosphere in 1,2-dichloroethane (DCE). GC-MS analysis showed that the major product of this reaction was 2,3-*bis*(methylthio)benzo[*b*]thiophene. The Lewis-acidic nature of the catalyst and thiomethylation of benzo[*b*]thiophene at the 2- and 3-positions led to the assumption that the mechanism at work here would be similar to the one that takes place during Friedel-Crafts reactions. This initial result suggested that this type of C-S bond forming reaction might be of more general use. Firstly, a brief review of similar reactions will be given.

## 2.0.0 BACKGROUND

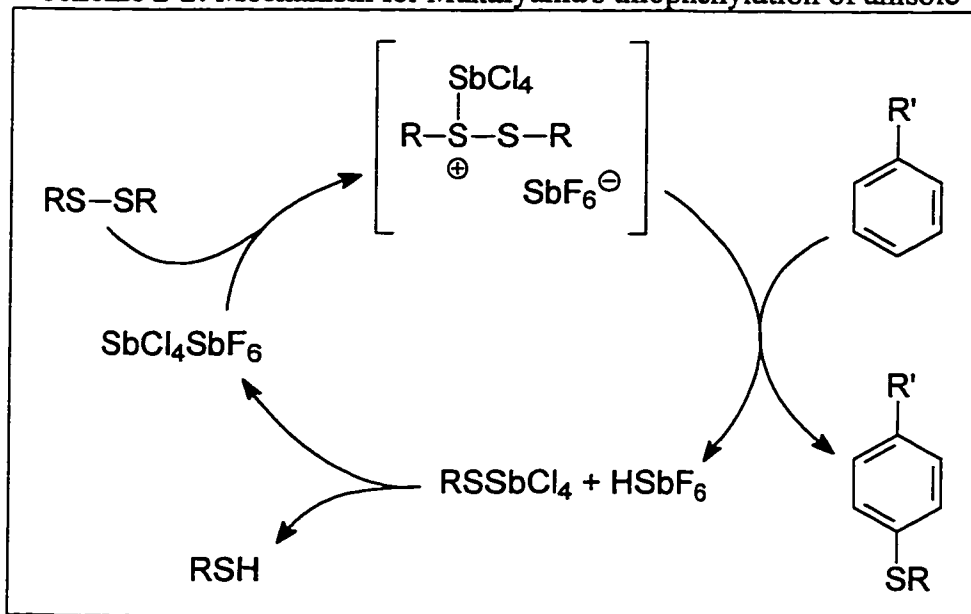
Mukaiyama has examined various Lewis acid catalysts to generate sulfenium cation equivalents in the thiophenylations of anisole (**Scheme 2-1**).<sup>70</sup> The highest yields were obtained with a 1:1 combination of SbCl<sub>5</sub> and AgSbF<sub>6</sub> although other Lewis acids such as FeCl<sub>3</sub> also showed moderate activity.

**Scheme 2-1:** Mukaiyama's mixed aromatic sulfide synthesis

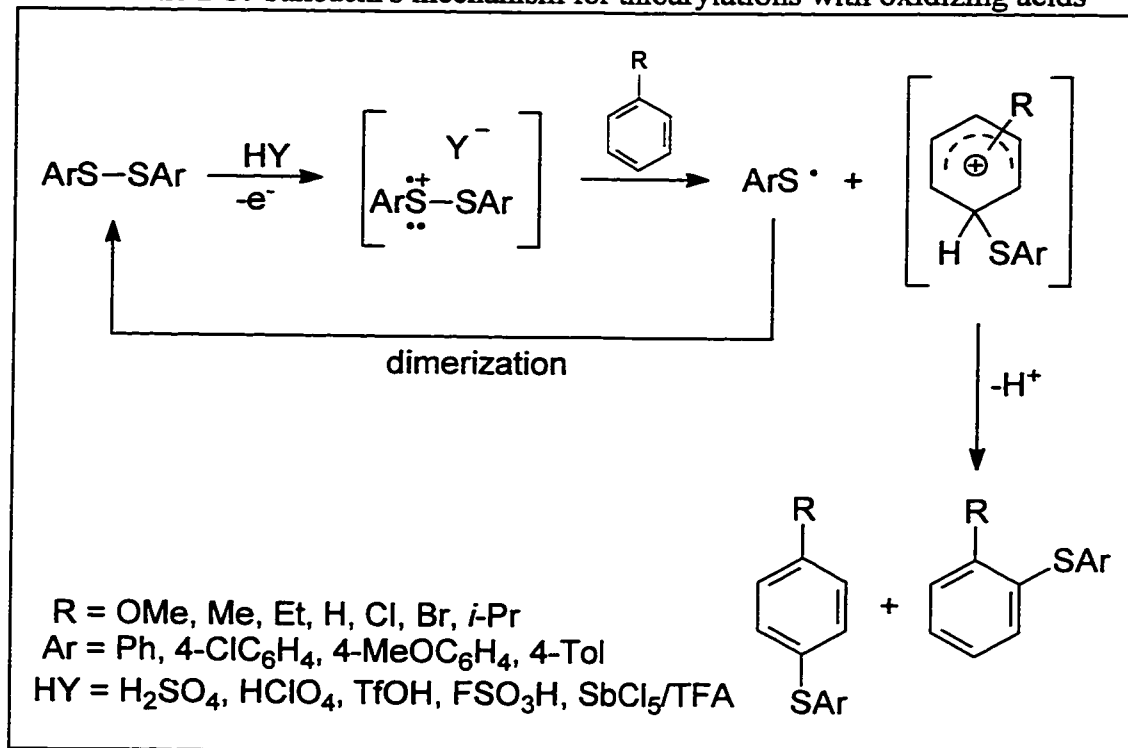


The mechanism is believed to involve an activated sulfenium ion equivalent which results from co-ordination of  $\text{SbCl}_4^+$  to the disulfide. This species is then attacked by the aromatic substrate producing the desired thioalkylated arene. (**Scheme 2-2**).

**Scheme 2-2:** Mechanism for Mukaiyama's thiophenylation of anisole



Takeuchi, on the other hand, has evidence that a second mechanism may take place when oxidizing acids are employed.<sup>71</sup> He believes that a disulfide molecule is first oxidized to its radical cation and it is this species that is attacked by the aromatic molecule. The rest of the steps of this mechanism are shown in **Scheme 2-3**. Takeuchi dismisses the possibility that a simple protonation of the disulfide may be taking place because when non-oxidizing yet strong acids, such as  $\text{HCl}$ , are used under the same conditions, the reaction does not take place.

**Scheme 2-3:** Takeuchi's mechanism for thioarylations with oxidizing acids

## **2.1 THIOPHENES**

### **2.1.0 BACKGROUND**

Like many other five-membered heterocycles, thiophene is particularly sensitive towards acids and tends to polymerize readily. This is a fairly serious drawback particularly when a process calls for acidic conditions, and for this reason, thiophene was chosen to be one of the first compounds on which the newly discovered clay-catalyzed thiomethylation was performed.

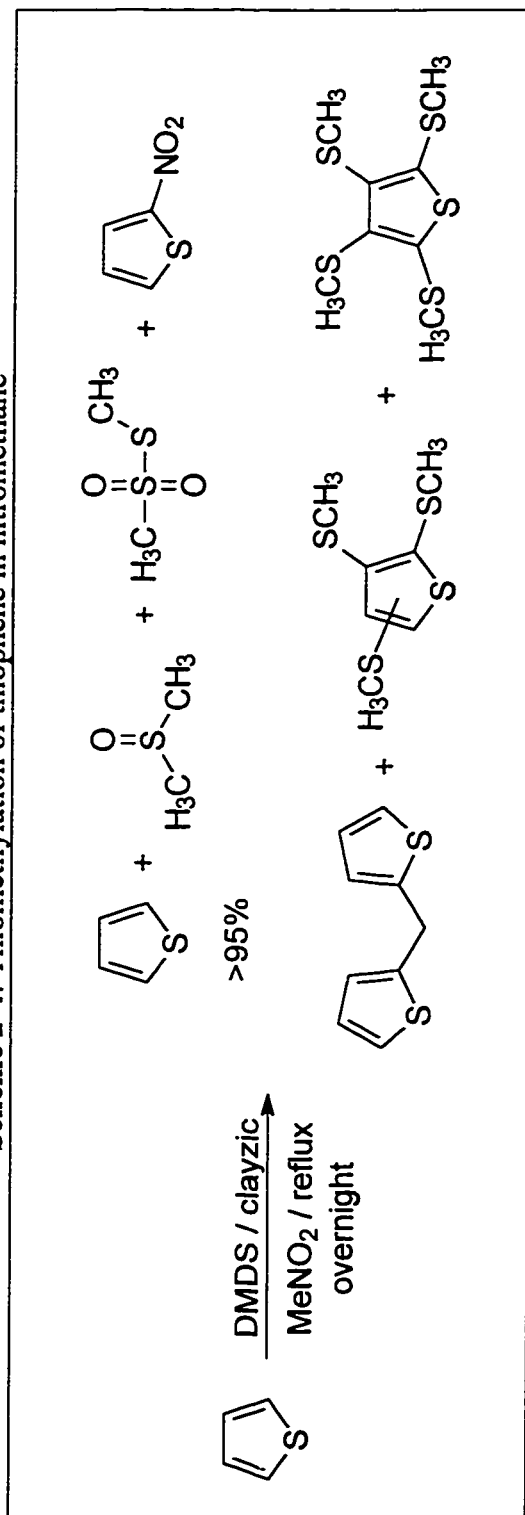
Several studies on clay-catalyzed reactions have been performed previously with thiophene,<sup>72,73,74</sup> particularly its benzylation with benzyl chloride, and these have shown that clays are very successful in arresting polymerization and, depending on the conditions used, high selectivity may be achieved.

#### **2.1.1 THIOMETHYLATION OF THIOPHENE**

##### **A. REACTIONS IN NITROMETHANE**

In this study, the first thiomethylation reaction of thiophene was performed at room temperature with clayzic as the catalyst in nitromethane. Nitromethane was the first solvent chosen because other work in our laboratories suggested that products were easily extracted from the porous structure of the clay with this solvent. However, the reaction did not proceed as expected with GC-MS analysis of the reaction mixture

**Scheme 2-4:** Thiomethylation of thiophene in nitromethane



showing mostly starting material with a trace (<1%) of two compounds that had the correct molecular ion for the mono- and di-thiomethylated products.

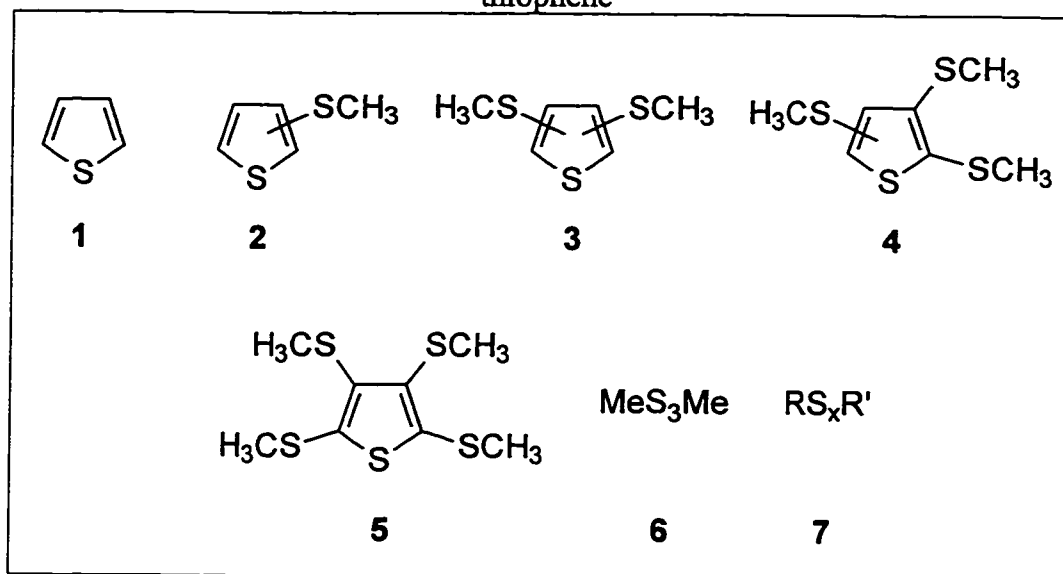
When the reaction mixture was heated under reflux overnight, GC-MS analysis showed that once again the main component of the reaction mixture was thiophene. This time, however, small traces of the more heavily thiomethylated tri- and tetra-substituted thiophenes along with dimethylsulfoxide, thiomethylsulfonylmethane, 2-nitrothiophene, and dithienylmethane were also present (Scheme 2-4). It should be noted that since many of the products observed were present in such minute quantities, their isolation would have been impossible, so their identification was made by comparing their mass spectra to those found in a computer database.<sup>75</sup> All compounds identified were found to have a 90% match or greater to the computer library data.

Another interesting feature of this reaction was that nitromethane was not inert during its course. In fact, a brown gas, presumably NO<sub>2</sub>, was being evolved copiously throughout the first hours of the reaction. This explains the traces of the oxidized methylsulfide products and that of 2-nitrothiophene in the reaction mixture. The generation of NO<sub>2</sub> was completely unexpected since, as was mentioned previously, nitromethane was used successfully for a variety of clayzic-catalyzed reactions with thiophene such as benzylations as well as in the syntheses of benzo[*b*]thiophenes.

## B. OTHER SOLVENTS AND CATALYSTS

Following the reactions with nitromethane, it was clear that more inert solvents had to be found. For the most part, the results using dichloromethane, 1,2-

**Figure 2-1:** Compounds observed by GC-MS during the thiomethylation of thiophene



**Table 2-1:** Thiomethylations of thiophene under varying conditions <sup>a</sup>

Run	Solvent	Co-catalyst	Composition of the crude product mixture (%) <sup>b</sup>					
			2	3	4	5	6	7
1	CH <sub>2</sub> Cl <sub>2</sub>	none	7	72	19	2	0	0
2	CHCl <sub>3</sub>	none	0	17	43	18	21	1
3	CHCl <sub>3</sub>	(i-Pr) <sub>2</sub> NEt	0	0	0	0	0	0
4 <sup>c</sup>	Thiophene	none	17	0	0	0	0	0
5	Thiophene	none	7	41	47	0	0	0
6	DCE	none	0	19	36	12	27	3
7	DCE	Al <sub>2</sub> O <sub>3</sub> /K <sub>2</sub> CO <sub>3</sub>	0	23	41	11	20	5
8 <sup>c,d</sup>	DCE	none	0	5	3	0	92	0
9 <sup>d</sup>	DCE	none	0	43	4	0	53	2
10	PhCl	none	0	29	55	12	3	0

<sup>a</sup> All runs were performed with claycic and all GC-MS samples were taken after 17 h of reflux unless stated otherwise.

<sup>b</sup> Based only on the integration of the areas under the GC-MS bands. The isolated crude in these reactions was usually 10% or less

<sup>c</sup> Stirred for 17 h at 20°C

<sup>d</sup> K10/H<sub>2</sub>SO<sub>4</sub> was used as the catalyst instead of claycic

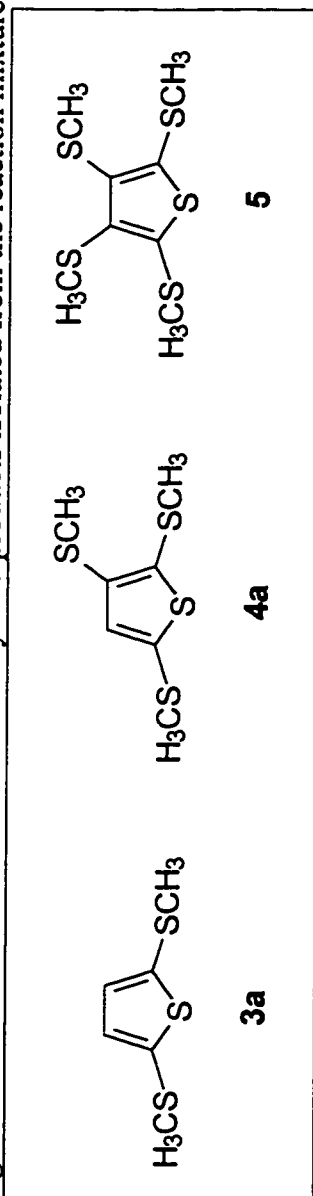


dichloroethane, chloroform, and thiophene itself (**Table 2-1**) were not very encouraging. In all cases the yields from reactions were low (<10%) for each solvent, and they produced complex mixtures of which the major components are shown in **Figure 2-1**. It should be noted that only a rough estimate for the percent compositions and percent yields in **Table 2-1** were made by using the areas of the GC peaks without application of any standards or response factors. When the final product mixtures were analyzed by  $^1\text{H}$ -NMR, it was discovered that there was a 5% discrepancy, at the most, between it and the GC-MS percent report.

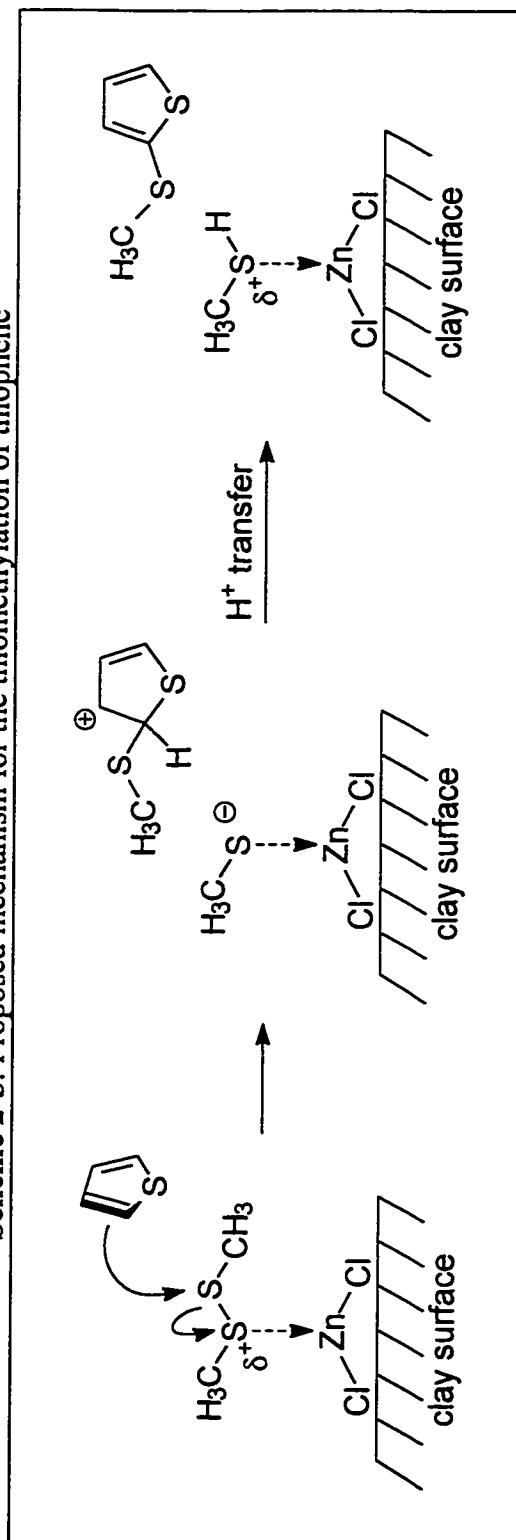
Entry 2 on **Table 2-1** shows the results obtained with chloroform. The reaction gave a mixture of the various thiomethylated thiophenes along with dimethyltrisulfide and a smaller amount of the tetrasulfide. Enough crude product was isolated to identify the main components (**Figure 2-2**) as 2,5-*bis*(methylthio)-thiophene (compound **3a**), which was oxidized to the disulfone and its structure confirmed by X-ray crystallography, 2,3,5-*tris*(methylthio)thiophene (compound **4a**), and 2,3,4,5-*tetrakis*-(methylthio)-thiophene (compound **5**). The addition of a non-nucleophilic base (Entry 3) completely stopped the reaction, presumably, by co-ordinating to the Lewis sites in the clay.

The substitution pattern of the thiophenes in these products suggests that indeed the reaction follows an electrophilic aromatic substitution mechanism (**Scheme 2-5**). First of all, a disulfide molecule co-ordinates to an active site in the clay. This gives the DMDS a partial positive charge activating it towards an attack by the  $\pi$ -system of the thiophene displacing the methanethiolate anion. The thiomethylated thiophene is formed after a proton exchange step takes place to regenerate the  $\pi$ -system on the thiophene and to form methanethiol.

**Figure 2-2:** Structure of the main thiomethylated products isolated from the reaction mixture



**Scheme 2-5:** Proposed mechanism for the thiomethylation of thiophene

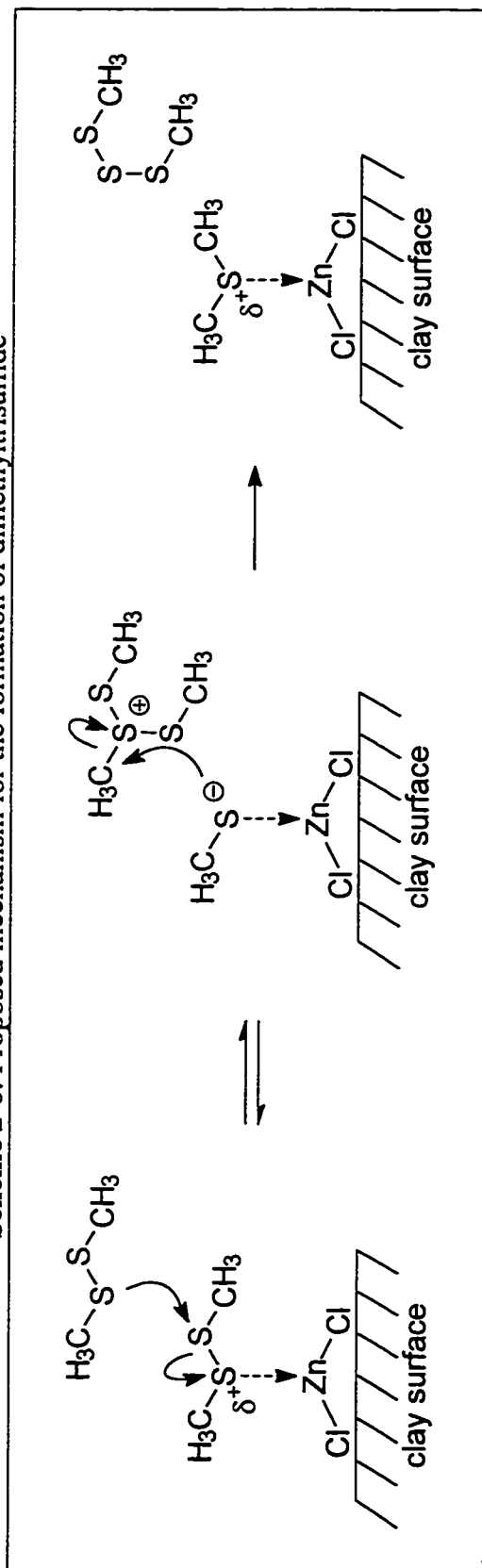


Reactions where thiophene is both the reactant and the solvent, as shown by entries 4 and 5 in Table 2-1, also produce the *bis*- and *tris*(methylthio) compounds. The formation of these products demonstrate that once a thioalkylation takes place, the products are either more reactive than thiophene itself, are trapped within the active site of the clay enhancing further reactions, or a combination of both. In particular, coordination of the product *via* -SCH<sub>3</sub> to an active site may help to localize a mono-thiomethylated product in the pores of the catalyst and, thus, enhance further reactions. From this point, it was clear that achieving control of the degree of substitution would be extremely difficult.

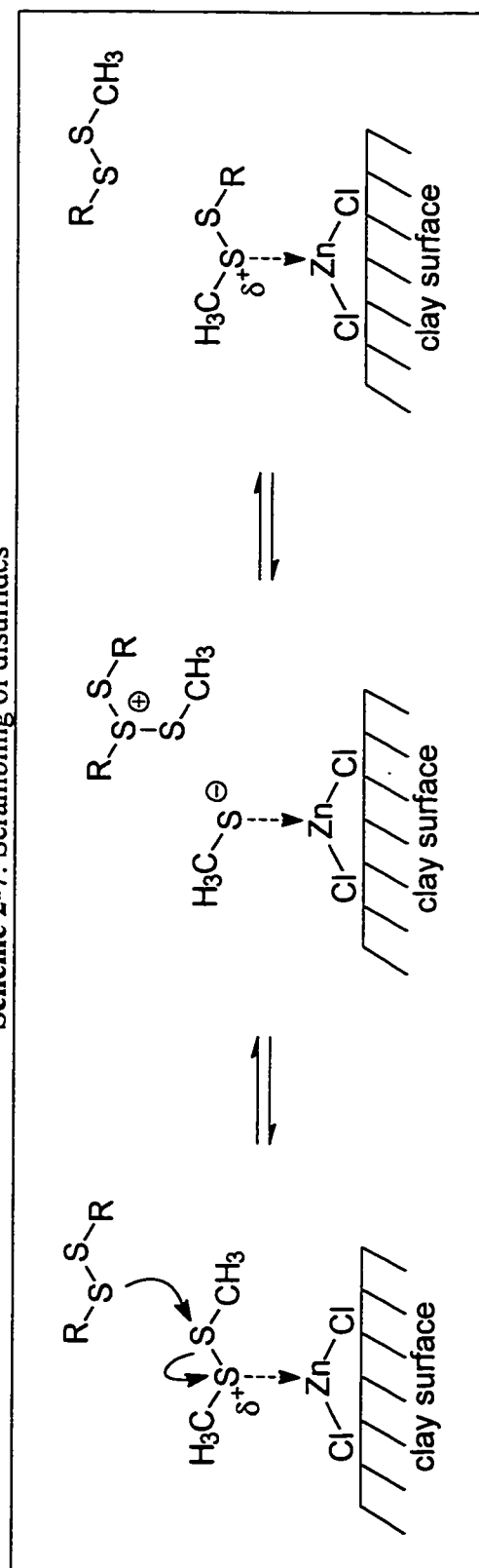
The next set of reactions, represented by entries 6 through 9, were performed in 1,2-dichloroethane (DCE). Reactions performed in this solvent with benzo[*b*]thiophene yielded 2,3-*bis*(methylthio)benzo[*b*]thiophene in a satisfactory yield.<sup>76</sup> It was hoped that, if anything, performing the reaction in dichloroethane with thiophene might increase the selectivity towards perhaps the disubstituted product. Once again, the results were far from what was expected. One observation, however, was made that provides evidence for the formation of methanethiol (or thiolate) during the reaction: large amounts of 1,2-*bis*(methylthio)ethane were observed by GC-MS along with dimethyltrisulfide. These observations, along with the results obtained from a reaction performed by refluxing a mixture of DMDS, clayzic, and DCE, provided enough data to propose a mechanism for the formation of the trisulfide (Scheme 2-6).

This mechanism, once again, relies on the existence of an activated form of the disulfide which is then attacked by a nucleophile. In this case, the attacking nucleophile is another molecule of disulfide forming a more or less free methyl-*bis*(thiomethyl)-

**Scheme 2-6: Proposed mechanism for the formation of dimethyltrisulfide**



**Scheme 2-7: Scrambling of disulfides**



sulfonium intermediate and a methanethiolate species. It is assumed that at this stage the reaction is reversible, but on occasion the thiolate will attack the one methyl group on the tricoordinated sulfur releasing dimethyltrisulfide and dimethylsulfide. The mechanism also helps explain a second and perhaps a more significant observation: when two different disulfides are mixed together under these conditions, they are immediately scrambled and a 1:2:1 mixture of the pure and mixed disulfides is quickly obtained (**Scheme 2-7**). If this mechanism is correct, then one must also contend with the possibility that the active species during the thiomethylation reactions is not an activated disulfide but the sulfonium intermediate. This may explain why the amounts of trisulfide are larger when thiophene (or other aromatics) are introduced into the system: the more methanethiolate formed during the normal thiomethylations (see **Scheme 2-5**), the more likely attack will occur on the sulfonium intermediate to produce the trisulfide. Another important conclusion that can be drawn from this is that as the reaction proceeds, the increased amounts of methanethiol produced take up more and more active sites on the catalyst, which has the effect of slowing down the reaction.

One final possibility remains. There is a chance that the mechanism taking place is something akin to what Takeuchi proposes for his thioarylation experiments (**Scheme 2-3**).<sup>71</sup> Although the conditions employed did not seem to be oxidizing enough for this type of mechanism to take place, a reaction employing the same conditions that Takeuchi employed was performed. Therefore, a mixture of thioanisole and diphenyldisulfide were stirred in dichloromethane for 2 hours in the presence of clayzic. As was expected, the reaction failed to give significant amounts of product and therefore it can be stated with a fair amount of certainty that this type of mechanism does not take place in the

thiomethylation of thiophene or other aromatic compounds when clayzic is employed as the Lewis acid.

The final entry on **Table 2-1** shows the results of an experiment in chlorobenzene. Not only did the yield of the crude product improve, but also the amount of the more heavily thiomethylated products increased. Unfortunately, the amounts of dimethyl trisulfide increased as well. The conclusion that can be drawn from this observation is that in order to obtain larger amounts of the fully thiomethylated thiophene **5**, the reaction must be performed at higher temperatures. Since chlorobenzene had shown itself to be the best solvent for this reaction, it was decided to try and optimize the conditions with this solvent.

### C. REACTIONS IN CHLOROBENZENE

In general, the reactions performed in chlorobenzene solution gave the best yields of thiomethylated products. Also, even though it is probable that the thiomethylations proceed *via* a Friedel-Crafts mechanism, no traces of thiomethylated solvent were ever seen indicating that even under these harsh conditions chlorobenzene remains inert.

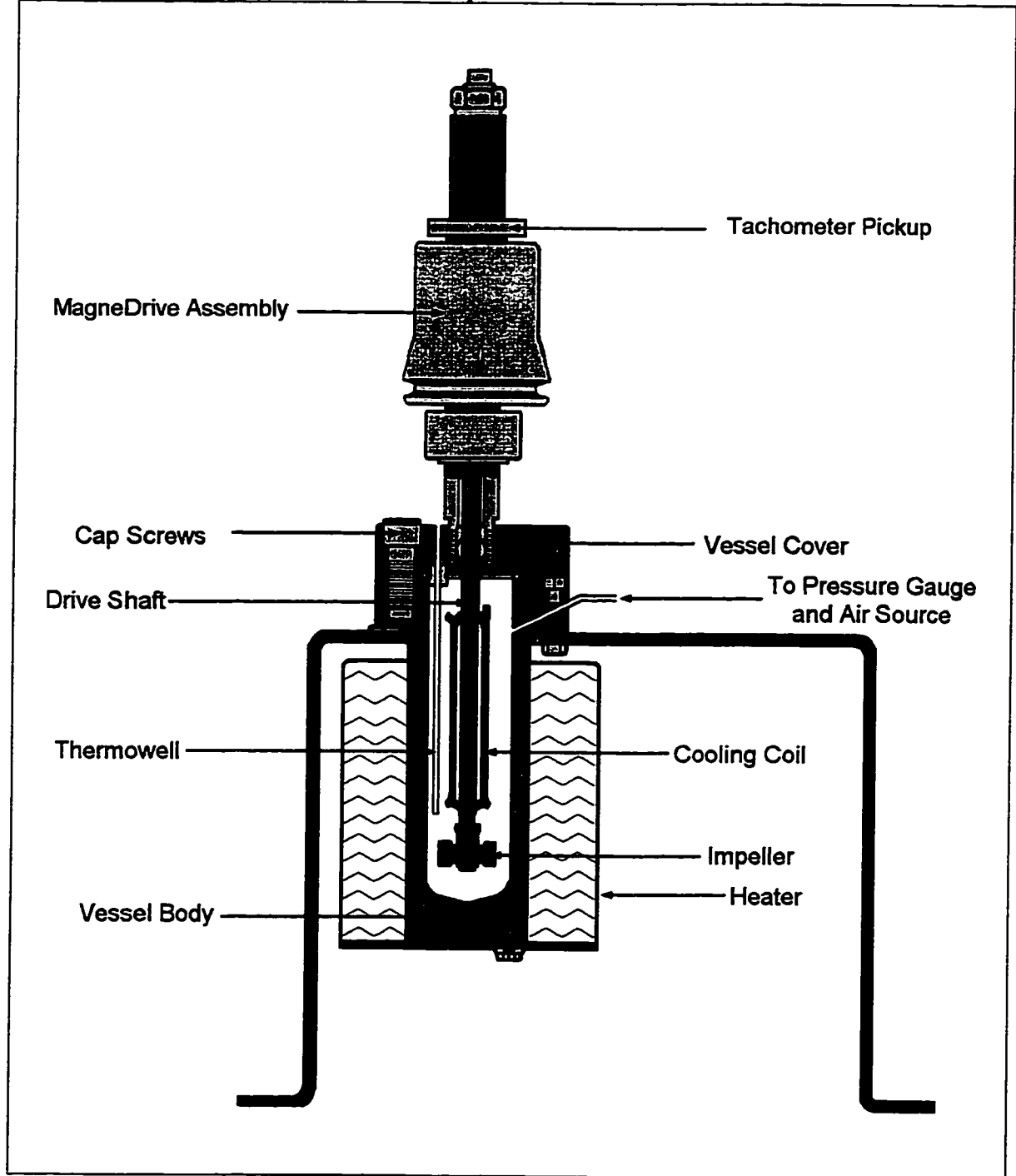
Entries **1** through **3** in **Table 2-2** show that even at the higher temperatures achieved with chlorobenzene, the reaction fails to produce the fully thiomethylated product exclusively. Although the more heavily substituted thiophenes are favoured in this mixture, even after 40 hours of refluxing, the amount of the *tetrakis* is far from being acceptable.

**Table 2-2:** Thiomethylations of thiophene in chlorobenzene <sup>a,b</sup>

Entry	Catalyst	Temp. (°C)	Time (h)	Atmosphere	Composition of crude product mixture (%)			Yield of crude product (%)
					3	4	5	
1	Claycic	Reflux	4	Air	59	31	10	-
2	Claycic	Reflux	17	Air	15	61	24	-
3	Claycic	Reflux	40	Air	8	48	43	17
4	Claycic <sup>c</sup>	Reflux	40	Ar (balloon)	8	52	40	21
5	Claycic <sup>d</sup>	Reflux	40	Air	0	89	11	10
6	Claycic <sup>d</sup>	Reflux	40	Air	32	68	0	18
7	Claycic	Reflux	96	Air	0	0	0	0
8	Claycic	Reflux	48	Air (stream) <sup>e</sup>	2	7	91	4
9	Claycic	Reflux	22	Air (balloon)	0	71	29	19
10	ZnCl <sub>2</sub>	Reflux	40	Air	0	0	0	0
11	ZnCl <sub>2</sub> (dry)	Reflux	40	Air	0	0	0	0
12	K10/CuCl <sub>2</sub>	20	2	Air	87	13	0	-
13	K10/CuCl <sub>2</sub>	20	20	Air	83	17	0	-
14	K10/CuCl <sub>2</sub>	20	48	Air	78	22	0	-
15	K10/CuCl <sub>2</sub>	Reflux	17	Air	47	44	9	11
16	<i>p</i> -TsOH	Reflux	17	Air	<1	0	0	<1
17	K10/TiCl <sub>4</sub>	Reflux	17	Air	<1	0	0	<1
18	K10/MnCl <sub>2</sub>	Reflux	17	Air	0	30	70	20
19	K10/MnCl <sub>2</sub>	Reflux	17	Argon	0	90	10	13
20	MnCl <sub>2</sub> ·4H <sub>2</sub> O	Reflux	17	Air	0	0	0	0
21	MnCl <sub>2</sub>	Reflux	17	Air	0	0	0	0

<sup>a</sup> 8 equivalents of DMDS were used for all reactions<sup>b</sup> Compound 2 was not observed in this set of reactions<sup>c</sup> Amount of claycic used was increased by 50%<sup>d</sup> Amount of claycic used was reduced by 75%<sup>e</sup> Dry air was bubbled into the reaction mixture

**Figure 2-3:** Schematic representation of the autoclave used





Clayzic, however, was not the only catalyst used in these experiments. As was demonstrated in other studies (see **Chapter 1.3**), unsupported zinc chloride was a very poor catalyst for promoting thiomethylation (Entries 10 and 11). The results with other catalysts employed are shown in entries 12 through 21, but none of these reactions, save two, achieved yields comparable to those obtained with clayzic. The catalyst that seemed to work even better than clayzic is shown in Entry 18. K10 impregnated with manganese(II) chloride, or clayman, gave a much cleaner reaction than clayzic. Not only was the reaction free of isomerization products, but the yields were slightly higher and very little dimethyl trisulfide was formed. This was extremely puzzling because manganese(II) is not known to be a good Lewis-acid catalyst.

Since it was believed that the formation of methanethiol was somehow responsible for the reduction in the reaction rates with clayzic, it was decided to introduce air into the reaction mixture by means of a bubbler in order to oxidize methanethiol back to DMDS (Entry 8). However, due to the high volatility of thiophene, it was lost from the system and therefore very little product was observed. The next logical step was to perform the reactions in a closed system and this was achieved by using an autoclave of the type shown in **Figure 2-3**.

The first run performed with such a system used the same conditions that gave the best results under reflux with the exception that enough air was introduced into the autoclave so as to oxidize any methanethiol formed. The autoclave was kept at 150°C for five hours. As entry 1 in **Table 2-3** shows, the results much improved. Virtually pure *tetrakis*-(methylthio)thiophene was isolated in a 56% yield. As expected, the formation of dimethyl trisulfide was almost completely stopped, which lends strength to the

**Table 2-3:** Thiomethylations of thiophene performed under pressure

Entry	Catalyst	Eq. of DMS	Temp. (°C)	Time (h)	Gas used	Pressure (KPa) <sup>a</sup>	Composition of crude product mixture (%)			Yield of crude product (%) <sup>b</sup>
							3	4	5	
1	Clayzic	8	150	5	Air	6900	3	9	88	57
2	Clayzic <sup>c</sup>	8	150	5	Air	6900	0	0	0	0
3	Clayzic <sup>d</sup>	8	150	5	Air	6900	10	29	61	52
4	Clayzic	8	150	5	Argon	6900	21	66	13	41
5	Clayzic	8	240	5	Air	6900	0	0	0	0
6	Clayzic	0.5	150	5	Air	1310	33	50	18	11
7	Clayzic	2	150	5	Air	4400	6.6	15	78	38
8	Clayzic <sup>e</sup>	8	150	5	Air	6900	26	73	0	33
9	K10/MnCl <sub>2</sub>	8	150	5	Air	6900	4	10	86	47

<sup>a</sup> Initial pressure of the vessel at room temperature.<sup>b</sup> Calculated from the weight of the isolated crude product and the percent composition obtained from the GC-MS.<sup>c</sup> Performed in an autoclave without a stirring mechanism<sup>d</sup> Performed in an autoclave equipped with a standard teflon stirring bar<sup>e</sup> Amount of clayzic was reduced by 75%

hypothesis that it is the methanethiol formed during the reaction that interferes with the active sites in the clayzic.

Subsequent entries in **Table 2-3** show the effect of changing various conditions on the thiomethylations done in the autoclave. Increasing the temperature to 240°C (Entry 5) caused decomposition of the reactants/products to a complex mixture of open-chained sulfides. As would be expected, the decrease of both the amounts of DMDS and clayzic used also reduces the yields as well as the amounts of *tetrakis* product observed.

Entries 2 and 3 show how important efficient stirring is for this reaction. The reaction shown in Entry 2 was performed in an unstirred autoclave with the result that the only products isolated were massive amounts of tri-, tetra-, and higher polysulfides as well as other decomposition products. Entry 3 was performed in an autoclave stirred with a conventional teflon stirring bar. Although there can be no doubt that the thiomethylation had taken place, the original results achieved with the Magedrive-stirred autoclave (which stirs at *ca.* 1000 rpm) are, by far, better.

The last entry in **Table 2-3** shows a run performed with clayman. This time, the results are comparable to those obtained with clayzic with the exception that the crude product was, for some reason, slightly less contaminated with impurities. Once again the question arises of why clayman is such a good thiomethylation catalyst.

#### D. CLAYMAN

The discovery that K10/MnCl<sub>2</sub> was a milder yet more effective catalyst for the thiomethylation of thiophene permitted to explore the possibility of preparing

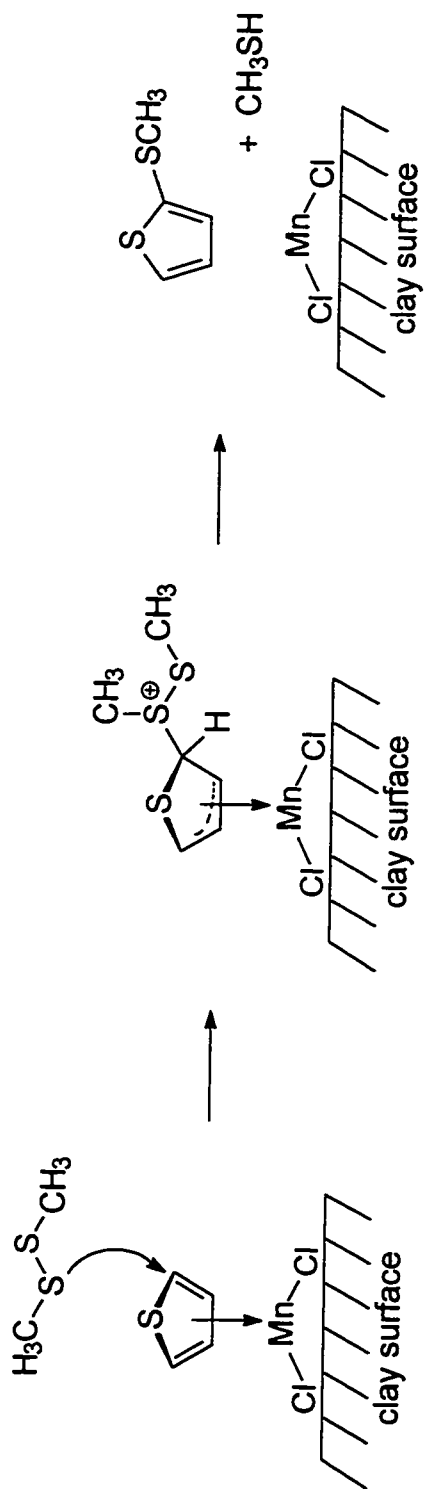
thioalkylated thiophenes bearing alkyl groups other than methyl. This was a particularly attractive possibility since reductive cleavage of groups other than methyl should facilitate conversion of these products to thiols (**Chapter 5**).

The fact that dimethyl trisulfide was not formed and that the final reaction mixture did not possess its usual intensely dark colour were the principal reasons that led to the conclusion that a different mechanism had to be taking place when clayman was used as the catalyst. But what could this mechanism be?

The first fact considered was that the trisulfide was hardly observed. This suggests that dimethyldisulfide is not activated in the same manner as it would be with clayzic (**Scheme 2-5**). Perhaps DMDS is oxidized in the same fashion as the aryl disulfides in Takeuchi's studies. This hypothesis was quickly disproved by performing the same reaction that Takeuchi investigated but with the clayman catalyst and observing that virtually no reaction took place.

If the DMDS is not co-ordinating to the clay, then perhaps it is the thiophene that is activated by co-ordination to a Mn(II) site.<sup>77</sup> Aryl-manganese complexes have been isolated previously, although these systems are usually stabilized by ligands such as carbonyls, cyclopentadienyls, etc.<sup>2,78,79</sup> It was therefore reasoned that if the thiophene does co-ordinate to the manganese, although in all likelihood this complex cannot be isolated, it might have a sufficiently long lifetime to react. Thus, by accepting some electron density from the thiophene's  $\pi$ -system, the thiophene would become electrophilic enough to react with an unactivated disulfide molecule (**Scheme 2-8**). It is worth noting that DMDS is capable of performing such nucleophilic attacks as observed in its reaction with itself and other disulfides (**Chapter 2.1.1.B**). If this mechanism were sound, then

**Scheme 2-8:** Possible mechanism for the thiomethylation of thiophene in the presence of clayman



there is a small chance that the thiophene might become activated enough to react with higher disulfides. Unfortunately this did not prove to be the case because when the reaction was attempted with both isopropyl and benzyl disulfides, only the original disulfides were isolated.

One final possibility remains. The DMDS does co-ordinate to the manganese in clayman although not as strongly as with clayzic. This may explain why it would react with thiophene although not with a second molecule of disulfide.

#### E. OTHER DISULFIDES

**Table 2-4** shows the results obtained when reactions with thiophene were performed with disulfides other than dimethyldisulfide. Most entries are straightforward except perhaps for entry 3. In this case, a 1:1 molar mixture of phenyl and benzyldisulfides was used in an attempt to exploit the scrambling properties of the clay and form benzylphenyldisulfide. The reasoning behind this idea was that if this compound were to react with thiophene, the thiophene would attack the sulfur bearing the benzyl group thus displacing SPh (the better leaving group). Unfortunately, no reaction was observed with this disulfide mixture.

It was clear from these results that only the simplest disulfides may be used in this kind of preparation and that by extending the length of the disulfide chain by anything more than one carbon, the rate of the reaction slows virtually to a standstill.

**Table 2-4:** Thioalkylations of thiophene with various disulfides <sup>a</sup>

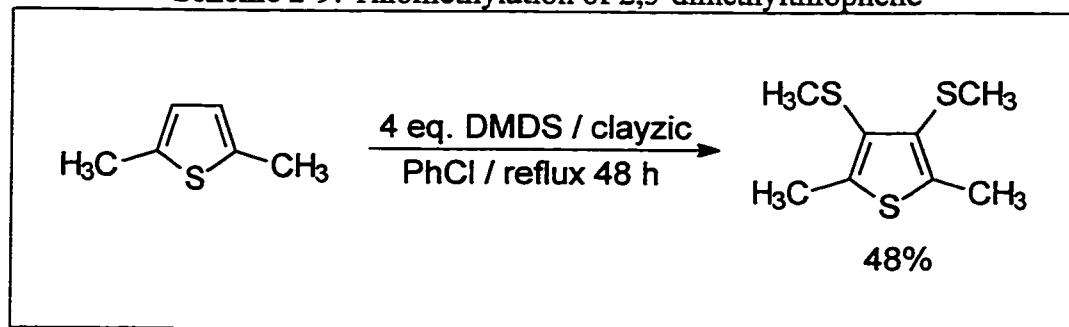
Entry	Catalyst	Disulfide	Results
1	Clayzic	Ethyl	13% Disubst. product
2	Clayzic	<i>n</i> -Hexyl	No reaction
3	Clayzic	Phenyl/Benzyl	No reaction
4	Clayzic	<i>i</i> -Propyl	No reaction
5	Clayman	<i>i</i> -Propyl	No reaction
6 <sup>b</sup>	Clayman	<i>i</i> -Propyl	No reaction
7	Clayman	Benzyl	No reaction

<sup>a</sup> All reactions were performed under refluxing chlorobenzene unless stated otherwise.  
<sup>b</sup> Performed in an autoclave under the conditions established previously

### 2.1.2 THIOMETHYLATION OF 2,5-DIMETHYLTHIOPHENE

The success obtained from the preparation of 2,3,4,5-*tetrakis*(methylthio)-thiophene led to the hypothesis that the reaction might proceed more easily if there were not so many available sites for reaction, and for this reason the symmetric 2,5-dimethylthiophene was chosen.

The reaction conditions employed were the same as those used with the thiophene (**Scheme 2-9**). In other words, the reaction mixture was heated under reflux in chlorobenzene and two equivalents of DMDS were used per available thiomethylation site (four equivalents in all). Although the reaction proceeded more slowly than with thiophene (it took 48 hours of refluxing to achieve almost complete thiomethylation), the final reaction mixture was considerably cleaner in comparison to reactions performed with thiophene. This is, perhaps, not very surprising since 2,5-dimethylthiophene is more stable than thiophene and, therefore, less prone to polymerization.

**Scheme 2-9: Thiomethylation of 2,5-dimethylthiophene**

One interesting observation from this reaction was that it completely failed to give any product unless a solution of 2,5-dimethylthiophene in chlorobenzene was added dropwise to a refluxing mixture of the other reagents. The inference that can be made from this observation is that 2,5-dimethylthiophene is sufficiently electron rich to compete with the DMS for the active sites in the catalyst. This does not seem to be the case with thiophene because no matter what order the reagents were introduced into the reaction mixture, the results were always similar.

The reaction with clayman, on the other hand, was not much different than that with clayzic, perhaps owing to the increased nucleophilicity inherent in the dimethylthiophene molecule itself.

### 2.1.3 DIBROMOTHIOPHENES

As it was mentioned in **Chapter 1**, tetrathiafulvalenes are compounds that can be converted into very efficient organic conductors. These compounds, however, belong to only one of the many classes of organic conductors that have been discovered to date. A

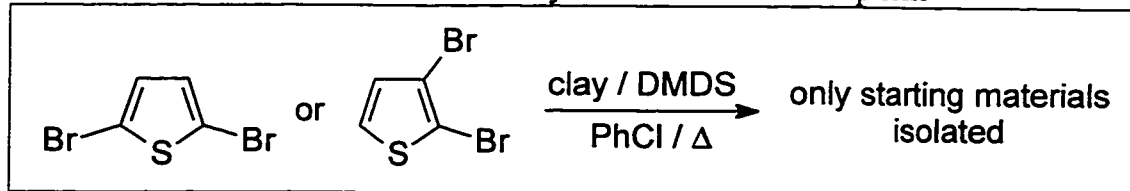


second class of compounds that has gathered quite a bit of interest is the polythiophenes, which are usually prepared by the polymerization of various dihalothiophene derivatives.

Current research has been focused on the preparation of variously functionalized derivatives of such compounds in order to improve their solubilities as well as their conducting properties. Attention was therefore directed to prepare the *bis*(methylthio) derivatives of 2,5-dibromo and 2,3-dibromothiophene. Not only would these compounds permit access to a large variety of thiophene-based tetrathiafulvalenes, but it would also be an effective means towards the synthesis of thiomethylated polythiophenes.

Once again, the same conditions as before were used with these compounds, but unfortunately no reaction was observed with either substrate. Autoclave reactions also failed to give anything but starting materials. It was therefore concluded that the bromine atoms deactivate the thiophene system much in the same way as the chlorine does in chlorobenzene. Another possibility is that the bromine atoms themselves co-ordinate to the active sites in the catalyst preventing the activation of DMDS molecules.

**Scheme 2-10:** Thiomethylation of dibromothiophene



#### 2.1.4 THIOALKYLATIONS OF THIOPHENE BY STANDARD HOMOGENEOUS METHODS

The failure to obtain the benzylthio- and the isopropylthio- adducts of thiophene by the clay-catalyzed method, compelled attempts to synthesize these compounds by the same techniques used by Tiecco,<sup>34</sup> Fanghänel,<sup>80</sup> and others (**Chapter 1.2**).

The initial reactions were performed in DMF at room temperature with the relatively inexpensive and commonly available 2,5-dibromothiophene. This compound was added to a solution of the appropriate sodium thiolate in DMF at room temperature. The reaction was monitored by GC-MS for five hours. Initially the results seemed to be very promising although slow. After five hours, significant amounts of a compound having the same mass ion as 2-bromo-5-isopropylthiothiophene were observed. Further stirring at room temperature did not seem to increase the quantity of this or the *bis*(thioalkylated) product, so the reaction mixture was warmed to 50°C and stirred at this temperature overnight. Unfortunately, the reaction mixture resulting from this treatment consisted of a multitude of products, none of which showed the desired mass ion when analyzed by GC-MS. Similar results were obtained when the reaction was performed with sodium ethanethiolate and sodium benzylthiolate.

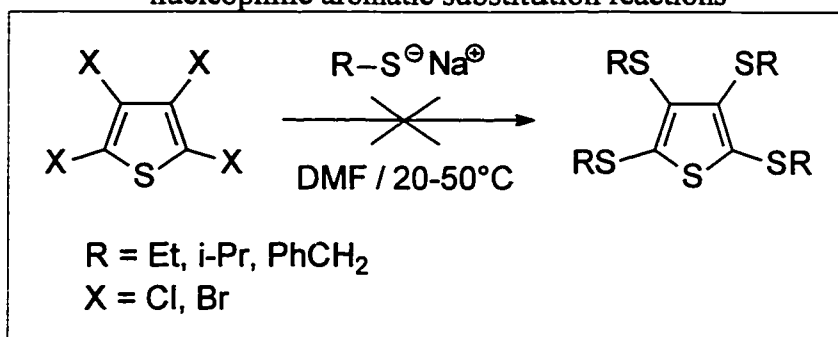
As Tiecco pointed out, the reactivity of the polyhalobenzenes is best when the halides used are fluorides and slightly less when the halides used are chlorides; therefore, it was decided to perform this reaction with tetrachlorothiophene and sodium benzylthiolate following the same procedure that gave Fanghänel success.

Tetrachlorothiophene was prepared by literature procedures<sup>81</sup> and added to a slight excess of sodium benzylthiolate dissolved in DMF. The reaction was allowed to

stir for three hours at which time a GC-MS analysis of the reaction showed that none of the desired product had been formed.

The complete failure of these reactions, both at room temperature and under mild heating, and the fact that such thioalkylated thiophenes have been traditionally prepared only by the reaction of thienyl lithiums with disulfides, may explain why this type of procedure has never been reported in the literature.

**Scheme 2-11:** Attempts at thioalkylating thiophene through nucleophilic aromatic substitution reactions



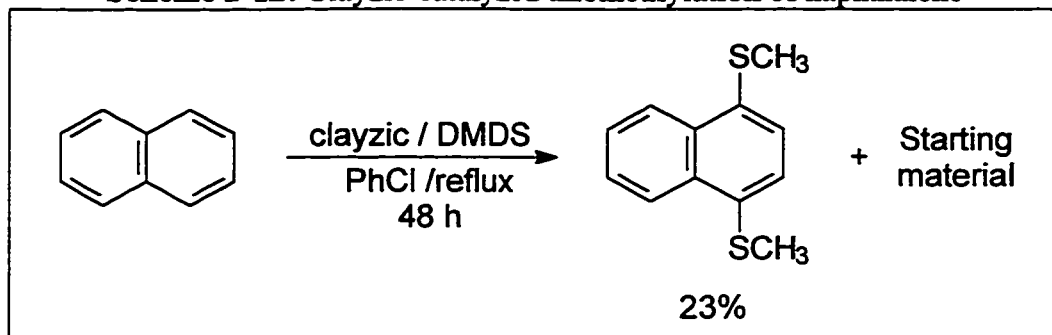
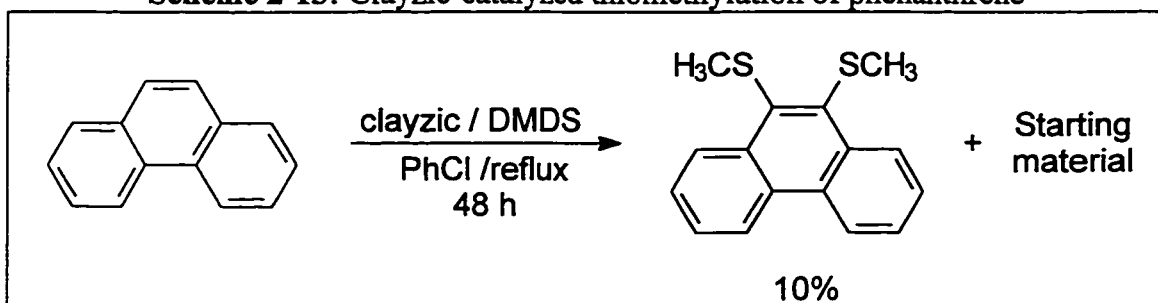
## 2.2 THIOMETHYLATION OF OTHER AROMATICS AND HETEROAROMATICS

### 2.2.0 BACKGROUND

Thiophene, toluene, anisole and various other benzene derivatives have been shown to be fairly easily thiomethylated with the various clay catalysts prepared in our laboratories.<sup>76,77,82</sup> It would, however, be more useful if a larger variety of aromatic compounds, in particular other heteroaromatics, were shown to react under similar conditions as the products of these reactions could be used to synthesize tetrathiafulvalene derivatives.

### 2.2.1 NAPHTHALENE AND PHENANTHRENE

These two compounds were surprisingly unreactive towards DMDS in the presence of the modified clay catalysts. Naphthalene, when compared to its heteroaromatic counterpart, benzo[*b*]thiophene, is much more difficult to thiomethylate. When the clayman-catalyzed reaction is refluxed in chlorobenzene, the only compounds isolated from the reaction mixture were 1,4-*bis*(methylthio)naphthalene (the standard electrophilic substitution pattern for naphthalene when electron-rich substituents are used), isolated only in a 23% yield and identified by <sup>1</sup>H-NMR, and naphthalene itself (**Scheme 2-12**). Phenanthrene was even less reactive yielding only about a 10% yield of the 9,10-*bis* compound (**Scheme 2-13**). Performing these reactions in the presence of clayzic results in much lower yields.

**Scheme 2-12:** Clayzic-catalyzed thiomethylation of naphthalene**Scheme 2-13:** Clayzic-catalyzed thiomethylation of phenanthrene

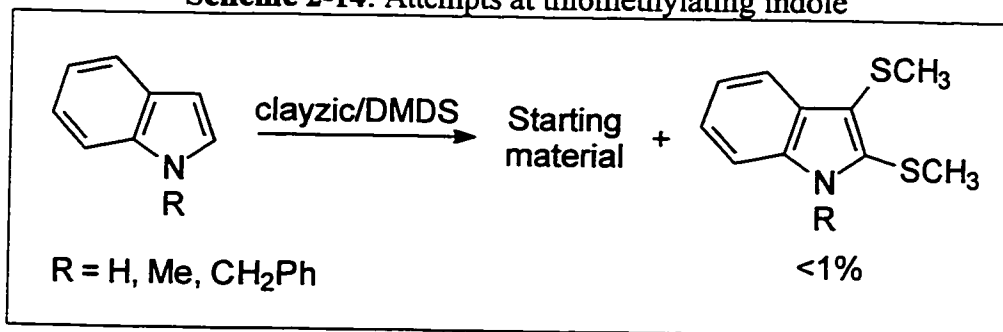
### 2.2.2 FURAN, PYRROLE AND INDOLE

These heteroaromatic compounds are more prone to polymerization than thiophene and, in general, very difficult to functionalize by standard electrophilic substitution processes. It would therefore be interesting to determine whether it is possible to obtain their thiomethylated derivatives using the clay-catalyzed methods.

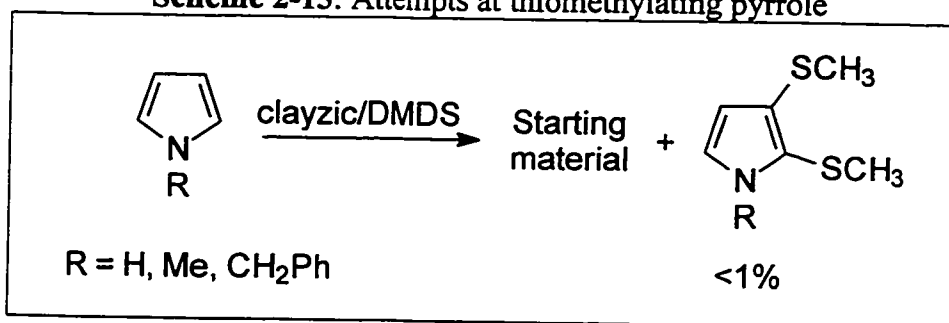
The first thiomethylation of thiophene was performed at the same time as those of pyrrole and indole. Unlike thiophene, when these compounds were subjected to the same conditions, only small traces of the thiomethylated product were observed by GC-MS. In addition to this, as soon as indole or pyrrole were added to the reaction mixture, the clay "swelled up", in other words, it behaved as if water or alcohol had just been added.

Hence, it was concluded that the nitrogen atom on these compounds was too basic and, therefore, able to co-ordinate rather strongly to the active sites in the clay. Likewise, the N-methyl and N-benzyl derivatives of pyrrole and indole failed to undergo thiomethylation with clay-promoted catalysts.

**Scheme 2-14:** Attempts at thiomethylating indole

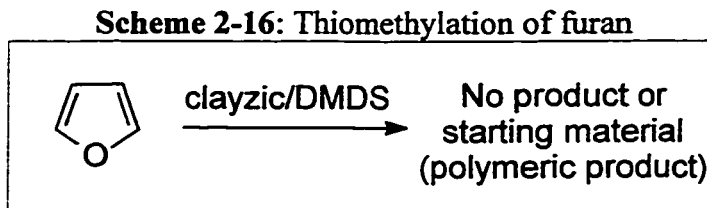


**Scheme 2-15:** Attempts at thiomethylating pyrrole



Furan, unlike pyrrole and indole, was much less stable in the presence of clay catalysts at standard reaction conditions yielding only polymeric products. Since furan is more sensitive towards acidic conditions, a new clay reagent was prepared to be used in conjunction with the standard catalyst. K10/K<sub>2</sub>CO<sub>3</sub> was prepared in much the same way as the other catalysts have been prepared and this was added along with clayzic or clayman in a 1:1 ratio. Once again no useful reaction took place. Thus, it seems that of

all these compounds, only the sulfur heterocycles react favourably towards the clay-catalyzed thiomethylation.



### 2.3 CONCLUDING REMARKS

The use of clay catalysts with DMS has been shown to be an effective method of introducing multiple sulfur atoms into various aromatic systems. Although the reactions with thiophene under standard conditions did not yield large amounts of the tetra-substituted product, by performing the reaction under a high pressure of air permitted the isolation of this new compound in good yield. The more stable 2,5-dimethylthiophene did not require such forcing conditions and therefore its *bis*-thiomethylated derivative could be prepared and isolated, once again in good yield.

It is unfortunate that clay-catalyzed thioalkylations may not be used with disulfides containing branched alkyl groups because these are more easily removed by reductive de-methylation techniques. Methods to produce such compounds under standard homogeneous conditions also failed although perhaps the more active fluorinated thiophenes may give better results.

The surprising effect of clayman in the thiophene-DMS reaction and the absence of side-products suggested that a completely different kind of mechanism may be

at work here. Whether or not this is the case, thioalkylations with this catalyst also failed to produce any products with heavier disulfides.

2,3- and 2,5-dibromothiophene along with indole, pyrrole and furan were either unreactive or too unstable under the reaction conditions employed. It is theorized that the dibromothiophenes, indole and pyrrole did not react because they are more basic than DMDS and that therefore they tie up all the active sites in the clay. Furan, on the other hand, seems to be too unstable even under these conditions because no trace of it or of any thioalkylated products is observed when the reaction is performed.



## CHAPTER 3

### CLAY-CATALYZED THIOMETHYLATION OF ALKENES

#### 3.0 INTRODUCTION

The clay-catalyzed thiomethylation of aromatic compounds has been proven to be a simple and reasonably high yielding process for introducing more than one  $\text{CH}_3\text{S}$ -functional group into the aromatic nucleus. One drawback, however, is that the reaction is not very selective, which makes controlling the number and position of the thiomethyl units introduced very difficult. One plausible solution to this problem would be to limit the possible sites of attack through the use of alkenes instead of arenes.

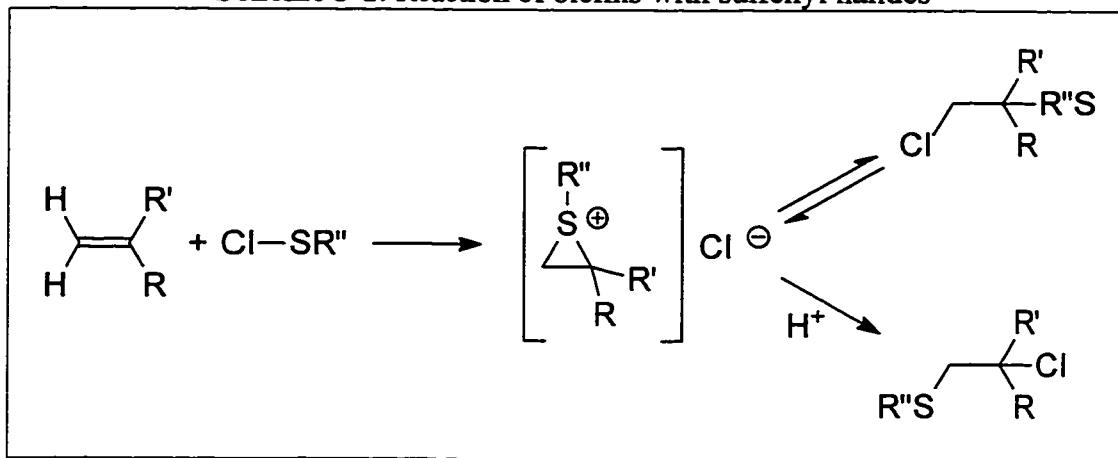
The addition of electrophilic substrates to electron-rich double bonds has been proven to be one of the most effective methods of preparing 1,2-disubstituted compounds. Preliminary work in our laboratories has shown that clay-catalyzed thiomethylation is also applicable for use with alkenes and results in products where addition of the disulfide molecule has added across the double bond.

##### 3.0.0 BACKGROUND

The addition of sulphenyl ion equivalents to olefins has been known for many years, and the best known family of this type of compound are the sulphenyl halides, whose synthesis and chemistry have been investigated extensively.<sup>83</sup>

The mechanism is fairly straightforward. The  $\pi$ -system of the alkene attacks the electrophilic sulfur, thus displacing the halide and generating an episulfonium intermediate. Under ordinary conditions, this species is then opened by the halide to give, due to steric effects, the Markovnikov adduct in an *anti*-configuration (Scheme 3-1). These may undergo a rearrangement under acidic conditions to give the more thermodynamically stable anti-Markovnikov adducts.

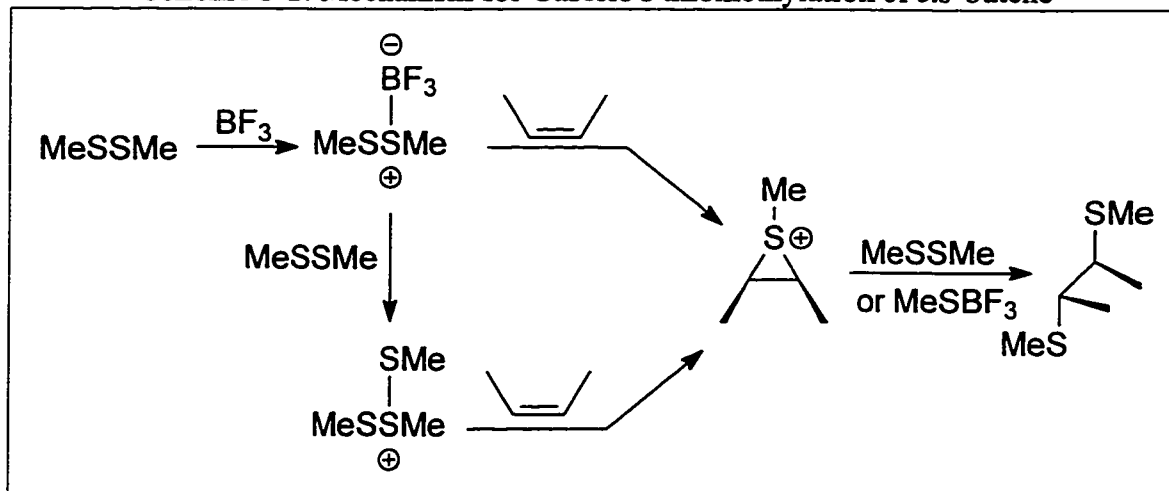
**Scheme 3-1:** Reaction of olefins with sulfenyl halides



Sulfenyl halides, however, are not the only sulfenyl ion equivalents that have been employed in the past. Caserio has used a catalytic amount  $\text{BF}_3 \cdot \text{Et}_2\text{O}$  to activate disulfides.<sup>84</sup> The mechanism that is proposed for this reaction is very similar to that which takes place with sulfenyl halides. In this mechanism,  $\text{BF}_3$  co-ordinates to the disulfide molecule and generates the sulfenyl ion equivalent. Caserio is not certain whether the active species in this reaction is fact the disulfide- $\text{BF}_3$  complex or the product of this species with another molecule of disulfide (Scheme 3-2). Either way, reaction with the olefin results in an episulfonium intermediate that is opened by another molecule

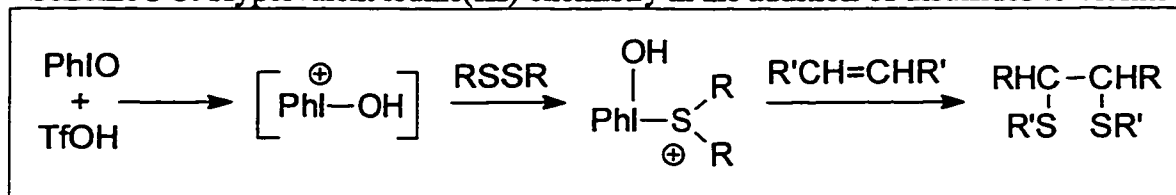
of disulfide or thiolate. Once again, this mechanism very effectively provides an explanation of why only the *anti*-addition product is observed in this reaction.

**Scheme 3-2:** Mechanism for Caserio's thiomethylation of *cis*-butene

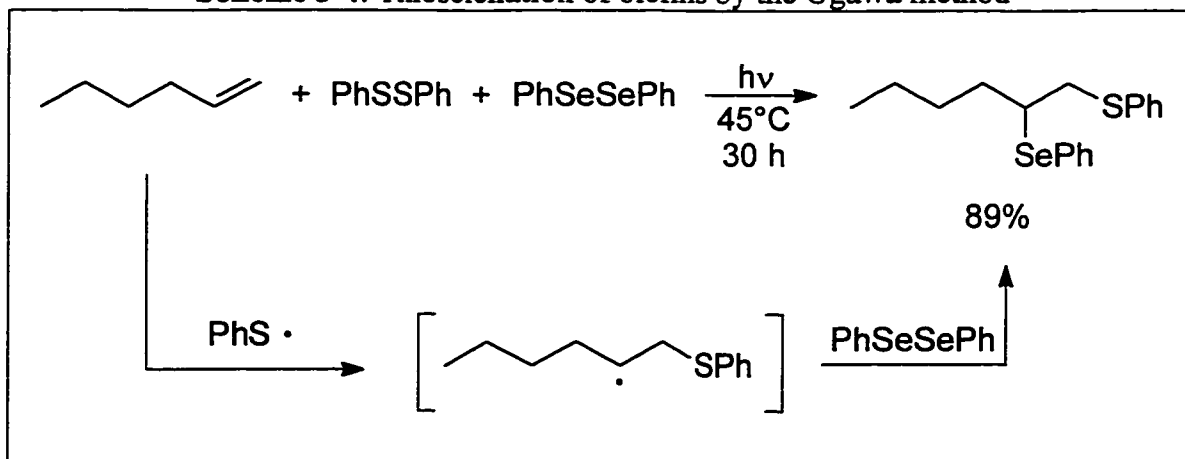


Francis has used an iodine-catalyzed variation of this method to determine the position of the double bond in various alkenes.<sup>85</sup> The mechanism is probably very similar to Caserio's the only difference being that the active species is an iodonium/alkene intermediate which is attacked by the disulfide molecule.

Kitamura has employed a less common iodine reagent to achieve more or less the same results.<sup>86</sup> The combination of iodosylbenzene (PhIO) with triflic acid formed the species [PhI<sup>+</sup>-OH], which served as the Lewis acid to activate the disulfide molecule in his reaction (**Scheme 3-3**). Once again, it is either this species or the dithiosulfonium ion, RS<sup>+</sup>(SR)<sub>2</sub>, that reacts with the olefin to generate the episulfonium ion.

**Scheme 3-3:** Hypervalent iodine(III) chemistry in the addition of disulfides to olefins

Ogawa used free-radical chemistry to achieve the same type of addition.<sup>87</sup> By using a PhSeSePh/PhSSPh couple and irradiation, he successfully synthesized the thioselenated product. According to the type of products obtained, Ogawa proposes that first the disulfide is homolytically cleaved and these radicals react with the alkene to give a second radical intermediate. Reaction of this arylthio-substituted radical with the diselenide gives the product. Depending on the nature of the alkene, this reaction can be highly selective in terms of the final positions of the sulfur and selenium atoms. Unfortunately the reaction is not highly stereoselective, although, in the case of cyclic olefins, the *trans* products were usually observed.

**Scheme 3-4:** Thioselenation of olefins by the Ogawa method

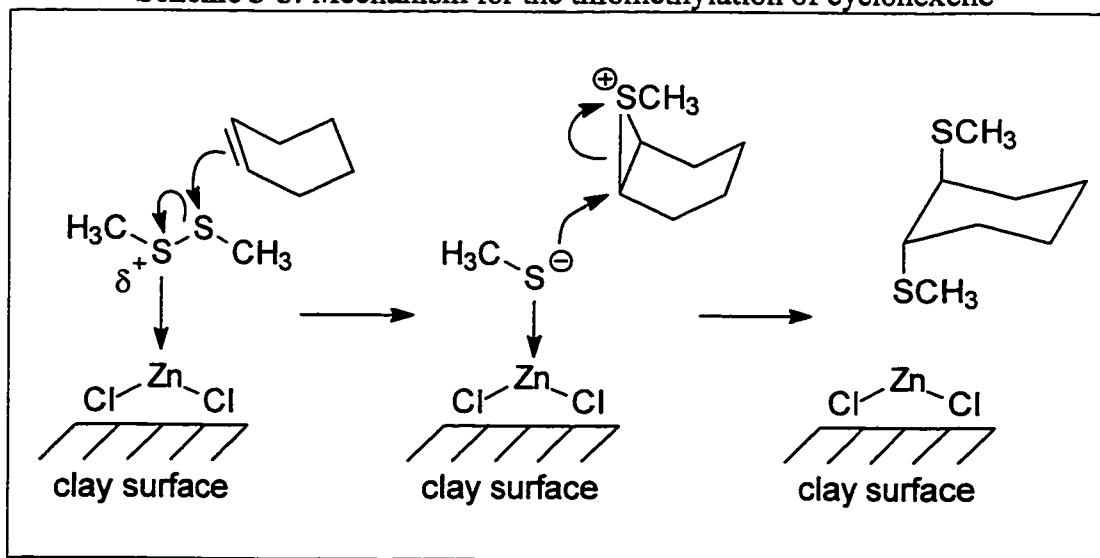
### 3.1 CYCLOHEXENE

#### 3.1.0 BACKGROUND

Cyclohexene is easily thiomethylated at room temperature with clayzic.<sup>88</sup> The reaction conditions could not be more straightforward: DMDS and cyclohexene are added to a mixture of clayzic and 1,2-dichloroethane and stirred at room temperature for two hours. Isolation simply consists of filtration of the reaction mixture and evaporation of the solvents.

The mechanism that is proposed for this reaction is very similar to the one that takes place with sulfenyl halides. As was the case with the thiophene reactions, the active species is a clayzic-activated DMDS molecule. This species is attacked by a cyclohexene molecule forming an episulfonium intermediate which is then opened by the remaining methylthiolate (**Scheme 3-5**)

**Scheme 3-5:** Mechanism for the thiomethylation of cyclohexene



*Trans*-1,2-bis(methylthio)cyclohexane, however, is not the only product isolated when the clay catalyst used is impregnated with metal salts. For example, along with the liquid product, a fair amount of colourless crystals were also isolated when the reaction is performed with clayzic. These crystals were soon identified as a zinc chloride complex of the product from its X-ray crystal pattern. Moreover, this proved beyond a shadow of a doubt that the configuration of the cyclohexane ring was *trans*, as was theorized from the mechanism. The observation of this complex also corroborates the suggestion that clayzic consists of free  $\text{ZnCl}_2$  on the surface of the clay.<sup>10</sup> All in all, the yield from these reactions rarely goes above 60%.

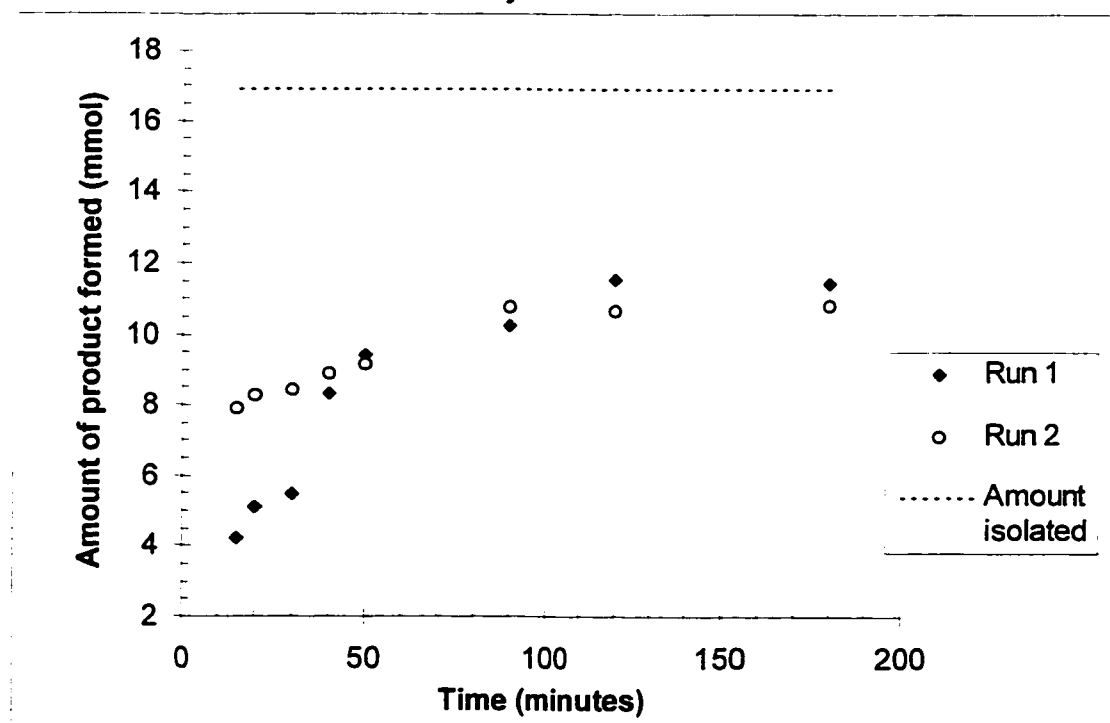
The formation of these complexes complicates matters somewhat in terms of isolation. In order to obtain the pure thiomethylated cyclohexane, the reaction mixture was first washed with an aqueous NaOH/EDTA solution before removal of the solvents. Fortunately, this is not necessary when the thiomethylation is performed with K10 alone. Although in this case the reaction proceeds much more slowly (usually requiring about twelve hours instead of just two), the product obtained is very pure. Once again, the highest yield obtained with this reaction was close to 60%.

In order to understand better the role that the catalyst plays in these reactions, it was decided to conduct a kinetic study with clayzic, K10, and other clay-based catalysts. It was hoped that this study would give more insight into the mechanism and perhaps reveal the nature of the active species involved.

### 3.1.1 KINETIC EXPERIMENTS

The study was to be fairly simple: the reaction would be performed as described above with the exception that an internal standard, hexadecane, would be added to the mixture along with the other reagents. Soon after the study began, however, it was realized that the formation of the complex would pose a serious problem in any attempt to accurately determine the concentration of the product at any particular time. It was therefore decided that the samples could not be directly injected into the GC, but rather they would have to be washed with aqueous base and perhaps even EDTA. This, of course, risked the contamination of the sample and perhaps even some loss of products or reactants from the solution, but it was deemed necessary.

**Figure 3-1:** Kinetic data obtained for the clayzic-catalyzed thiomethylation of cyclohexene



Two runs were performed and, surprisingly, the results obtained from these two runs varied significantly (**Figure 3.1**). Because the clay, solvents, and reagents came from the same batch and the conditions used for both runs were as identical as possible, this was very puzzling. Another interesting observation was that the amount of product isolated (in both runs) was much larger than what the GC analysis would lead to believe. Many possible explanations were put forward at this point: the complex was not being decomposed efficiently, the pre-injection treatment of the reaction solution was somehow changing the concentrations of its components in an unpredictable manner, some of the product was being left behind on the clay, etc. In addition to these possibilities, the fact that the yield of the reaction was never higher than 60%, even when conditions were optimized, was probably also a major cause of the inconsistent results. Not only was this reaction not quantitative, but it was also impossible to determine what was happening to the other 40%. At the end of the reaction, there was no trace of cyclohexene left in solution, and exhaustive washing of the clay with ethanol, methanol, water, and aqueous base failed to yield any more product or, in the case of clayzic,  $\text{ZnCl}_2$ -complex. Most probably, some cyclohexene underwent polymerization to an extent which prevented extraction of the polymer from the clay. In light of these facts, any results obtained from kinetic studies would be highly suspect and therefore kinetic work on this reaction was not pursued any further.



### 3.1.2 CLAYMAN

So far, the only catalysts that have been discussed with the thiomethylation of cyclohexene have been clayzic and ordinary K10. It seemed logical, therefore, to perform at least a few reactions with clayman since it showed itself a cleaner yet a more efficient catalyst in the thiomethylation of thiophene.

The clayman-catalyzed thiomethylation of cyclohexene proceeded much more slowly than at first expected. Whereas the reaction with clayzic was complete within a few hours, the reaction time with clayman was comparable to that of ordinary K10. After some thought and after reviewing the other differences between clayman and clayzic in the thiomethylation of thiophene, the reason became clearer.

As it was mentioned in **Chapter 2.1.1D**, the clayman-catalyzed reaction of DMDS with thiophene produces very little dimethyltrisulfide as a by-product. It was suggested that the reason behind this observation is that clayman does not activate DMDS in the same manner that clayzic does and that therefore the reaction must involve some other activated intermediate. The dramatic decrease in the reaction rate of the DMDS-cyclohexene reaction provides more evidence that DMDS is not activated in the presence of clayman (or, at the very least, it is not activated sufficiently to be attacked by the  $\pi$ -bond of cyclohexene).

In **Chapter 2**, one of the possibilities suggested for the high reactivity of clayman with thiophene (or, for that matter, with other aromatics), involved a thiophene-Mn(II) complex. If this hypothesis is correct, then the formation of such a complex is not possible with cyclohexene and this causes the reaction to fail. Because the

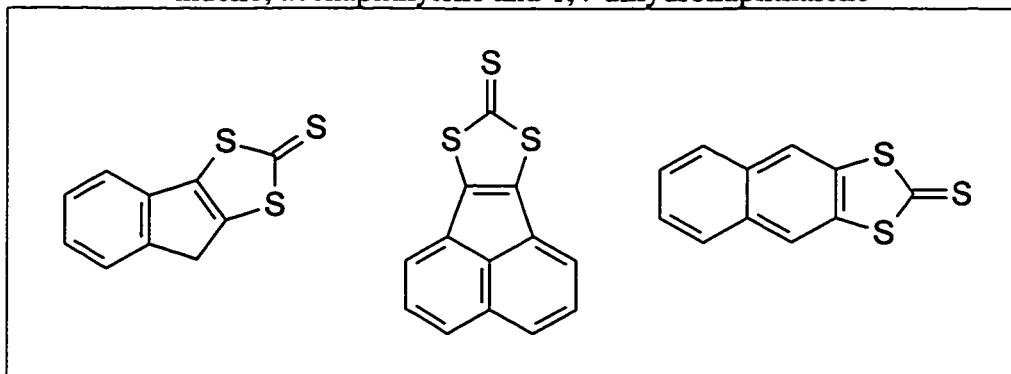
stereochemistry of the products is identical to that of the products from reactions with K10 or clayzic (*i.e.* the SCH<sub>3</sub> groups on the cyclohexane ring are in a *trans* configuration), it has been concluded that the small reactivity observed is due to trace Brønsted-acid sites on the clay and not due to the slow formation of a cyclohexene-Mn(II)  $\pi$ -complex.

## 3.2 INDENE, ACENAPHTHYLENE AND 1,4-DIHYDRONAPHTHALENE

### 3.2.0 BACKGROUND

In spite of the fact that the kinetic studies with cyclohexene failed to give reproducible results, which made it more difficult to establish the accuracy of the proposed mechanism, the reaction is quite successful in producing the DMDS-alkene adducts in respectable yields. Since the ultimate goal of this project, as stated in previous chapters, was to prepare various TTF derivatives, it was decided to prepare the DMDS adducts of three interesting olefins with the intent of re-generating the  $\pi$ -bond between the 1,2-positions and then transforming the compound into the TTF precursor.

**Figure 3-2:** 1,3-dithiol-2-thione derivatives that could be prepared from indene, acenaphthylene and 1,4-dihydronaphthalene

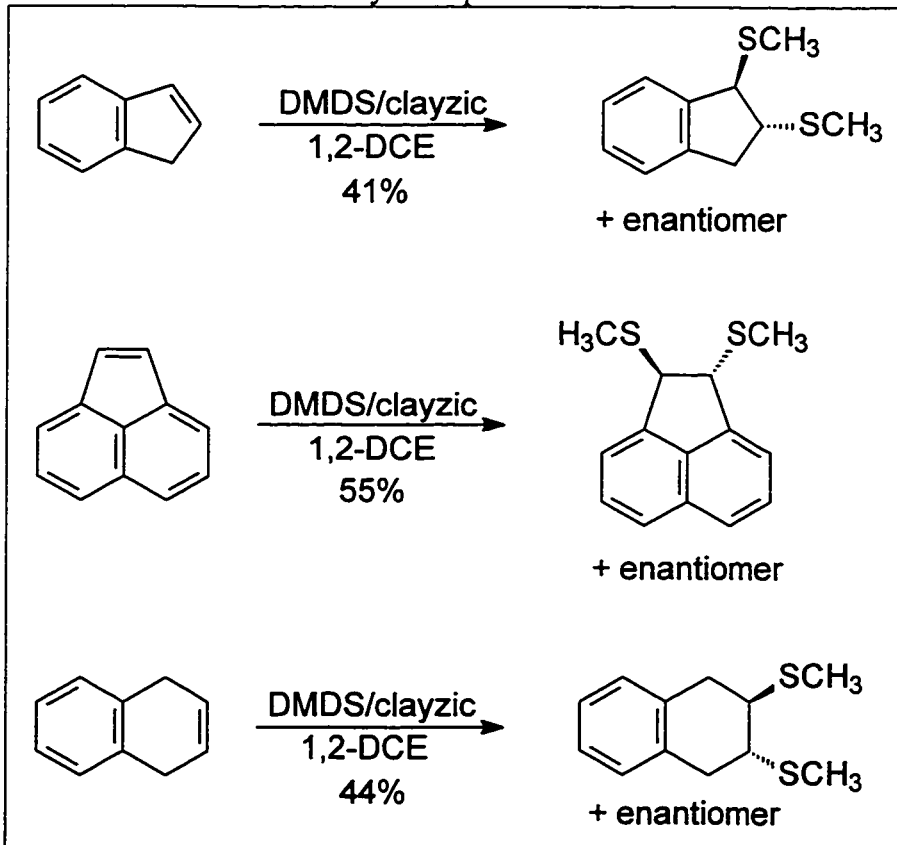


### 3.2.1 THIOMETHYLATION RESULTS

The thiomethylation of the three olefins may be accomplished with the same procedure used for reaction of cyclohexene to yield the previously unknown (a surprising

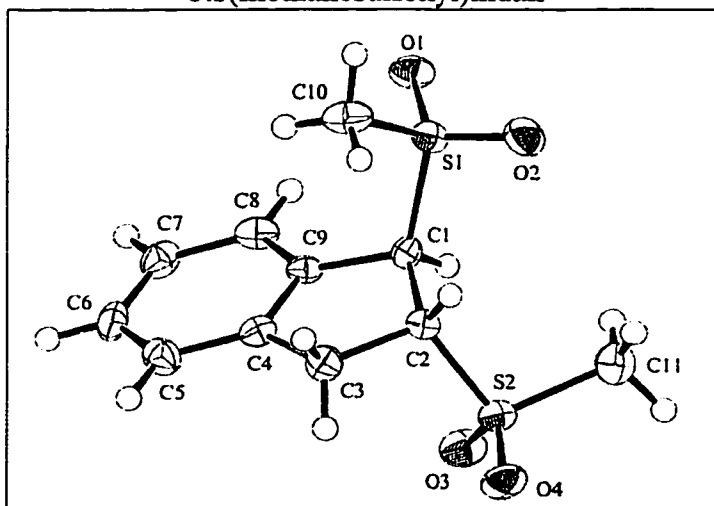
fact considering the simplicity of these compounds) adducts in moderate yields. In each case, the olefin was stirred at room temperature in a solution of 1,2-dichloroethane and DMDS with clayzic or K10 as the catalysts. One interesting observation, however, was made in the case of acenaphthylene and indene: if these compounds were added to the clay/solvent mixture before the DMDS, then the reaction failed to give any product at all. Instead of the thiomethylated product, once the solvent had been removed, a highly insoluble solid was obtained in both cases. A mass spectrum of these solids suggests that they are mixtures of high molecular weight compounds. A likely explanation for this observation is that the double bond in indene and acenaphthylene is reactive enough for it to co-ordinate to the catalyst thus promoting polymerization of the alkene.

**Scheme 3-6:** Thiomethylation of indene, acenaphthylene, and 1,4-dihydronaphthalene



Although the configuration around the rings in both of these products was expected to be *trans*, this was more difficult to prove than in the case of cyclohexene. The  $^1\text{H}$ -NMR spectrum of the indene adduct showed that the product consisted of two isomeric compounds roughly in a 1:10 ratio. Unlike with cyclohexene, the zinc complex of these products failed to give X-ray quality crystals and therefore a definite identification had to be achieved by other means. For this reason, both the indene and acenaphthylene adducts were oxidized and their corresponding disulfones isolated in an attempt to determine their configuration through their X-ray crystal structures. Unfortunately, good quality X-ray crystals could only be obtained for the indene adduct (**Figure 3-3**), thus proving that the major product of this reaction is indeed *trans*.

**Figure 3-3:** ORTEP diagram of *trans*-1,2-*bis*(methanesulfonyl)indan



**Table 3-1:** Selected bond lengths for *trans*-1,2-*bis*(methylthio)indan (see **Appendix** for more detail)

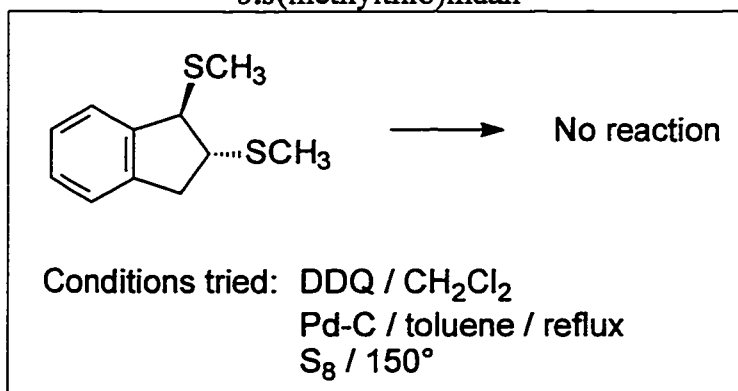
Atom	Atom	Distance (Å)	Atom	Atom	Distance (Å)
S(1)	C(1)	1.795	S(2)	C(11)	1.755
S(2)	C(2)	1.789	C(1)	C(2)	1.549
S(1)	C(10)	1.751			

### 3.2.2 DEHYDROGENATION RESULTS

Having introduced adjacent sulfur atoms into the target molecules, the rest of the dithiole ring had to be constructed. This would, of course, require the sulfur atoms to be on a *cis* double bond, and so the only question remaining would be when to introduce it. Since the double bond could be, in theory, introduced at some later point in the synthesis of the TTF or immediately after the thiomethylation, both avenues were examined. The thiomethylated olefins were either subjected to a reductive de-methylation (see **Chapter 4**) or to dehydrogenation.

#### A. INDENE ADDUCT

**Scheme 3-7:** Attempts at the dehydrogenation of 1,2-bis(methylthio)indan

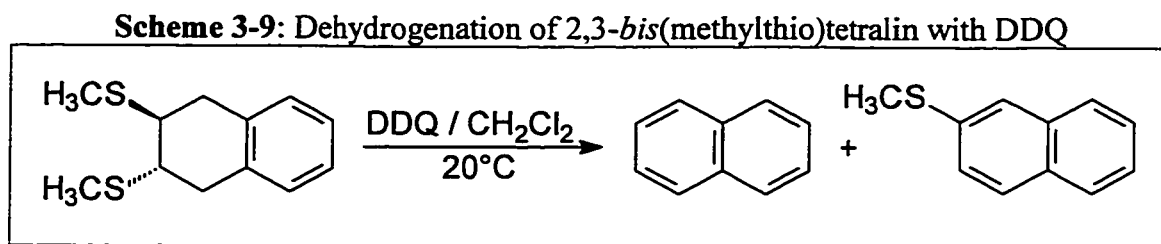


The indene adduct was subjected to the three most common procedures for dehydrogenation.<sup>89</sup> Heating the compound in sulfur (both neat and in the presence of diphenyl ether as solvent) only succeeded in complete decomposition of the starting material. Dehydrogenation with DDQ and with palladium on carbon simply failed to



would be a simple matter of dehydrogenating this compound in order to obtain the desired 2,3-*bis*(methylthio)naphthalene.

This seemingly simple task soon showed itself very difficult. Initial attempts at dehydrogenation with DDQ yielded only naphthalene and a small amount of the monothiomethylated naphthalene (**Scheme 3-9**).



Both *o*- and *p*-chloranil (tetrachlorobenzoquinone) were used next. Whereas *o*-chloranil gave a similar result to DDQ, *p*-chloranil failed to react at all. Reactions with sulfur at high temperatures also failed to give the desired product. Finally, dehydrogenations with palladium on carbon were tried; however, these reactions were speculative because the high thiophilicity of the palladium atom would probably result in the poisoning of the catalyst.

### 3.3 CONCLUDING REMARKS

Although it was not possible to carry out a kinetic study of this type of reaction, the positive results obtained with olefins that are prone to polymerization show that clays may be used very effectively as catalysts to add dimethyldisulfide across an alkene  $\pi$ -bond. It is interesting to note that the synthesis of the *bis*(methylthio)-substituted



derivatives of indene and acenaphthylene had never been attempted before. One may speculate that the reason for this is that these compounds are very prone to polymerization and therefore standard catalysts, such as  $\text{BF}_3 \cdot \text{Et}_2\text{O}$ , are not suitable to carry out these types of reactions on activated double bonds. Clay-catalysis offers a new possibility to carry out reactions such as these under very mild and extremely simple conditions.

## CHAPTER 4

### METAL-AMINE REDUCTIONS OF SULFIDES

#### 4.0 INTRODUCTION

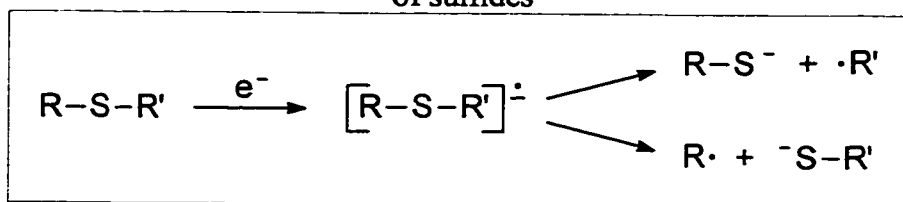
Dissolving metal reductions have been known and exploited for many decades. The best known of these is the Birch reduction of benzene to 1,4-cyclohexadiene.<sup>90</sup> These reactions proceed by free radical mechanisms and involve one-electron transfer from the metal (or the "solvated electron") to the LUMO of the compound to be reduced.

These reductions may also be used to cleave sulfides to their corresponding alkyl or aryl thiols. The elegance of this reaction, if it may be described this way, is that it has been successfully used to reduce multiple sulfide units residing on the same molecule leaving behind, in its most dramatic example to date, six thiol units.<sup>80,91</sup>

##### 4.0.1 BACKGROUND

Both aryl ethers and thioethers may be reduced with this method to the corresponding phenols or thiophenols and, in most cases, the same chemistry may be applied to explain both processes. The first step of this mechanism is an electron transfer to the substrate (**Scheme 4-1**). The species formed is a radical anion which undergoes fragmentation to form an alkoxide (or thiolate) and an alkyl (or aryl) radical. One might ask, therefore, which way would the fragmentation go?

**Scheme 4-1:** General mechanism for the dissolving metal reduction of sulfides



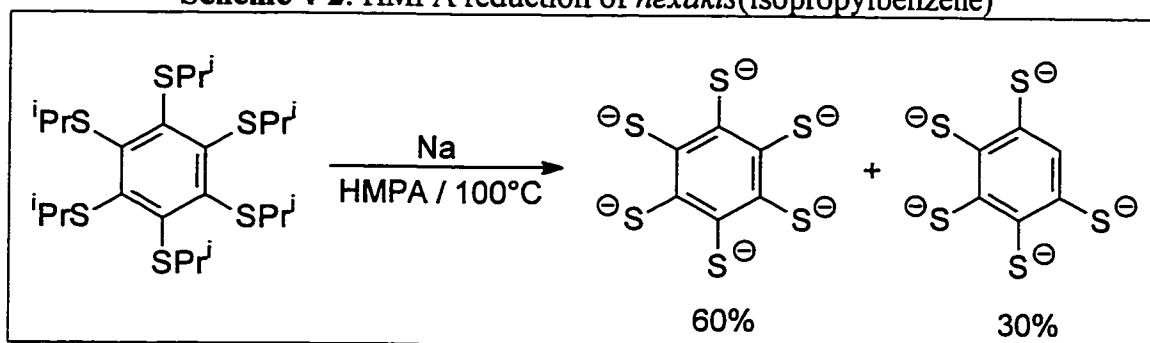
The direction of cleavage depends on the stability of the various possible alkyl radicals as well as on the basicity of the possible thiolates.<sup>92</sup> So, if one were to perform a reduction with, for example, *tert*-butylmethylsulfide, one would produce methanethiolate and a *tert*-butyl radical because, although the basicities of the thiolates are roughly equivalent, the stability of a *tert*-butyl radical is vastly greater than that of a methyl radical. On the other hand, if one performed a reduction of thioanisole (phenylmethylsulfide), one would find that the product would be primarily benzenethiolate and a methyl radical. In this case the factor which most strongly influences the direction of the fragmentation is the greater basicity of methane thiolate with respect to benzene thiolate (the formation of the least basic thiolate being favoured the most).

#### 4.0.1 PREVIOUS SYNTHESSES OF POLYTHIOLS

Tiecco, in connection with his syntheses of polyalkylthiobenzenes (see **Chapter 1.2.1**),<sup>34</sup> also studied the reduction of his products with sodium in HMPA.<sup>91</sup> In almost all instances he obtained the desired polymercaptobenzenes in good yield. In one case, however, Tiecco found an unexpected aryl-sulfur bond cleavage in the more crowded

*hexakis*(isopropylthio)benzene. Reduction of this compound caused the formation of significant amounts of pentamercaptobenzene along with the expected hexamercaptobenzene (**Scheme 4-2**). Tiecco postulated that with *hexakis*(isopropylthio)benzene the steric relief obtained by the fragmentation of an aryl-sulfur bond compensates for such an unfavourable process. This is never observed with 1,3-*bis*, 1,4-*bis*, or 1,3,5-*tris*(isopropylthio)benzene. Furthermore, based on this reasoning, he proposed that the undesired aryl-sulfur bond cleavage occurs at the beginning of the entire process.

**Scheme 4-2:** HMPA reduction of *hexakis*(isopropylbenzene)

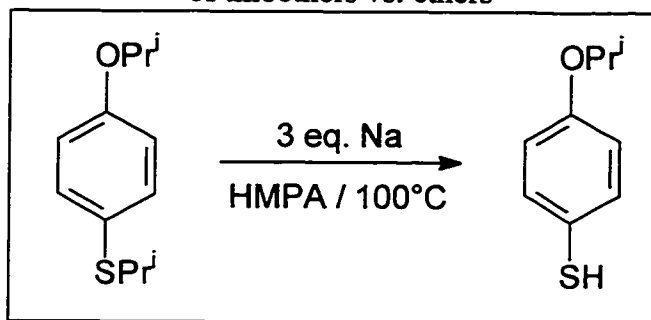


When dealing with multiple alkylthio groups on a molecule, as Tiecco has done, one may ask oneself one last question: why are further reductions possible once the first thiolate is formed? After all, the molecule already contains a negative charge and so it does not seem logical for the molecule, as the extreme case of the *hexakis* compound demonstrates, to acquire five additional negative charges. Tiecco did not offer any kind of experimental evidence, but he suggested<sup>91</sup> that the arenethiolates formed are not present as the free anions but are closely associated with a sodium cation. This would

prevent a delocalization of the negative charge into the aromatic ring making further reductions less prohibitive and, therefore, possible.

In another series of experiments, Tiecco reduced *bis*-sulfides whose alkyl groups were different.<sup>35</sup> Again, as others before him, he observed the trend that fragmentation occurs at a benzyl group more easily than at a methyl group. Finally, when an alkoxy and an alkylthio group are present in the same molecule, fragmentation always occurs to give the thiol (**Scheme 4-3**).

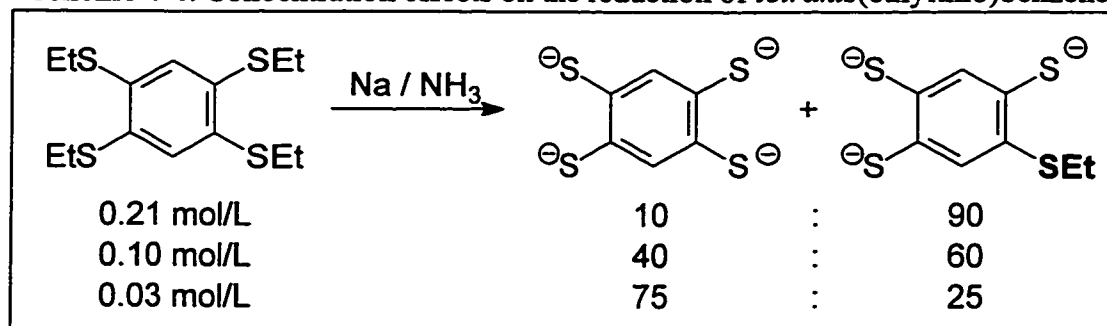
**Scheme 4-3:** Preference towards the reduction of thioethers vs. ethers



Pastor, on the other hand, did not wish to use HMPA in his synthesis of 1,2,4,5-tetramercaptobenzene<sup>93</sup> due to its potentially carcinogenic effects and this led him to perform a series of reactions to determine some of the factors that are responsible for types of products obtained. He performed the reduction of 1,2,4,5-*tetrakis*(ethylthio)-benzene with sodium in liquid ammonia, sodium in ammonia/THF, and lithium in *n*-propylamine. Pastor found that in the case of the reactions in liquid ammonia, a relatively high ratio (4:1) of the completely reduced product vs. the partially reduced product was obtained only when the concentration of the reactant was low (**Scheme 4-4**).

By employing lithium in *n*-propylamine, Pastor was able to obtain a better 9:1 ratio of products with a 45% final yield of tetramercaptobenzene.

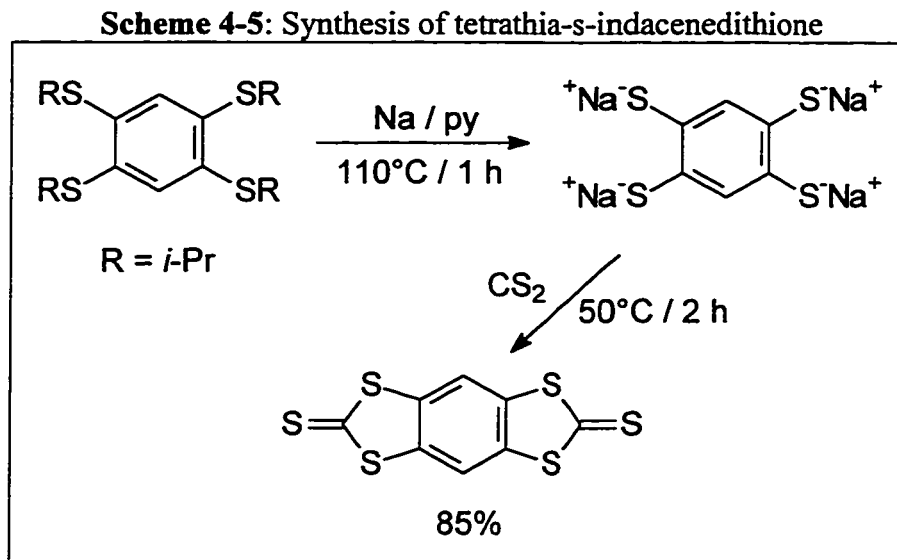
**Scheme 4-4:** Concentration effects on the reduction of *tetrakis*(ethylthio)benzene



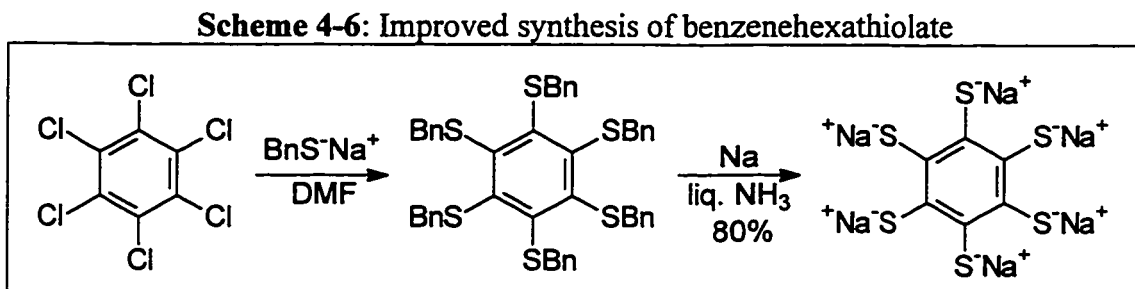
These results, especially when considering the liquid ammonia reactions, indicate that if one wishes to increase the amount of the fully reduced product, one has to somehow increase the amount of its precursor in solution. This is crucial because it infers that no matter how labile the alkyl may be, if the solubility is not adequate and the compound precipitates out before it is fully reduced, then the reaction will stop. This explains Tiecco's success with HMPA and, although he makes no mention of this, why a reaction in liquid ammonia may fail with these highly thioalkylated aromatic compounds.

Müllen and co-workers also undertook the synthesis of 1,2,4,5-benzenetetrathiol although they chose slightly different conditions to prepare this compound.<sup>94</sup> The compound to be reduced was *tetrakis*(isopropylthio)benzene and they treated it with sodium in pyridine at 100°C. Although Müllen did not isolate the tetrathiol, the reaction seems to have worked even better than Pastor's Li/MeNH<sub>2</sub> method: the crude reaction mixture, after quenching with water, was treated with carbon disulfide to give the

dithione in 85% yield (**Scheme 4-5**). Reynolds (see **Chapter 1.2.1**)<sup>40</sup> based his synthesis of thiophene 3,4-dithiol on this method.



By far, the best results for the synthesis of benzenehexathiol were achieved by Fanghanel.<sup>80</sup> Initially he synthesized this compound using Tiecco's method, but like Pastor he was concerned about the hazards that large amounts of HMPA could pose. Probably hoping that the lability of the benzyl group would be enough to overcome any solubility problems encountered in liquid ammonia, he prepared *hexakis*-(benzylthio)benzene and reduced it to afford the hexasodium salt in 80% yield.



Besides the improved yield, this method has another advantage over Tiecco's: liquid ammonia is much easier to remove than HMPA. After evaporation of the ammonia, workup simply consisted of adding water and extracting the solution with ether to remove organics. Cooling the aqueous phase in an ice bath caused the hexasodium salt to precipitate out in a form that was sufficiently pure to conduct further experiments.

From all of these studies one arrives at an important conclusion: the lability of the alkyl group is paramount especially if the solubility of the partially reduced compound is not very high in the solvent chosen. Unfortunately this means that the thiomethyl groups in the compounds prepared in **Chapter 2** would not be as easily cleaved as it had been hoped.



## **4.1 RESULTS AND DISCUSSION**

### **4.1.0 INTRODUCTION**

As was demonstrated in the previous section, there are no examples where the reduction of multiple thiomethyl groups was achieved successfully. Therefore, the failure to introduce the isopropylthio or benzylthio functional groups into thiophene and other aromatic or olefinic compounds by means of clay-catalysts cast some doubt on whether the reduction could be performed on the thiomethylated compounds.

In addition to this, there are no publications on the synthesis or even the attempted synthesis of 2,3,4,5-thiophenetetrathiol. Fanghänel has demonstrated that the fully deprotonated as well as the fully protonated benzenhexathiol is stable enough for isolation. Numerous others have prepared thiophene thiols and dithiols. So why has there never been a synthesis of the tetrathiol?

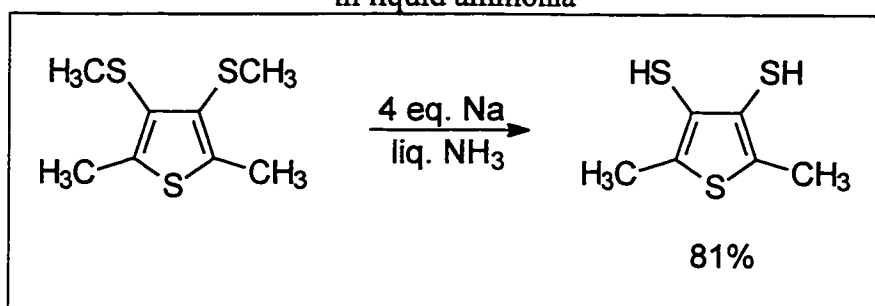
#### **4.1.1 2,5-DIMETHYLTHIOPHENE-3,4-DITHIOL**

The first reduction attempted was with the thiomethylated product derived from 2,5-dimethylthiophene because the synthesis of this product is simpler (the use of an autoclave is not required) and its isolation is more straightforward. Another reason for using this compound to test the metal/amine method was that, because the methylthio-derivatives were being employed instead of the more common isopropylthio derivatives, there was some concern that the reaction would not work well. It was believed that a

reaction with 2,5-dimethyl-3,4-*bis*(methylthio)thiophene not only would be easier because of the smaller number of sulfide units involved, but also it would yield 2,5-dimethylthiophene-3,4-dithiol. This compound has been prepared in the past, it is fairly stable, and so the success or failure in making it would provide a good idea of whether the methodology was sound.

A reaction with sodium (4 eq.) in liquid ammonia was performed and the mixture was stirred until the ammonia evaporated off. Isolation of the product gave an 81% yield of crude thiol (**Scheme 4-7**). GC-MS analysis showed that it was at least 90% pure. Since the purity of the product was sufficient for the intended purposes and any further handling would require significant precautions against atmospheric oxygen, no further attempts at purification were made and the compound was taken to the next step in the synthesis (see **Chapter 5**).

**Scheme 4-7:** Reduction of 2,5-dimethyl-3,4-*bis*(methylthio)thiophene in liquid ammonia

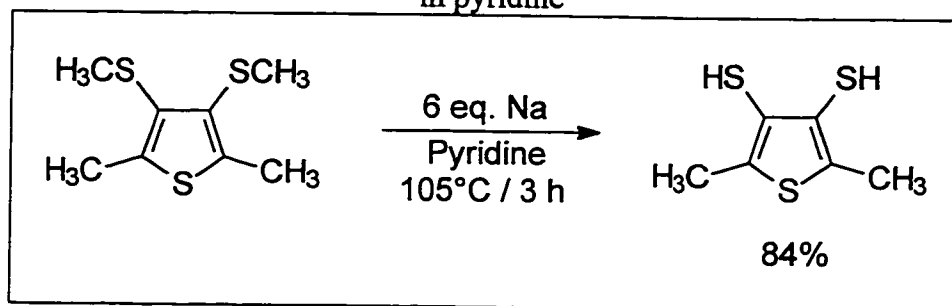


Although this method worked very well with this compound, the results with 2,3,4,5-*tetrakis*(methylthio)thiophene were less than encouraging (see below, **Chapter 4.1.1**). After coming across Reynolds' use of pyridine in his synthesis of thiophene-3,4-

dithiol (**Scheme 1-24**), the viability of this method was first tested, as in the previous case, on the 2,5-dimethyl compound.

The sulfide was dissolved in pyridine and the solution was heated to 100-105°C. This time, however, more sodium was required for full demethylation and so six equivalents (instead of the usual four) were added. After workup, 84% of crude was isolated which, as in the case with the reaction in liquid ammonia, was pure enough to perform further experiments (**Scheme 4-8**).

**Scheme 4-8:** Reduction of 2,5-dimethyl-3,4-*bis*(methylthio)thiophene in pyridine



#### 4.1.2 2,3,4,5-THIOPHENETETRATHIOL

As mentioned earlier, the reduction of 2,3,4,5-*tetrakis*(methylthio)thiophene was performed after the reduction of 2,5-dimethyl-3,4-*bis*(methylthio)thiophene proved successful. The first reduction of the *tetrakis* compound was performed in liquid ammonia with eight equivalents of sodium (*i.e.* two equivalents per SCH<sub>3</sub> unit, as was the norm for such reduction in liquid ammonia) and the reaction mixture was stirred until the blue colour of the "solvated electron" disappeared. Since the ultimate goal of this project was to synthesize TTF derivatives and since the resulting tetrathiol was expected to be

highly air sensitive, no attempt at isolation was made and the product mixture was immediately reacted with thiophosgene after the usual workup. After this second reaction was complete, no trace of dithione or other identifiable product was observed.

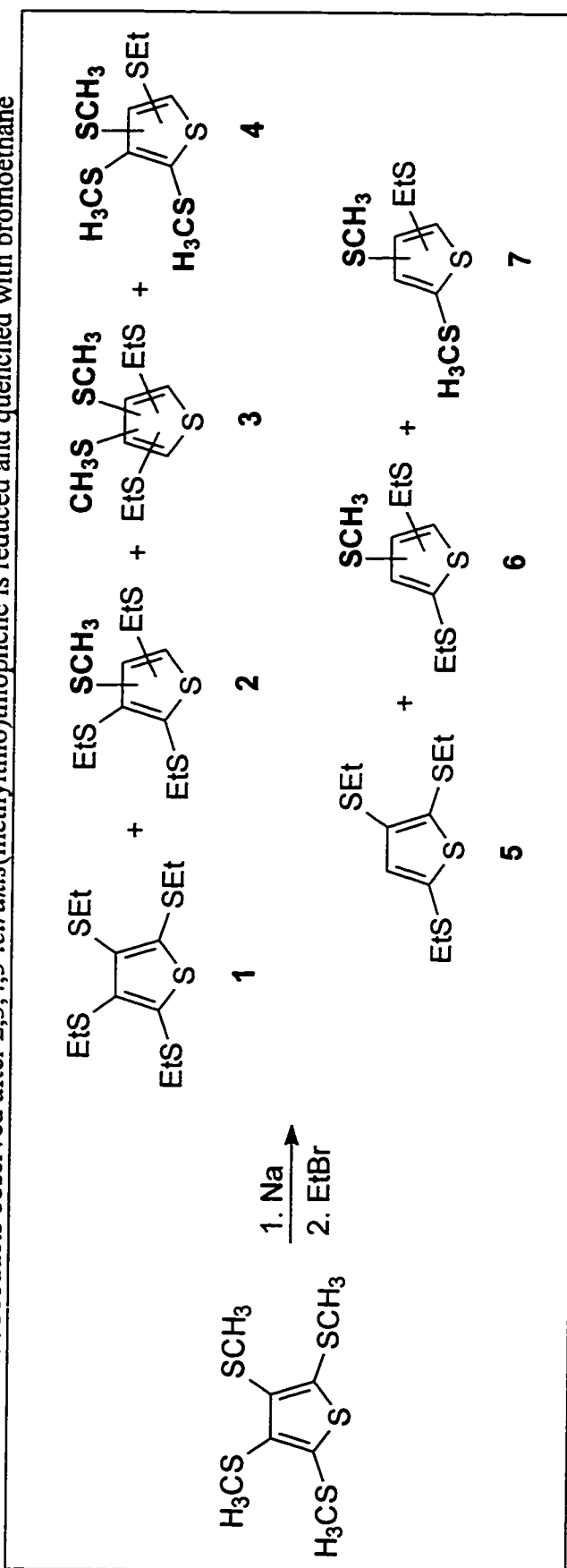
#### A. REDUCTIONS IN LIQUID AMMONIA

The reaction obviously failed but what was unclear was at which point did it fail. Was it the reduction itself or the final reaction with thiophosgene? In order to clarify matters, it was decided to quench the reduction mixture with bromoethane in order to determine to what extent reduction was taking place.

**Scheme 4-9** shows a general reduction reaction with most of the possible products that may be obtained. In an ideal situation, compound **1** would be obtained exclusively, but when the reduction was repeated under the same conditions as above, the product mixture only contained roughly <1% of compound **1**. The remainder consisted of the partially demethylated compound **2** (21%) and **3** (12%) as well as, surprisingly, the partially dethiomethylated compound **6** (65%).

A careful re-examination of Tiecco's work provided a possible explanation for the observed de-thiomethylation: fragmentation was occurring at the less favourable thiophene-sulfur bond because this may provide some steric relief for the system. Although this is a likely explanation, one must take into account that Tiecco was working with a system containing six bulky isopropyl groups instead of four smaller methyl groups. In fact, when the reduction is performed with the *pentakis*(iso-

**Scheme 4-9:** Products observed after 2,3,4,5-*tetrakis*(methylthio)thiophene is reduced and quenched with bromoethane



propylthio)benzene, the pentathiol is obtained in good yield without any unfavourable dethioalkylations.

For the moment, at least, it seemed that the unfavourable cleavage would be something that would have to be accepted as an unfortunate turn of events. Hoping that at some future stage in the synthesis it would be possible to separate the two products, it was decided to proceed with this reaction in an attempt to answer one more unanswered question.

As mentioned previously, all four methyl groups were not being cleaved in the reduction, which resulted in that the bulk of the product consisted of a complex mixture of the partially de-methylated sulfides. There were two possible explanations for this: either the intermediate thiolates were too insoluble to allow for any further reaction, or they were not reactive enough at these conditions. In order to clarify these questions, a study was undertaken in order to determine what type of conditions are necessary in order to maximize the amounts of compound **1** produced. The following table (**Table 4-1**) shows a series of reactions done in liquid ammonia.

**Table 4-1:** Reductions of 2,3,4,5-*tetrakis*(methylthio)thiophene in liquid ammonia with 8 equivalents of metal

Entry	Co-Solvent	Conc. of S.M.	Metal Used	Product Distribution (%)						
				1	2	3	4	5	6	7
1	None	40	Na	0.2	21	12	1	2	65	0
2	None	80	Na	5	0	8	10	38	40	0
4	Et <sub>3</sub> N (25%)	40	Na	13	22	0	0	42	23	0
5	None	40	Li	0	7	0	0	4	90	0
6	None	40	K	9	16	18	0	32	25	0

**Table 4-1** shows that changing the amount of solvent used and adding co-solvents has little effect in increasing the amounts of **1** in the reactions with liquid ammonia. There is a significant improvement by changing the alkali metal used, but it was felt that the results were not encouraging enough to continue the studies in ammonia. Since both Müllen and Reynolds had a great deal of success with pyridine, the next set of reactions studied was performed in this solvent.

## B. REDUCTIONS IN PYRIDINE

Unlike the experiments in liquid ammonia, reactions in pyridine showed a marked increase in the amounts of tetrathiolate formed. Entries **1** through **4** in **Table 4-2** show the results obtained with sodium under these conditions. Even after only half an hour, the amount of tetrathiolate formed is much greater than with liquid ammonia. Unfortunately, just as in the case with liquid ammonia, cleavage of a thiophene-sulfur occurs here as well. In order to determine the extent of this de-thiomethylation as well as to confirm the position of the thiophene C-S bond that was being cleaved, the reaction was quenched with iodomethane. This would result in a simple mixture of the *tris* and *tetrakis*(methylthio) compounds whose relative percent composition, as has been shown in **Chapter 2**, may be easily determined by GC-MS and <sup>1</sup>H-NMR. The isolated mixture consisted of roughly 1:1 *tetrakis* and 2,3,5-*tris*(methylthio)thiophene. The <sup>1</sup>H-NMR spectra of these compounds were identical to those obtained for the compounds prepared by the clay-catalyzed thiomethylation method (**Chapter 2.1**).

An increase in the amount of sodium used did result in a slight increase in the amount of tetrathiolate formed (entry 5). The use of excess sodium proved problematic, however, because the large amount of solids formed caused the mixture to become fairly thick and difficult to stir. Since increasing the amount of solvent did not alleviate this problem, it was decided to try out different alkali metals.

**Table 4-2:** Reductions of 2,3,4,5-*tetrakis*(methylthio)thiophene in pyridine at 105°C

Entry	Metal	Equiv.	Time (h)	Product Distribution (%)						
				1	2	3	4	5	6	7
1	Na	12.8	0.5	4	5	49	4	0	17	21
2	Na	12.8	1	13	17	27	2	6	32	3
3	Na	12.8	1.5	21	10	19	0	14	31	4
4	Na	12.8	4	19	8	21	0	17	33	2
5	Na	16	2	32	12	22	0	8	22	4
6	Li	4.8	4	0	0	25	43	0	0	27
7	Li	4.8	24	0	0	39	22	0	0	40
8	Li	12.8	4	0	2	38	21	0	5	35
9	K	4.8	4	0	0	32	46	0	4	15
10	K	8	4	0	3	39	47	0	4	5

Entries 6-8 in Table 4-2 depict the reactions performed with lithium. These reactions gave similar results as to those obtained with liquid ammonia. An observation made with the sodium reactions may offer an explanation for this result in pyridine. It was observed that before the distinctive purple colour of the reaction appeared, the sodium pieces had to first melt in the vigorously stirred solvent. The molten metal had a very fresh exposed surface, and this was, most likely, responsible for the high reactivity. Since the melting point of lithium is much higher than the boiling point of pyridine, the reaction probably never had a chance to get started.



Entries 9-10 were reactions performed with potassium. Once again, this metal failed to give any significant amount of the fully de-methylated product. Two possible explanations could clarify this result. Either the metal is too reactive under these conditions and reacts with the solvent before it has a chance to reduce the starting material, or there is insufficient covalent character in the K-S bond, as was postulated by Tiecco, to allow for three (and much less four) reductions to take place.

### C. REDUCTIONS IN HMPA

The various reductions done in pyridine once again demonstrated that this solvent was inadequate to promote full de-methylation of the *tetrakis* compound. With some misgivings, it was decided to use HMPA as solvent. Aside from the fact that HMPA is an odourless, carcinogenic solvent, it is also very difficult to remove, which could pose some problems during the isolation of the products.

**Table 4-3:** Reductions of 2,3,4,5-*tetrakis*(methylthio)thiophene in HMPA at 105°C

Entry	Metal	Equiv.	Time (h)	Product Distribution (%)						
				1	2	3	4	5	6	7
1	Na	8	1	51	0	0	0	49	0	0
2	Na	4.8	4	18	5	20	30	21	7	0
3	Na	7.2	1	39	8	15	0	36	2	0
4	Na	8	0.25	15	7	23	13	9	16	17
5	Li	8	1	5	0	15	33	13	5	30
6	K	8	1	42	0	0	13	0	0	0

**Table 4-3** shows some of the results obtained with this solvent. Without a doubt, as entry 1 demonstrates, HMPA is the most effective solvent at carrying out complete de-methylation of *tetrakis*(methylthio)thiophene. Having achieved the first goal in this stage

of the study, some attention had to be devoted towards the second one, that is, to prevent the formation of thiophenetrithiolate, which, as is shown in entry 1, was still occurring. In order to determine why de-thiomethylation was occurring, a few reactions, under varying conditions, were performed in an attempt to understand this process better and perhaps find a way to inhibit it.

Initially it was thought that de-thiomethylation in HMPA was occurring simply because two equivalents of sodium per sulfide unit was too much and had the result of over-reducing the starting material. Unfortunately this turned out not to be the case because roughly one equivalent of sodium was not enough to achieve full demethylation (entry 2). These results are comparable to the reactions in pyridine where 8 equivalents of sodium were used. Entry 3 shows that even a slight reduction in the amount of sodium used per each SCH<sub>3</sub> unit (10% less in this case), caused a decrease in the amount of fully de-methylated material produced.

Entry 4 shows that this process was occurring at the earliest stages in the reaction because even after only 15 minutes, the ratio of the combined percentages of the *tetrakis* and *tris* substituted compounds is already roughly 1:1 even though de-methylation was not complete. As mentioned previously, Tiecco encountered a similar problem in his reduction of *hexakis*(isopropylthio)benzene and he invoked steric factors to explain his data. The final entries in Table 4-3 show that sodium is indeed the best metal for the reduction of this compound. Once again, lithium failed to react, while potassium failed to give complete reduction.

#### D. ISOLATION OF THIOLS

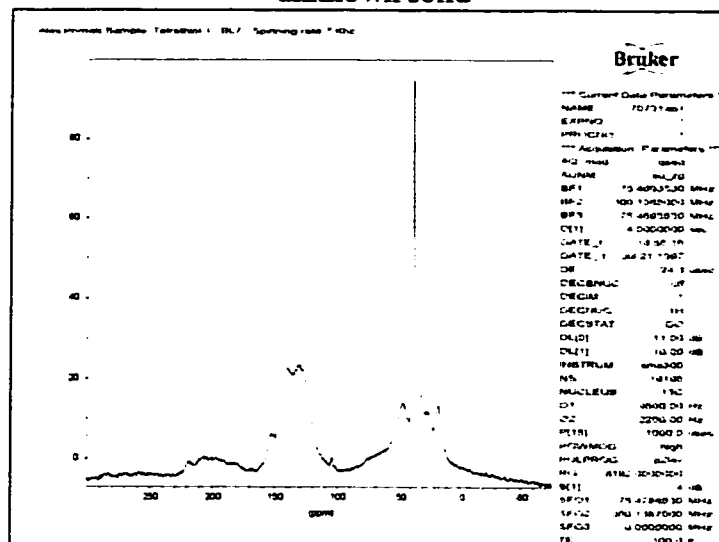
The reduction of *tetrakis*(methylthio)thiophene was most efficiently performed in HMPA, and so an attempt at obtaining the TTF derivatives directly from the crude reaction mixture was made immediately after the reaction was stopped (to be discussed in more detail in **Chapter 5**). However, since these thiophene polythiols were previously unknown compounds, some effort was also diverted into their isolation and characterization.

One of the first and most obvious steps towards achieving this goal would be to quench the reaction mixture and then acidify it in order to obtain the protonated thiols. Upon acidification, a yellow-orange solid immediately precipitated out of the aqueous HMPA solution and this was followed by an unpleasant odour reminiscent of H<sub>2</sub>S. This solid turned out to be extremely insoluble in all solvents. It was partially soluble in amines as well as dilute ethanolic KOH. There was little doubt that this solid was acidic in nature and it was hoped that it was in fact the mixture of tri- and tetrathioms in question. Little doubt remained that this was the case after extraction of the filtered aqueous solution failed to yield any significant amount of organic material.

Unfortunately, the solid did not seem to be very stable. Samples of this compound kept at -20°C and sealed in a vial under an argon atmosphere emitted a strong H<sub>2</sub>S-like odour after only a few hours. Also, the compound became less and less soluble in alkali as time went by. A mass spectrum analysis of this solid failed to give any results. All these things pointed to a polymer. A solid-state <sup>13</sup>C-NMR spectrum of this compound was obtained (**Figure 4-1**) and the broadness of the signals suggested that

indeed this was a polymer (note that the strong, sharp signal at ~38 ppm is consistent with that of the methyl groups on HMPA).<sup>95</sup>

**Figure 4-1:** Solid-state  $^{13}\text{C}$ -NMR spectrum of the unknown solid

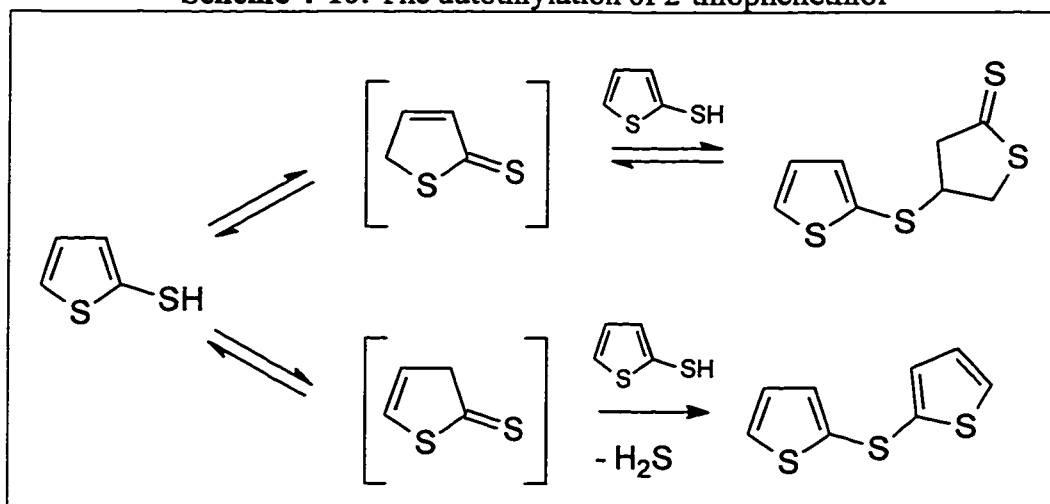


Ordinarily, thiols exposed to atmospheric oxygen will slowly oxidize to the corresponding disulfides, but, if this was indeed the case, this process seemed to be highly accelerated. A review of the literature regarding thiophene thiols provided a possible explanation.<sup>96,97</sup> 2-Thiophenethiol undergoes a reversible autothiolation and the mechanism involves its tautomer (**Scheme 4-10**). This autothiolation is usually accompanied by a side-reaction whose product is *bis*(thienyl)sulfide.

It is believed that something similar is happening to the tetrathiol (and to the trithiol). The presence of four additional thiol units not only increases the possible number of tautomers available for the system, but, most likely, also increases their respective stabilities. **Scheme 4-11** is proposed as a possible mechanism for the

polymerization of this molecule. It is worth to note that **Scheme 4-11** only shows two of the large number of possible products that can arise from such mechanisms.

**Scheme 4-10:** The autothiylation of 2-thiophenethiol

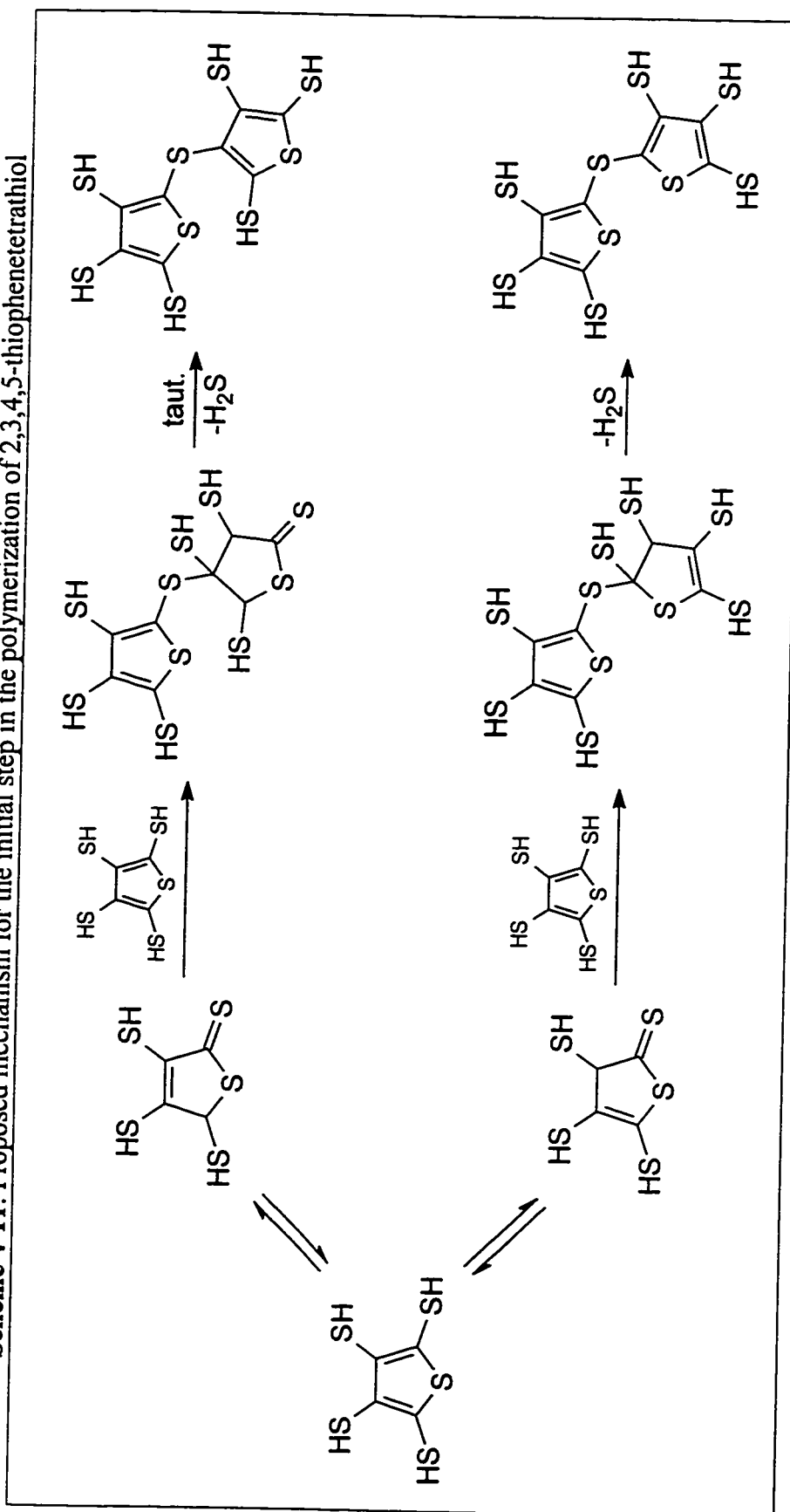


The spontaneous polymerization of the tri and tetrathiol removed all hopes of isolating and studying these compounds. Attention had to be re-directed to somehow functionalizing and then separating these two compounds. The first attempt involved the isolation of the crude sodium salts of the polythiols from the reaction mixture. Fanghänel has shown that it is possible to recrystallize the hexasodium salt of benzenhexathiol very effectively from an ice-cold aqueous solution.<sup>73</sup> However, all attempts to use this procedure failed. This was probably due to the large amounts of water that were necessary in the removal of the HMPA from the reaction mixture.

The high boiling point of HMPA along with its solubility in water and organic solvents was proving to be a more difficult problem than what was previously expected. The solvent responsible for the success of the reduction was now interfering with the isolation of the products. It was decided that the best course of action would be to protect

the thiol groups directly in the reaction mixture and then isolate these compounds. Three protective groups were chosen for this purpose: benzoyl, cyanoethyl, and trimethylsilyl.<sup>98</sup> Unfortunately, all attempts to prepare these compounds failed to give any trace of the desired products.

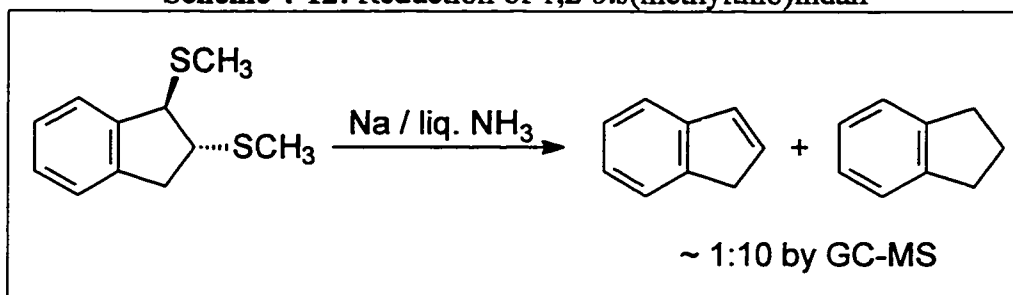
**Scheme 4-11:** Proposed mechanism for the initial step in the polymerization of 2,3,4,5-thiophenetetrathiol



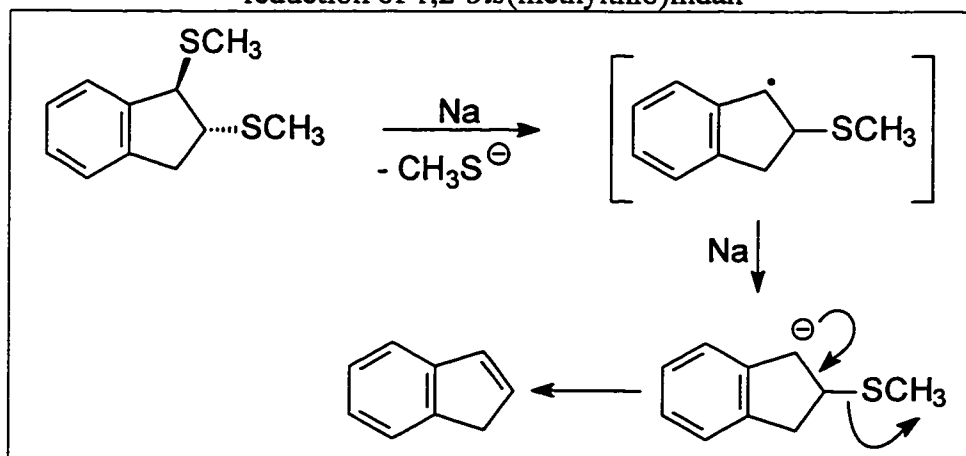
### 4.1.3 1,2-INDANDITHIOL AND 1,2-ACENAPHENEDITHIOL

Standard reductions of 1,2-*bis*(methylthio)indan were completely unsuccessful and only gave its corresponding desulfurized products (**Scheme 4-12**). After reviewing the mechanism, the reason for this became obvious very quickly. Once the electron transfer took place, fragmentation occurred at the benzylic carbon to generate the more stable radicals.

**Scheme 4-12:** Reduction of 1,2-*bis*(methylthio)indan



**Scheme 4-13:** Proposed mechanism for the formation of indene in the reduction of 1,2-*bis*(methylthio)indan





It is interesting to note that indene is a product being generated here as well. The reason for this could be that once the first fragmentation takes place, the radical is reduced once again to form a carbanion intermediate. Thiolate is then eliminated *via* an  $E_{AI}$  mechanism to form indene which may then be reduced to the indan by the slight excess of sodium present (**Scheme 4-13**).

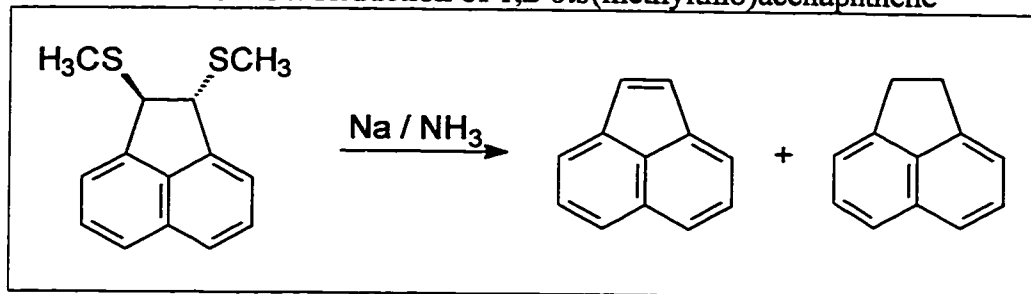
Melloni reported that when the reduction of anisole is performed in non-polar solvents such as toluene or heptane, the ratios of demethylation vs. demethoxylation were reversed.<sup>99</sup> These observations led Melloni to conclude that solvation effects play critical roles in the competition between the type of fragmentation observed: the tighter the ion pair in these solvents, the more favoured the demethoxylation.

It was hoped that a similar reversal would be observed if the reduction of 1,2-*bis*(methylthio)indan were carried out in toluene. Unfortunately, it is evident that this applies only when basicities of the resulting alkoxides (or thiolates) differ significantly, and, therefore, the difference between benzylthiolate anions and methanethiolate anions is not large enough to justify such reversal of selectivity.

**Table 4-4:** Reduction of 1,2-*bis*(methylthio)indan

Entry	Solvent	Metal	Temp. (°C)	Product Distr. (%)	
				Indene	Indan
1	NH <sub>3</sub>	Na	-33	9	91
2	Toluene	K	90	41	59
3	Heptane	K	90	18	82

The reduction of the DMDS/acenaphthylene adduct proceeded in a similar fashion yielding a mixture of both acenaphthylene and acenaphthene presumably for the same reasons as described in the case of the indene (**Scheme 4-14**).

**Scheme 4-14: Reduction of 1,2-bis(methylthio)acenaphthene**

The same results were achieved when 1,2-bis(methylthio)acenaphthylene (obtained from the dehydrogenation of the acenaphthene derivative with DDQ, **Chapter 3.2.2**) was reduced in liquid ammonia. Again, there is precedence for this type of result<sup>100</sup> and therefore one may conclude that the preparation of tetrathiafulvalenes from compounds such as acenaphthylene (and most likely indene as well) is not possible with this methodology.

## 4.2 CONCLUDING REMARKS

The preparation of 2,5-dimethyl-3,4-thiophenedithiol was successfully accomplished by the reduction of its precursor, 2,5-dimethyl-3,4-bis(methylthio)-thiophene. Given that the synthesis of this compound may be carried out very easily and in better yields through clay-catalyzed thiomethylations rather than through the more standard halogen-lithium exchange reaction, it is believed that this method is better suited to the synthesis of thiophene thiols.

The complete reduction of *tetrakis*(methylthio)thiophene was achieved only when the reaction was performed in hot HMPA although this was accompanied by substantial amounts of de-thiomethylation. It is believed that the de-thiomethylation occurs at the

earliest stages in the reaction in order to alleviate unfavourable steric interactions between neighbouring thiomethyl groups. There is some doubt to the validity of this argument because this type of side-reaction has been known only to occur when much more hindered systems have been employed. Because the synthesis of *tetrakis*(isopropylthio)thiophene has been successfully achieved (although in very small quantities, **Chapter 1.2**), it would be interesting to determine whether such a process would still occur with the bulkier yet more labile isopropyl group.

Isolation of thiophenetetrathiol itself was not possible because of the spontaneous polymerization of this compound that occurs upon acidification of the reaction mixture. Based upon studies on the autothiylation of 2-thiophenethiol, a likely explanation for this observation is that the tetrathiol tautomerizes very easily and subsequently undergoes nucleophilic attack by other polythiol molecules.

Although there was no time to properly study the polymerization process and the polymer itself, it is possible that this substance has interesting electrical properties. As was briefly mentioned in **Chapter 2.1.3**, polythiophenes are another class of organic compounds that are capable of conducting electricity, and this polymer resembles these compounds to some extent. It might be possible to control the polymerization process and then alkylate whatever thiol units remain on the polymer to produce a more soluble version of this compound. It would be interesting to determine whether this substance has, due to its heavier sulfur content, a higher conductivity than its polythiophene analogues.

The tetrathiolate itself reacts easily with alkyl halides and this led to the possibility of protecting the thiol groups in the hope of separating and purifying this

compound. Although some common protecting groups for the thiol moiety have been tried without success, it is possible that this may yet be achieved with other, more robust groups, that exist.

The reductive de-methylation of the addition products of DMDS and olefins failed to give the desired compounds. Instead, only the completely desulfurized products were observed. This is in agreement with the established mechanism which stipulates that, under these conditions, benzylic and vinylic C-S bonds will break in preference to methyl C-S bonds.

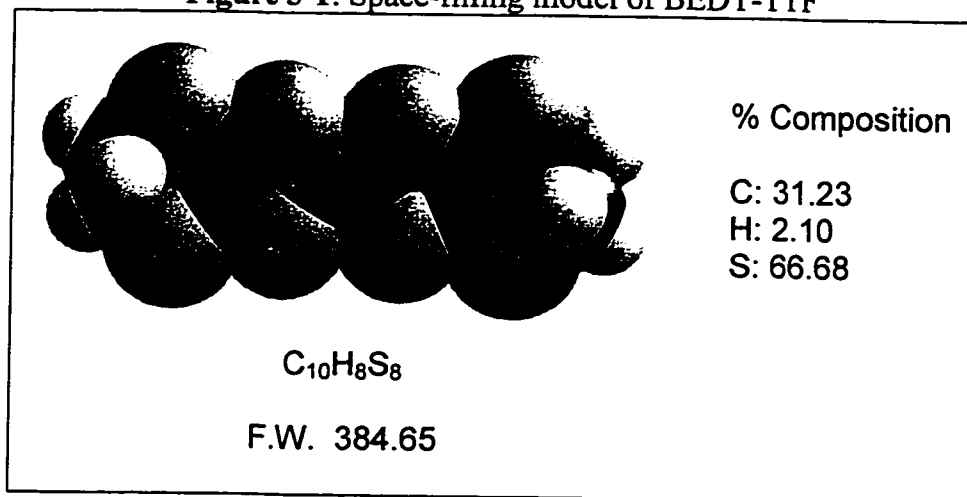
## CHAPTER 5

### SYNTHESIS OF TETRATHIAFULVALENE DERIVATIVES

#### 5.0 INTRODUCTION

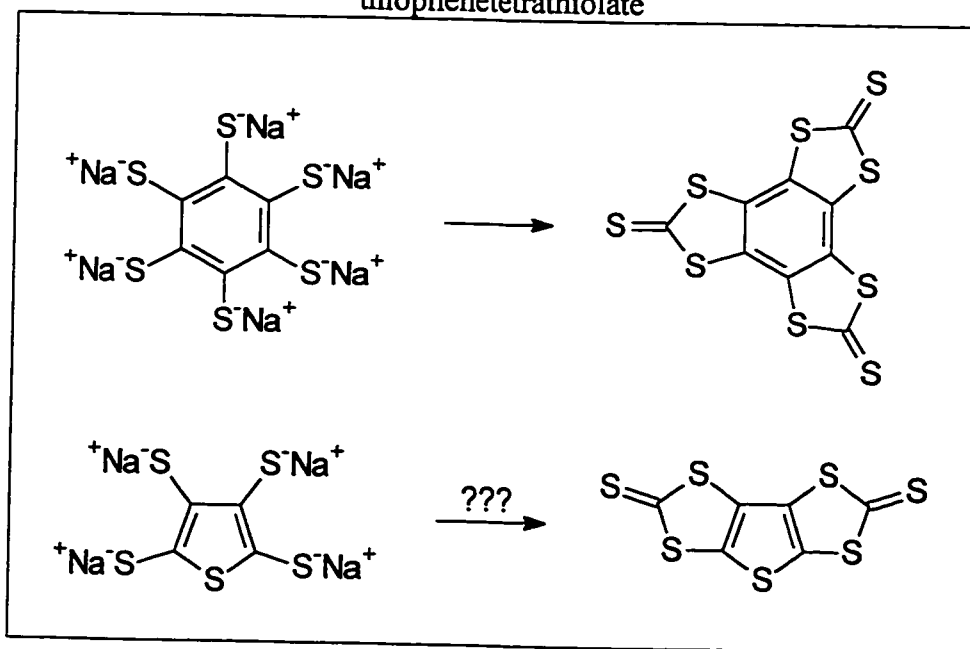
The initial goal of this project was only to investigate the clay-catalyzed thiomethylation of aromatic and olefinic compounds. Very early on, however, the question of usefulness arose. Is there a discernible need for these heavily chalcogenated compounds? Once synthesized, what could a compound such as 2,3,4,5-*tetrakis*(methylthio)thiophene be possibly used for? The answer came in the form of BEDT-TTF (**Figures 1.6 and 5.1**). This unusual molecule contains eight sulfur atoms, which makes its sulfur content close to seventy percent!

**Figure 5-1:** Space-filling model of BEDT-TTF



Further research of the literature uncovered a field of chemistry where the possibilities seemed endless. In particular, one series of studies stood out from the rest because it involved a compound that was, in some ways, very similar to the *tetrakis*(methylthio) derivative. Fanghänel's work involved a molecule with a benzene nucleus that had been exhaustively thiobenzylated in much the same way as the thiophene nucleus in the *tetrakis* compound.<sup>80,101,102,103</sup> Fanghänel reduced this compound, obtained the hexathiol, and was able to selectively introduce one, two, or three 1,3-dithiole-2-thione functionalities. Immediately, it was realized that it might be possible, if the reduction of the *tetrakis* compound could be accomplished, to prepare similar 1,3-dithiole-2-thione derivatives based on thiophene (**Figure 5-2**) and, perhaps, on the other compounds that had been thiomethylated.

**Figure 5-2:** 1,3-dithiole-2-thiones from benzenehexathiolate and thiophenetetrathiolate



## 5.1 COMPOUNDS BASED ON THIOPHENE

### 5.1.0 BACKGROUND

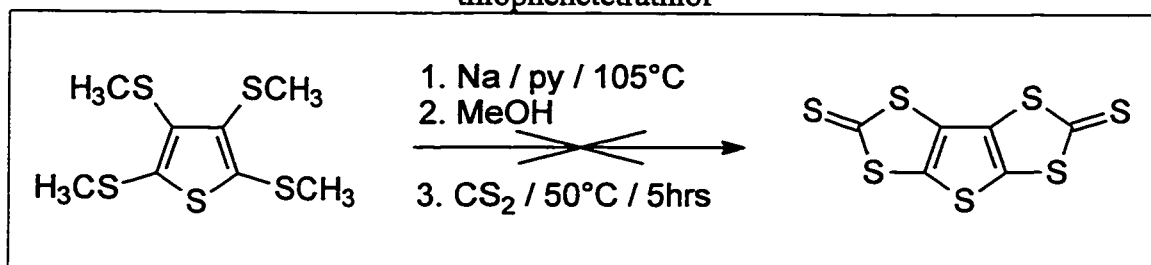
As was discussed in **Chapter 4**, the reduction of *tetrakis*(methylthio)thiophene had never been able to be carried out satisfactorily. The best results were obtained by performing the reaction in HMPA at 105°C with 8 equivalents of sodium. Even under these “optimized” conditions, the reaction failed to give the desired product exclusively. Protonation of the resulting polythiols revealed that these compounds were highly unstable, and all attempts to prepare their protected derivatives proved fruitless.

Some effort, however, was put into preparing the dithiolethione derivative directly from this reaction mixture. It was hoped that even under these unfavourable conditions, at least a small amount of the desired product could be isolated.

### 5.1.1 RESULTS

Attempts to prepare the 1,3-dithiole-2-thione derivatives directly from the reaction mixture of the reduced *tetrakis* compound were first made when pyridine was used as the solvent despite that complete demethylation had not occurred. After the reaction had taken place, the mixture was quenched with ten equivalents of methanol, and a large excess of carbon disulfide was added. This procedure was based on the one Müllen had used in his synthesis of tetrathia-s-indacenedithione (*cf.* **Scheme 4-5**). Workup of this reaction failed to give any of the desired products (**Scheme 5-1**).

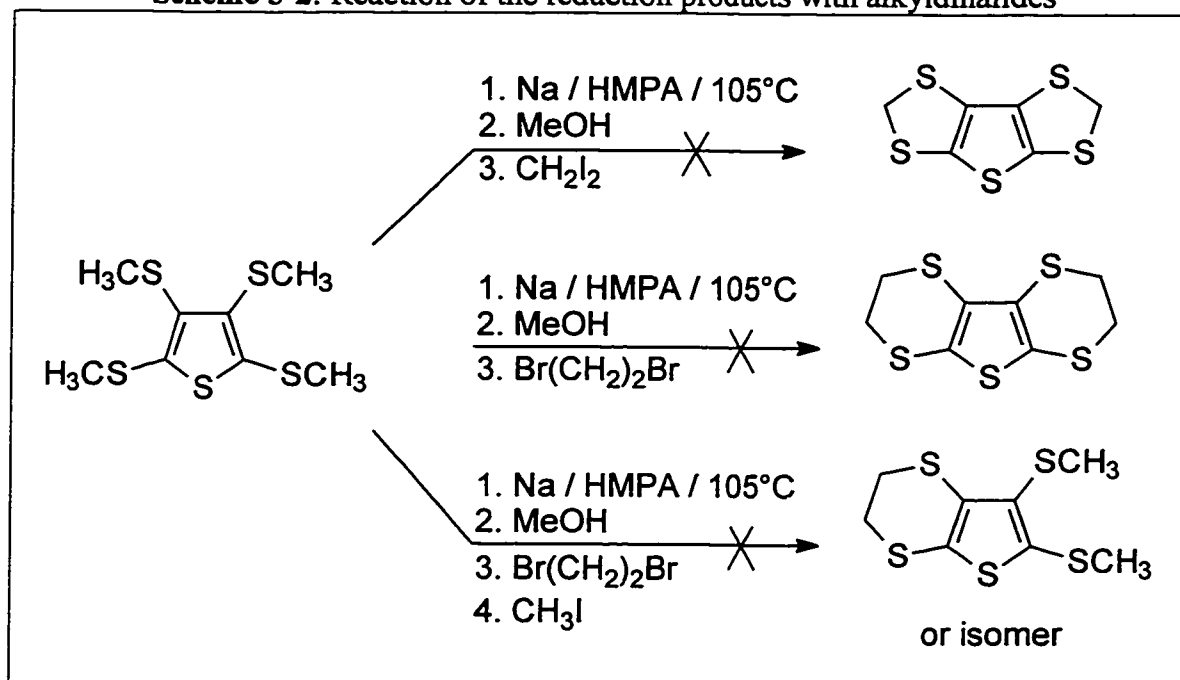
**Scheme 5-1:** Attempted synthesis of the *bis*(1,3-dithiole-2-thione) from thiophenetetrathiol



The possibility existed that this reaction failed because the first dithiole ring was forming around the sulfur atoms on carbons 3 and 4, thus preventing the formation of the second ring and making the molecule prone to polymerization. Performing a second reaction with only one equivalent of carbon disulfide and then quenching it with iodomethane quickly disproved this possibility. Once again, analysis of the crude product mixture showed only a multitude of compounds that could not be identified. At this point it became clear that the large number of different compounds produced from the reduction in pyridine were preventing the formation of the desired dithioles.

The improved results obtained when the reduction was performed in HMPA increased the likelihood that an *in situ* reaction with carbon disulfide might work. Unfortunately, this also failed. It seemed that the only compounds that react satisfactorily with the products from the reduction were iodomethane and bromoethane. It was therefore decided to react diiodomethane and 1,2-dibromoethane with the reduction products in an attempt to see whether they would form 5- and 6-membered rings around the thiophene nucleus (**Scheme 5-2**). Again, no success was achieved in preparing these compounds.



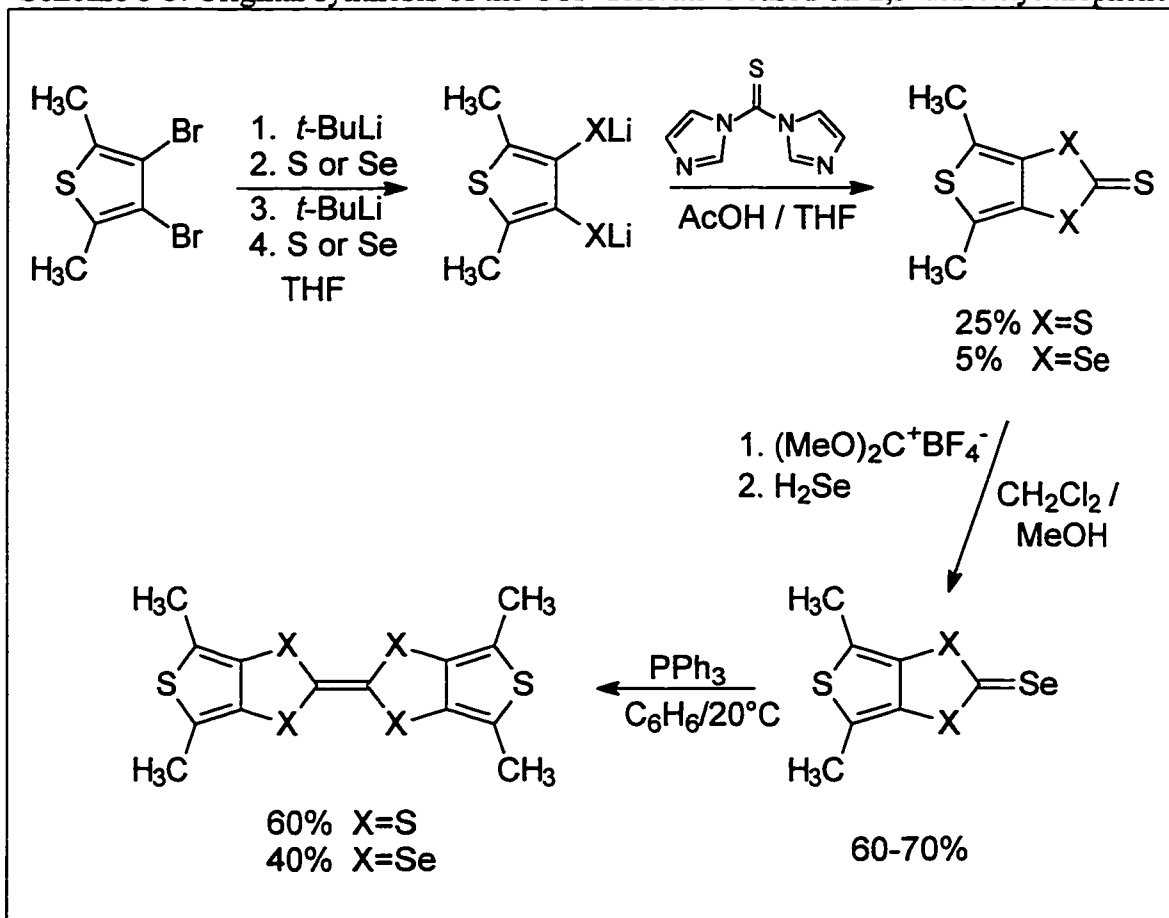
**Scheme 5-2:** Reaction of the reduction products with alkyldihalides

## 5.2 COMPOUNDS BASED ON 2,5-DIMETHYLTHIOPHENE

### 5.2.0 BACKGROUND

Although this compound has been prepared in the past, the synthesis was not very high yielding (**Scheme 5-3**).<sup>104</sup> However, one advantage that this type of approach has is that not only can sulfur be introduced into the system, but selenium and tellurium as well.

**Scheme 5-3:** Original synthesis of the TTF-derivative based on 2,5-dimethylthiophene



This scheme suffers from three drawbacks. First, although the article does not make any mention of this, 3,4-dibromo-2,5-dimethylthiophene is not a commercially available compound, and therefore one additional step must be added to the overall synthesis. Second, the use of the halogen-lithium exchange reaction in generating the thiols (or selenols) decreases the possible yield obtained dramatically. Finally, although the use of the selenone derivative permits the final coupling to occur under mild conditions and with relatively high yields, its preparation involves the use of hydrogen selenide, which is an extremely toxic gas.

The synthesis used in this study, although only applicable to the thione derivative, can boast of comparable yields, if not higher, at least in its first two steps. As was demonstrated in **Chapter 4**, the reduction of 2,5-dimethyl-3,4-*bis*(methylthio)thiophene proceeds very effectively both in liquid ammonia and in hot pyridine giving access to the dithiol much more efficiently than with existing methods.

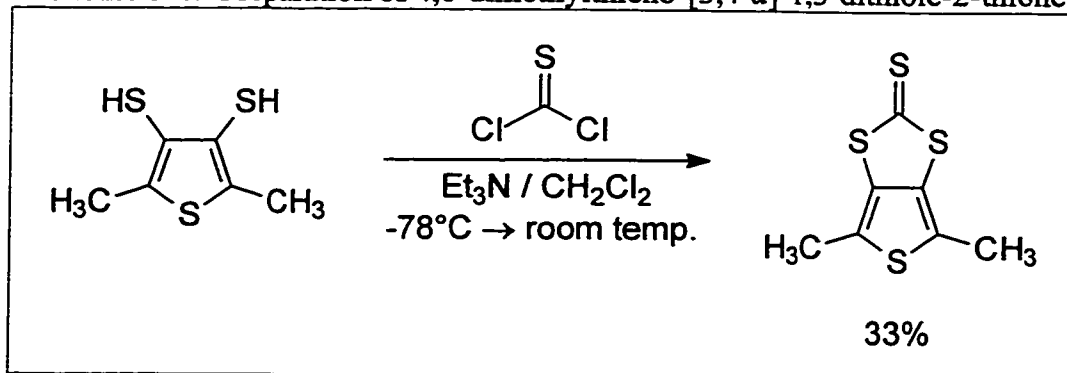
### 5.2.1 4,6-DIMETHYLTHIENO[3,4-*d*]-1,3-DITHIOLE-2-THIONE AND ITS TTF

The preparation of the 1,3-dithiole-2-thione derivative of 2,5-dimethylthiophene was fairly straightforward. Two methods were used in the preparation of this compound and both were equally successful.

In the first method, the crude dithiol (see **Chap. 4.1.1**) was dissolved in dichloromethane after which N,N-diisopropylethylamine was added. The reaction was cooled to -78°C and a thiophosgene solution was slowly added dropwise.<sup>105</sup> After

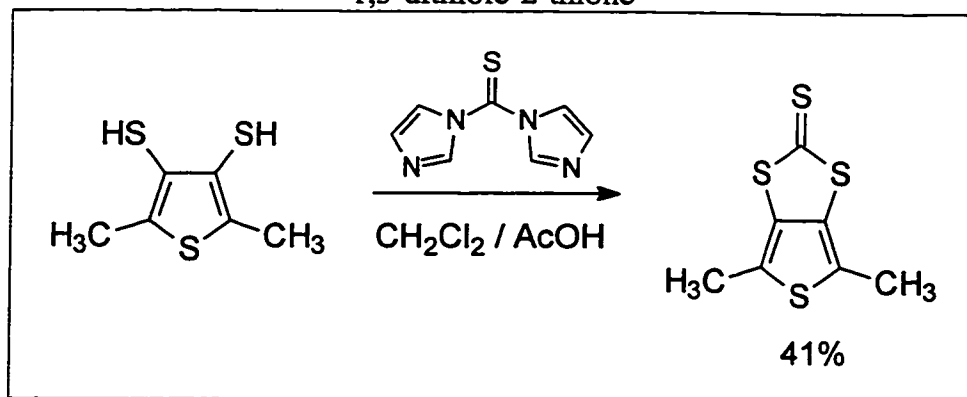
workup, the product was recrystallized from 2-propanol to give 4,6-dimethylthieno-[3,4-*d*]-1,3-dithiole-2-thione (DMT) in a 33% yield (**Scheme 5-4**).

**Scheme 5-4:** Preparation of 4,6-dimethylthieno-[3,4-*d*]-1,3-dithiole-2-thione



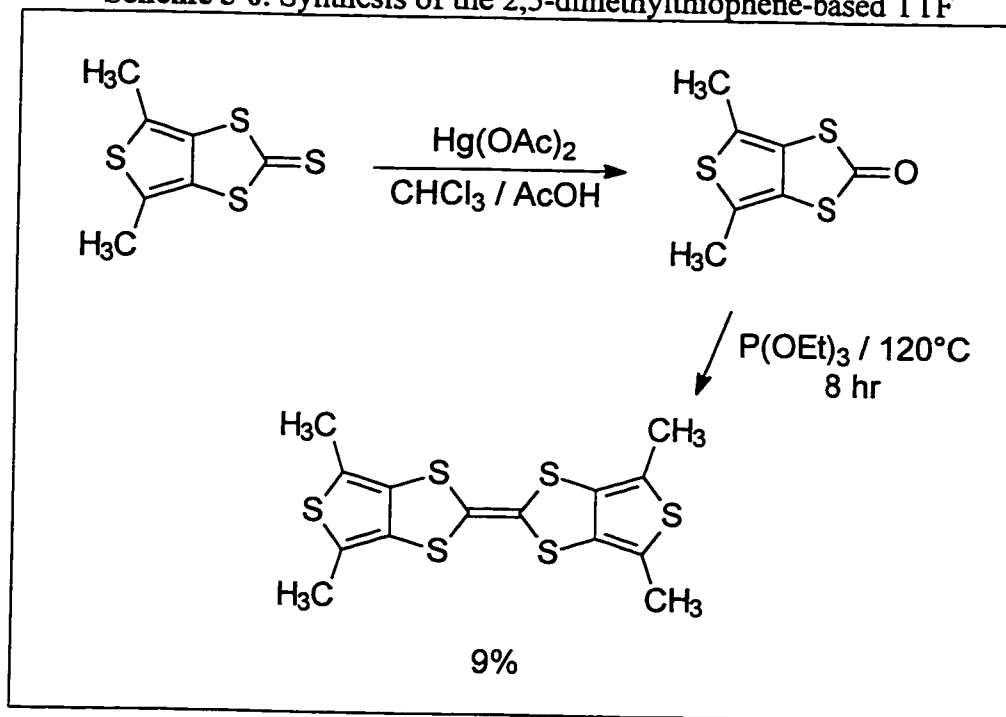
The second method is just a variation of the previous one and follows the procedure of Lestrup<sup>104</sup> and others.<sup>106,107</sup> Instead of using thiophosgene, the thiocarbonylating agent used was *N,N*-thiocarbonyl-*bis*-imidazole. The reagent was added to a solution of dichloromethane/acetic acid (10:1) and the dithiol. After stirring for 3 hours, the solution was worked up and the product was recrystallized from 2-propanol to afford a final yield of 41%.

**Scheme 5-5:** Variation in the preparation of 4,6-dimethylthieno[3,4-*d*]-1,3-dithiole-2-thione



The coupling of this compound is notoriously sluggish (as was mentioned earlier, previous syntheses required a transformation from the thione to the selenone in order to achieve the coupling in good yield). The thione derivative itself refused to undergo coupling under all conditions employed. However, after reviewing more recent work,<sup>108</sup> it was discovered that these types of reactions usually proceed somewhat more easily if a 1,3-dithiol-2-one system is used. Therefore, DMT was modified by standard methods to the corresponding carbonyl and coupling of this compound was achieved in a 9% yield.

**Scheme 5-6:** Synthesis of the 2,5-dimethylthiophene-based TTF

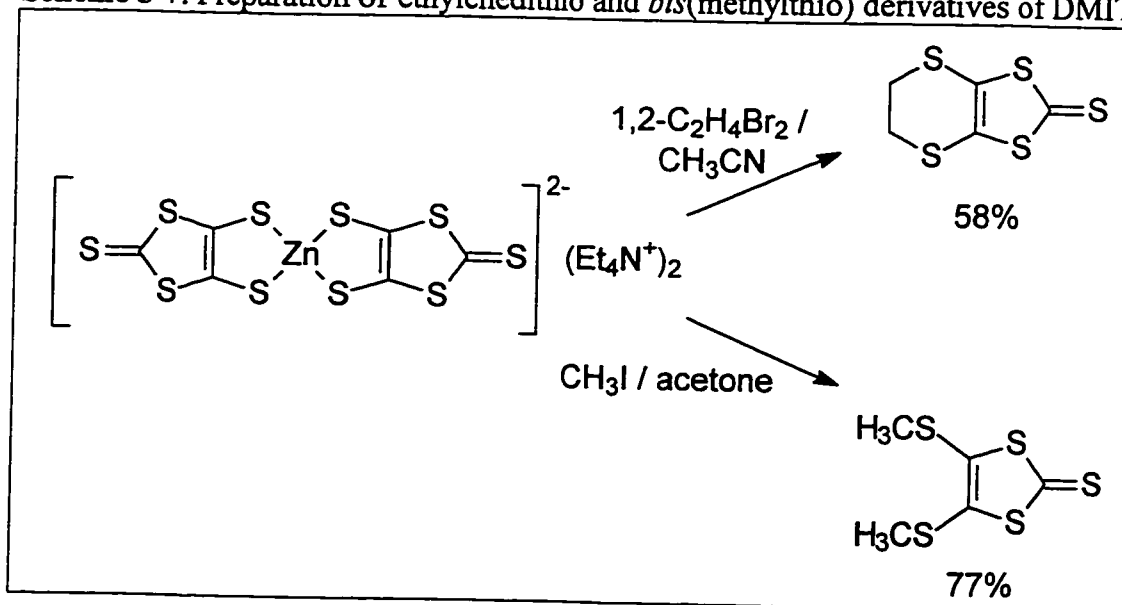


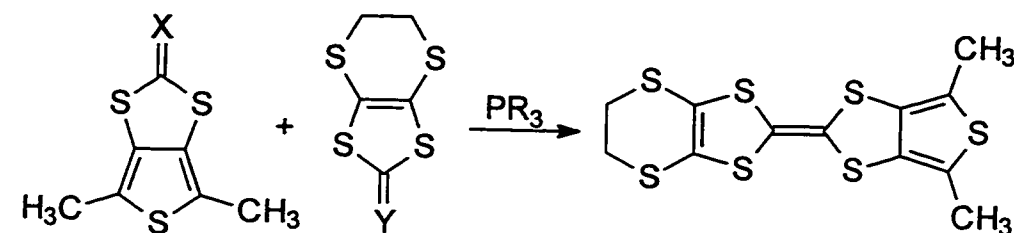
### 5.2.2 OTHER DERIVATIVES

Since the tetrathiafulvalene based on 2,5-dimethylthiophene has been synthesized previously, it was decided to prepare some mixed TTF derivatives based on this compound. For this purpose, four different reagents bearing groups that could be coupled to DMT were prepared. The first two compounds are derivatives of the zinc complex of 1,3-dithiole-2-thione-4,5-dithiolate and whose synthesis was based on literature procedures (**Chapter 1.3.1, Scheme 1-28**).<sup>50</sup>

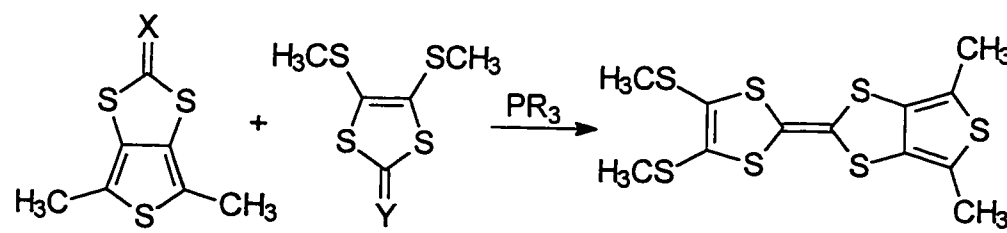
Following the preparation of  $(\text{NEt}_4)_2\text{Zn}[\text{DMIT}]_2$ , its two most common derivatives were prepared, once again, following established procedures. The synthesis of 4,5-ethylenedithio-1,3-dithiole-2-thione (or ET, although in the literature this refers to the TTF obtained from this compound) and 4,5-*bis*(methylthio)-1,3-dithiole-2-thione (BMT) is straightforward and simply involves alkylation of Zn-DMIT with the appropriate halide (**Scheme 5-7**).<sup>108</sup>

**Scheme 5-7:** Preparation of ethylenedithio and *bis*(methylthio) derivatives of DMIT



**Table 5-1:** Coupling of ET with DMT


X	Y	Conditions	% Yield
S	S	P(OMe) <sub>3</sub> , 100°C, 17 h	0
S	S	P(OEt) <sub>3</sub> , 125°C, 17 h	0
O	S	P(OEt) <sub>3</sub> , 100°C, 17 h	0
S	O	P(OMe) <sub>3</sub> , 100°C, 17 h	<1
S	O	P(OEt) <sub>3</sub> , 125°C, 90 min	13

**Table 5-2:** Coupling of BMT with DMT


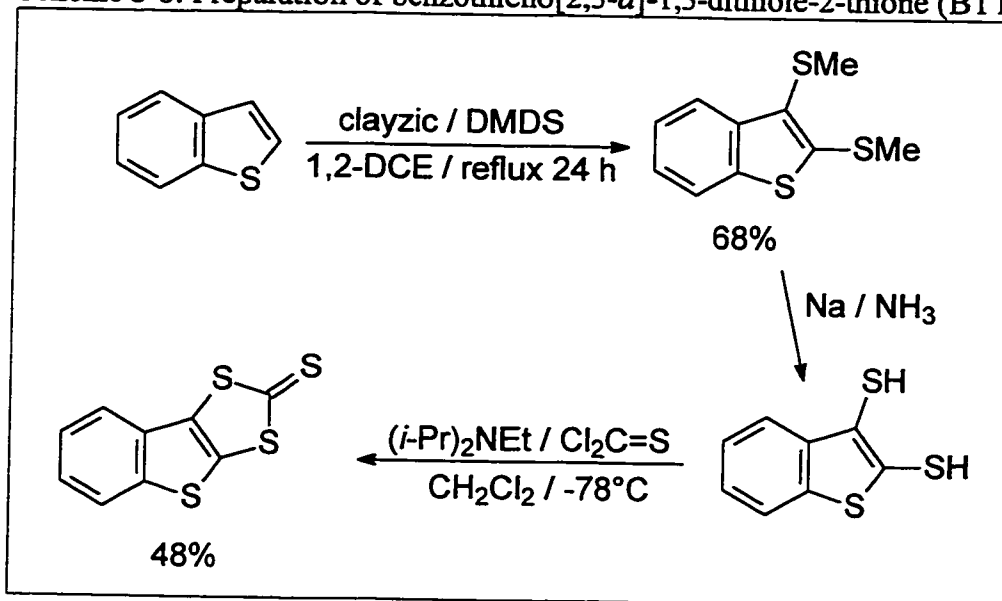
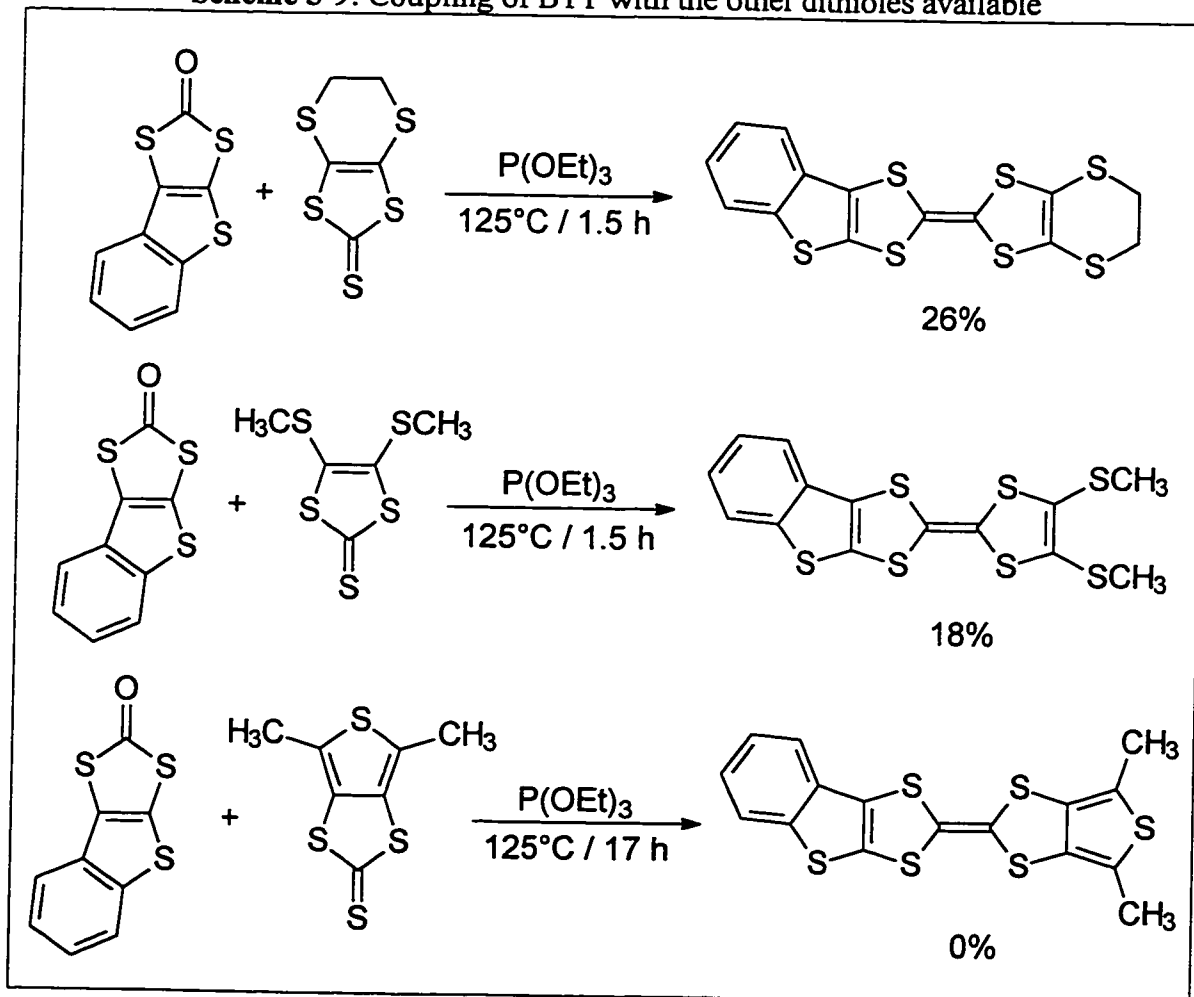
X	Y	Conditions	% Yield
S	S	P(OMe) <sub>3</sub> , 100°C, 17 h	0
S	S	P(OEt) <sub>3</sub> , 125°C, 17 h	0
O	S	P(OEt) <sub>3</sub> , 125°C, 17 h	0
S	O	P(OMe) <sub>3</sub> , 100°C, 17 h	0
S	O	P(OEt) <sub>3</sub> , 125°C, 1 h	5

Reaction of DMT with either ET or BMT in the presence of phosphite failed to give any product whatsoever. Therefore, a series of reactions with either the thiones or their oxygen analogues were performed in order to optimize reaction conditions (**Tables 5-1** and **5-2**). From these two tables, as well as from the preceding results, it is apparent that DMT is not a compound that reacts to form tetrathiafulvalenes very easily. However, as the last entries in these tables demonstrate, some product could be obtained only when the oxygen analogues of ET and BMT were reacted with the unchanged DMT.

The third compound to be used to couple with DMT was prepared by using a procedure developed by another member of our laboratories. As was mentioned at the beginning of **Chapter 2**, initial reactions with clayzic and DMDS were carried out with the test compound benzo[*b*]thiophene. The product of this reaction, 2,3-*bis*(methylthio)benzo[*b*]thiophene, may be reduced and thiocarbonylated in a similar manner as 2,5-dimethyl-3,4-*bis*(methylthio)thiophene. Therefore, a clayzic-catalyzed thiomethylation on benzo[*b*]thiophene was carried out followed by a sodium/ammonia reduction to produce 2,3-benzo[*b*]thiophenedithiol (**Scheme 5-8**). Finally, reaction with thiophosgene yielded benzothieno[2,3-*d*]-1,3-dithiole-2-thione (BTT) in good yield.

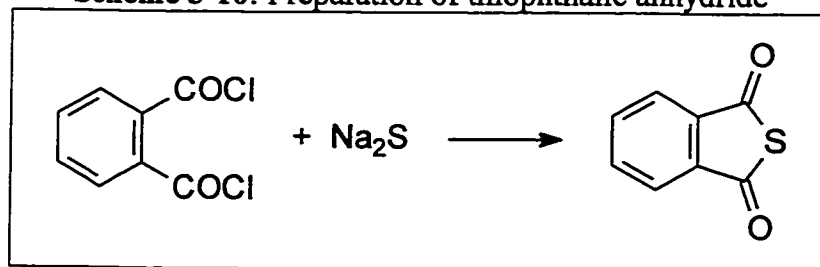
Coupling reactions of this compound with ET, BMT and DMT were performed using the same type of approach as above and once again could only be achieved with the oxygen analogue of BTT (**Scheme 5-9**). The yields with ET and BMT were fairly good for this type of reaction, but, once again, DMT has shown its reluctance to under all conditions employed.



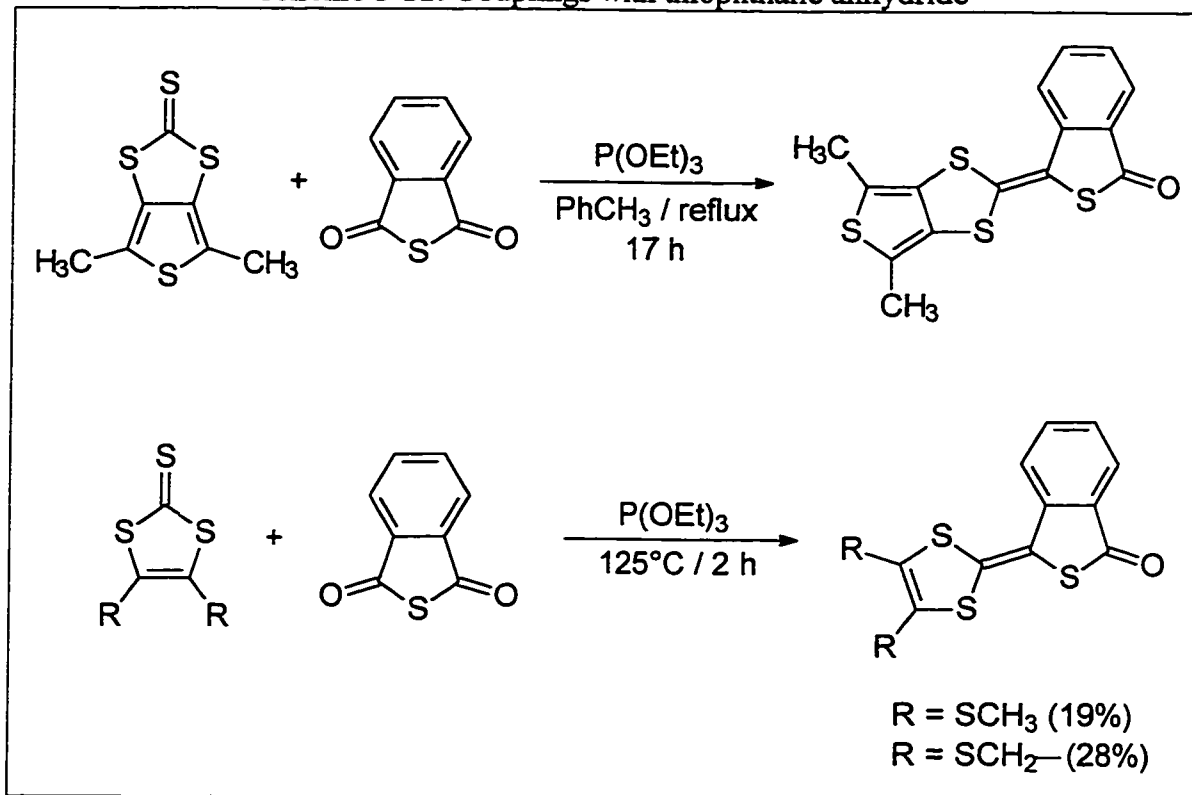
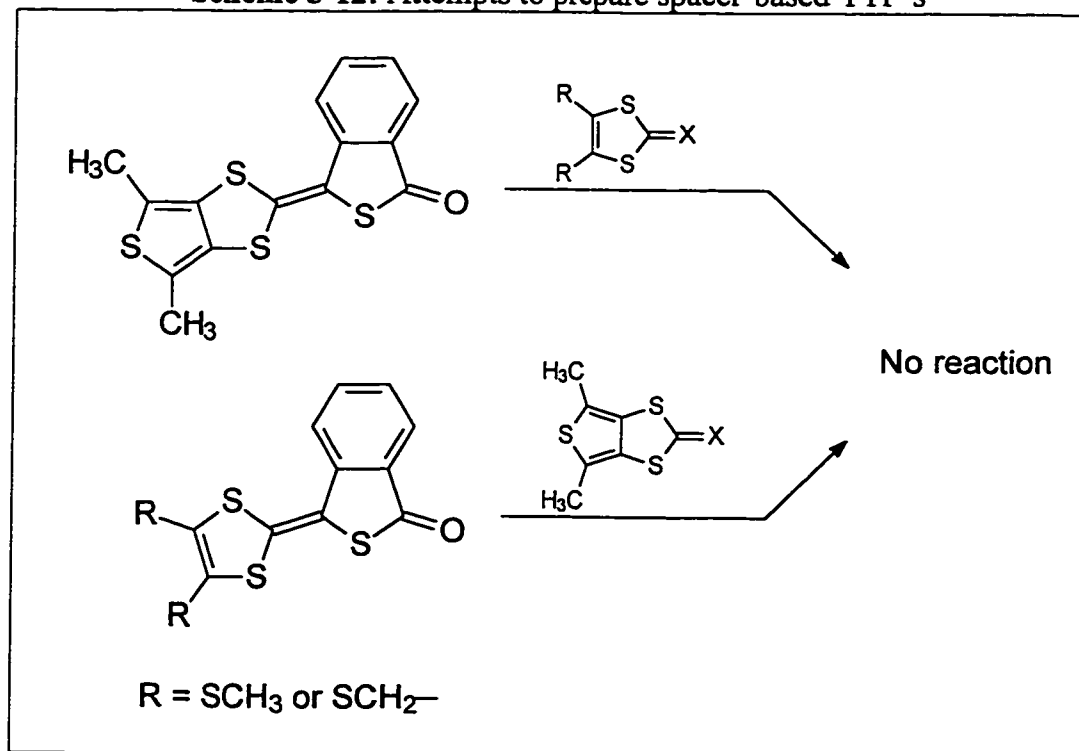
**Scheme 5-8:** Preparation of benzothieno[2,3-*d*]-1,3-dithiole-2-thione (BTT)**Scheme 5-9:** Coupling of BTT with the other dithioles available

The fourth compound prepared was not a 1,3-dithiole-2-thione derivative. Instead, it was a benzo[*c*]thiophene derivative that was to be used as a spacer between the various dithiole rings. It was prepared following an old literature procedure by reacting phthaloyl chloride with sodium sulfide (Scheme 5-10).<sup>109</sup> Since ET and BMT tetrathiafulvalenes based on this compound are known, it was decided to prepare some mixed TTF's containing one of these molecules at one end and DMT at the other.

**Scheme 5-10:** Preparation of thiophthalic anhydride



The first part of the coupling proceeded fairly smoothly both with DMT as well as ET and BMT (Scheme 5-11). However, because these products were highly insoluble and because they were unstable, it was not possible to fully characterize them. In addition to this, all reactions to couple these compounds to obtain the TTF derivatives failed no matter what conditions were tried or in what compounds were coupled (Scheme 5-12).

**Scheme 5-11: Couplings with thiophthalic anhydride****Scheme 5-12: Attempts to prepare spacer-based TTF's**

### 5.3 CONCLUDING REMARKS

For the moment, the only tetrathiafulvalenes that have been successfully synthesized from compounds generated by clay-catalyzed thiomethylations were based on 2,5-dimethylthiophene and benzo[*b*]thiophene. It is hoped, however, that this methodology may be used to prepare a wider range of TTFs especially if it can be adapted to be used with alkenes.

TTFs based on 2,5-dimethylthiophene have shown themselves to be fairly difficult to prepare. Since systems based on 1,3-dithioles bearing electron-withdrawing groups, such as the easily removable carboxylic acid derivatives, have been shown to undergo phosphite-mediated coupling fairly easily, these compounds may be used to prepare a larger variety of TTFs more easily and in larger yields.

## CHAPTER 6

### EXPERIMENTAL SECTION

#### 6.0 GENERAL COMMENTS

All organic reagents were purchased from the Aldrich Chemical Company and were used without further purification unless stated otherwise. Solvents were dried and purified according to standard procedures. Acenaphthylene was repeatedly recrystallized from hexane to remove any acenaphthene. Indene was fractionally distilled prior to use. Dimethyldisulfide was purchased from Aldrich, washed with 1M aqueous HCl to remove trace amines, and was distilled prior to use. Montmorillonite K10 was purchased from the Fluka Chemical Company and used without further purification.  $K_2CO_3$ ,  $CuCl_2$ ,  $ZnCl_2$  and  $MnCl_2 \cdot 4H_2O$  were purchased from BDH and were used without further purification. IR spectra were obtained on a Mattson 4030 galaxy series FT-IR spectrometer. Spectra of compounds with low melting points were obtained from molten films of these compounds supported on KBr plates. NMR spectra were obtained on a Bruker ACE200 or AM400 spectrometers. Chemical shifts are reported in parts per million (ppm) internally referenced to TMS. Mass spectra were obtained on a Hewlett Packard HP5890. Melting points were taken on a Fisher-Johns melting point apparatus and are uncorrected. Kgelrohr distillations were performed in a Bchi GKR-51 apparatus. Elemental analyses were obtained by the Canadian Microanalytical Service,

Ltd. and by D. Fox on a Control Equipment Corporation 440 EA, in the Analytical Service Laboratories of the Department of Chemistry at the University of Calgary.

#### *Preparation of the clayzic catalyst*

In a 3L round bottomed flask equipped with a mechanical stirrer, montmorillonite K10 (300 g) was added to a solution of  $\text{ZnCl}_2$  (81.6 g, 2 mmol/g of K10) in methanol (1 L). The mixture was stirred overnight and the solvent was removed by rotary-evaporation. The residue was crushed to a fine powder in a large mortar and returned to the rotary evaporator to remove any remaining traces of solvent. Once the catalyst had been thoroughly dried, it was placed in a 150°C vacuum oven to activate overnight and was stored in a polyethylene bottle after cooling. Prior to every reaction, the appropriate amount of catalyst was weighed out, returned to the oven for 2 h, and cooled in a vacuum dessicator over  $\text{P}_2\text{O}_5$ .

#### *Preparation of other clay catalysts*

The same procedure described for the preparation of clayzic was used in the preparation of K10/ $\text{CuCl}_2$ , K10/ $\text{K}_2\text{CO}_3$ , and clayman. In the case of K10/ $\text{K}_2\text{CO}_3$ , it was found that a 1:1 water/methanol mixture had to be used instead of pure methanol in order to dissolve the salt.

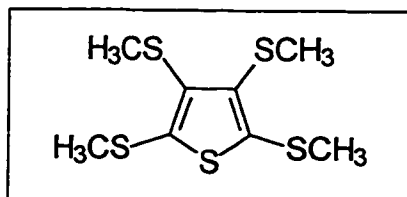
## 6.1 REACTIONS PERTAINING TO CHAPTER 2

### 6.1.1 REACTIONS UNDER HIGH AIR PRESSURE

The reagents were placed in a 300 mL capacity autoclave equipped with a MagneDrive® II drive assembly and fitted with an internal cooling coil, thermocouple, and pressure gauge (see **Figure 2-3**). The system was sealed and pressure tested with air to 1000 psi (6900 KPa). If no leaks were detected, the pressure was adjusted to attain a quantity of oxygen sufficient to oxidize any thiols produced in the course of the experiment (*i.e.* one mole of oxygen for every four moles of thiol produced). After the autoclave had been heated to the desired conditions, cooling of the system was accelerated by passing water through the internal cooling coil. After a slow depressurization, the contents of the autoclave were filtered through a fine frit and the clay was washed with toluene until the washings were practically colourless. The solvents and excess DMDS were removed on a rotary evaporator equipped with an activated carbon trap to contain odours.

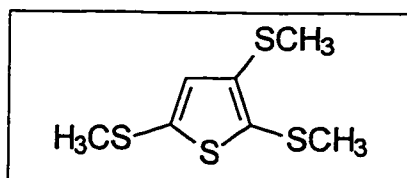
After removal of the solvent, the crude mixture was purified by Kgelrohr distillation and was recrystallized from hexanes or ethanol. The resulting product is usually contaminated with minute traces of methylpolysulfides, which give the products a strong and repulsive odour. If it is so desired, these impurities may be removed by treatment with zinc dust in a methanolic HCl solution

*2,3,4,5-Tetrakis(methylthio)thiophene.*



Kügelrohr distillation of the product mixture from the reaction of thiophene (5 mL, 62.5 mmol) with DMDS (8 eq) gave 9.5 g of crude *tetrakis* product. After purification and recrystallization from ethanol or hexanes, the product was obtained as white needles (7.96 g, 47.5%); m.p. 34-35°C (EtOH); b.p. 105°C/0.01 mm Hg; IR (neat) 2983, 2917, 1430  $\text{cm}^{-1}$ ;  $\delta_{\text{H}}$  (200 MHz) 2.52 (s, 6H), and 2.42 (s, 6H);  $\delta_{\text{C}}$  (50 MHz) 19.2 ( $\text{CH}_3$ ), 19.6 ( $\text{CH}_3$ ), 136.4 (qt.), and 140.8 (qt.);  $m/z$  268 ( $\text{M}^+$ , 100%); Analysis calculated for  $\text{C}_8\text{H}_{12}\text{S}_5$ : C 35.79%, H 4.51%; Found: C 35.48%, H 4.53%.

*2,3,5-Tris(methylthio)thiophene.*

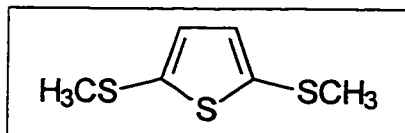


Kügelrohr distillation of the product mixture from the reaction of thiophene (5 mL, 62.5 mmol) with DMDS (0.5 eq) gave 0.68 g (4.9%) of the *tris* product. Spectral and physical data were identical to those described by Gronowitz.<sup>110</sup> B.p. 90°C at 0.01 mmHg (lit. 113-114°C/0.2 mm Hg); IR (neat) 2985, 2916, 1430  $\text{cm}^{-1}$ ;  $\delta_{\text{H}}$  (200 MHz) 6.90



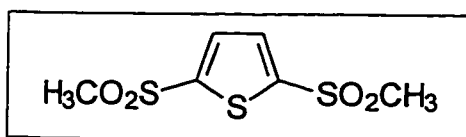
(s, 1H), 2.49 (s, 3H), 2.46 (s, 3H), 2.45 (s, 3H);  $\delta_{\text{C}}$  (50 MHz) 138.4 (qt.), 137.0 (qt.), 131.3 (CH), 115.8 (qt.), 20.4 (CH<sub>3</sub>), 21.4 (CH<sub>3</sub>), 17.6 (CH<sub>3</sub>);  $m/z$  222 ( $M^+$ , 100%).

*2,5-Bis(methylthio)thiophene.*



Kügelrohr distillation of the product mixture from the reaction of thiophene (5 mL, 62.5 mmol) with DMDS (0.5 eq) gave 0.41 g (3.7%) of the *bis* product. Spectral and physical data were identical to those reported by Gronowitz. B.p. 60°C at 0.01 mmHg (lit.<sup>110</sup> 59-61°C/0.15 mm Hg);  $\delta_{\text{H}}$  (200 MHz) 6.87 (s, 2H), 2.47 (s, 6H);  $m/z$  176 ( $M^+$ , 100%).

*2,5-Bis(methanesulfonyl)thiophene*



A solution of potassium permanganate (1.74 g, 10.96 mmol) in water (50 mL) was added to a solution of 2,5-*bis*(methylthio)thiophene (0.484 g, 2.7 mmol), benzoic acid (0.33 g, 2.74 mmol), tetraethylammonium chloride (0.07 g, 0.43 mmol) in dichloromethane (25 mL) and the reaction mixture was stirred vigorously for 4 h.

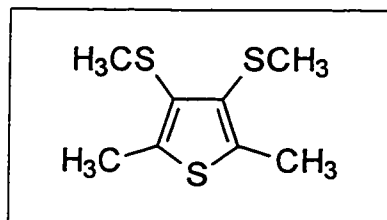
Aqueous concentrated sodium metabisulfite solution was added until the mixture attained an almost white colour. The resultant mixture was filtered through a celite pad and the organic layer was washed with 1 M aqueous hydrazine hydrochloride solution (1×20 mL), 2 M sodium bicarbonate solution (1×20 mL) and brine (1×20 mL). After drying of the organic phase over  $\text{MgSO}_4$  and evaporation of the solvent, a white solid was obtained which was recrystallized from ethanol to yield the product as white prisms (0.56 g, 85%); m.p. 168-171° (lit. 174-175°C); IR (KBr) 3018, 2929, 2365, 1314, 1136, 1041, 958, and 762  $\text{cm}^{-1}$ ;  $\delta_{\text{H}}$  (200 MHz) 7.86 (s, 2H) and 3.38 (s, 6H);  $\delta_{\text{C}}$  (50 MHz) 148.9 (qt.), 134.0 (CH), and 45.9 ( $\text{CH}_3$ );  $m/z$  240 ( $\text{M}^+$ , 100); Analysis calculated for  $\text{C}_6\text{H}_8\text{O}_4\text{S}_3$ : C 29.99%, H 3.36%; Found: C 29.57, H 3.73%.

## 6.1.2 REACTIONS AT ATMOSPHERIC PRESSURE

### *Reactions with Thiophene*

In a typical experiment, thiophene (5 mL, 62 mmol) was added to a 250 mL round bottomed flask equipped with a condenser and containing a refluxing mixture of clayzic (20 g, 31 mmol  $\text{ZnCl}_2$ ), DMDS (45 mL, 0.5 mol), and chlorobenzene (100 mL). Yields and other conditions employed are described in **Tables 2-1, 2-2, and 2-4**. After the appropriate time had elapsed, the mixture was filtered and the products were isolated in a similar manner as described in the previous section (**Chapter 6.1.1**).

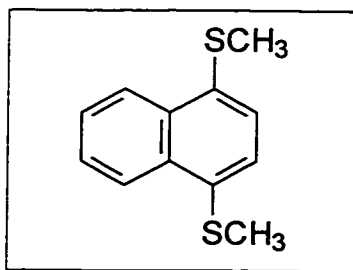
#### *2,5-Dimethyl-3,4-bis(methylthio)thiophene.*



A solution consisting of 2,5-dimethylthiophene (7.1 mL, 62.5 mmol) in chlorobenzene (20 mL) was added dropwise over 30 minutes to a refluxing mixture of clayzic (20 g) and DMDS (23 mL, 0.25 mol) in chlorobenzene (80 mL). After refluxing for 2 days, the mixture was cooled, filtered through a fine frit and the clay was washed with toluene. After removal of the solvents and excess DMDS, Kugelrohr distillation of the crude product gave a clear oil (7.53 g 58.9%); b.p. 60°C at 0.01 mmHg; IR (neat) 2983, 2916, 1513, 1435, 1420  $\text{cm}^{-1}$ ;  $\delta_{\text{H}}$  (200 MHz) 2.50 (s, 6H), 2.26 (s, 6H);  $\delta_{\text{C}}$  (50

MHz) 138.5 (qt), 133.9 (qt), 20.1 (CH<sub>3</sub>), 14.7 (CH<sub>3</sub>);  $m/z$  204 ( $M^+$ , 100); Analysis calculated for C<sub>8</sub>H<sub>12</sub>S<sub>3</sub>: C 47.02%, H 5.92 %; Found: C 47.01%, H 5.84%

*1,4-Bis(methylthio)naphthalene.*



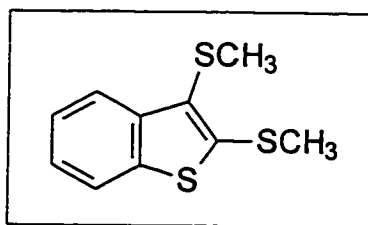
*Preparation in the presence of clayzic*

Naphthalene (3.20 g, 25 mmol) was added to a mixture of clayzic (18 g) and DMDS (13.5 mL, 0.15 mol). After refluxing for 2 days, the mixture was filtered and the solvents removed by rotary evaporator. Sublimation of the product yielded a cream-coloured solid (1.13 g, 20.5%) whose spectral characteristics were identical to those reported previously.<sup>111</sup> M.p. 78-81°C (lit. 94-95°C [AcOH]); IR (neat) 3054, 2980, 2915, 1584, 1488 cm<sup>-1</sup>;  $\delta_H$  (200 MHz) 8.32 (dd, 2H), 7.57 (dd, 2H), 7.35 (s, 2H), and 2.53 (s, 6H);  $\delta_C$  (50 MHz) 133.8 (qt.), 132.1 (qt.), 126.5 (CH), 125.1 (CH), 124.6 (CH), 16.7 (CH<sub>3</sub>);  $m/z$  220 ( $M^+$ , 100%)

*Preparation in the presence of clayman:*

The conditions used were identical to the ones described above with the exception that 15.6 g of clayman were used as the catalyst. Sublimation of the crude gave 3.57 g (64%) of a product whose spectral and physical data were identical to the ones above.

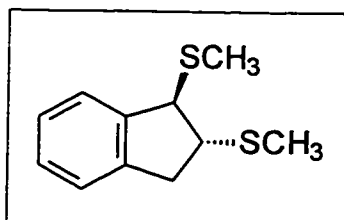
*2,3-Bis(methylthio)benzo[b]thiophene*



Benzo[b]thiophene (2.00 g, 14.9 mmol) was added to a mixture consisting of 20 g of clayzic, DMDS (13.5 mL, 0.15 mol), and 1,2-dichloroethane (100 mL). After refluxing for 17 h, the reaction mixture was cooled, filtered, and the clay was washed with dichloromethane (5×20 mL). After removal of the solvent and any excess DMDS *in vacuo*, the product was dissolved in hexane and the solution was filtered once again to remove any zinc chloride or its complex with *bis*(methylthio)ethane. Kugelrohr distillation of the crude gave the product as a clear oil (2.31 g, 68%); b.p. 110°C/0.10 mm Hg; IR (neat) 3053, 2986, 2917, 1465, 1416 cm<sup>-1</sup>;  $\delta_{\text{H}}$  (200 MHz) 7.88 (dd, 1H), 7.75 (dd, 1H), 7.41 (m, 1H), 7.32 (m, 1H), 2.66 (s, 3H), 2.37 (s, 3H);  $\delta_{\text{C}}$  (50 MHz) 145.1 (qt.), 140.7 (qt.), 138.6 (qt.), 124.9 (CH), 124.7 (qt.), 124.0 (CH), 122.1 (CH), 121.9 (CH), 18.4 (CH<sub>3</sub>), 18.1 (CH<sub>3</sub>);  $m/z$  226 (M<sup>+</sup>, 87%).

## 2.2 REACTIONS PERTAINING TO CHAPTER 3

### *Trans-1,2-bis(methylthio)indan*



### *Preparation in the presence of clayzic*

To a well stirred mixture of clayzic (15.92 g), DMDS (2.25 mL, 25 mmol), and 1,2-dichloroethane (35 mL), a solution of indene (2.92 mL, 25 mmol) in 1,2-dichloroethane (15 mL) was added dropwise over 15 minutes. After stirring for 3 hours, the mixture was filtered and the clay washed with dichloromethane (5×50 mL). After removal of the solvent, a white solid precipitated from the oily residue. The solid was filtered and washed with hexane to yield 0.218 g of a complex.

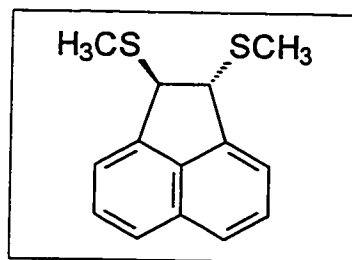
The hexane washings were combined and extracted with an EDTA solution (2×100 mL), water (1×100 mL), dried over  $\text{MgSO}_4$ , and after removal of the solvent, 3.51 g of crude product were isolated. High-vacuum distillation gave the product as a clear oil (2.14 g, 41%); b.p. 106°C at 0.01 mmHg; IR (neat) 3068, 3022, 2973, 2913, 2831, 1604, 1474, 1433  $\text{cm}^{-1}$ ;  $\delta_{\text{H}}$  (400 MHz) 7.36 (m, 1H), 7.21 (m, 3H), 4.21 (d, 1H), 3.50 (m, 2H), 2.93 (m, 1H), 2.19 (s, 3H), 2.06 (s, 3H);  $\delta_{\text{C}}$  (50 MHz) 141.4 (qt.) 141.0 (qt.), 127.9 (CH), 127.1 (CH), 125.2 (CH), 124.6 (CH), 56.3 (CH), 51.3 (CH), 38.6

(CH<sub>2</sub>), 14.5 (CH<sub>3</sub>) 13.6 (CH<sub>3</sub>);  $m/z$  210 ( $M^+$ , 100%); Analysis calculated for C<sub>11</sub>H<sub>14</sub>S<sub>2</sub>: C 62.81%, H 6.71%; Found: C 63.12% H: 6.82%

*Preparation in the presence of K10*

Indene (10.1 mL, 0.10 mol) was dissolved in 1,2-dichloroethane (20 mL) and the resulting solution was added dropwise to a well-stirred mixture of K10 (10 g), DMDS (36.0 mL, 0.40 mol) and 1,2-dichloroethane (60 mL). After stirring at room temperature for four days, the mixture was filtered and the clay was washed with dichloromethane (5×100 mL). After removal of the solvent and Kugelrohr distillation of the crude, 13.07 g (62.1%) of 1,2-*bis*(methylthio)indan were isolated. The spectral and physical data of this compound were identical to the ones obtained in the previous experiment.

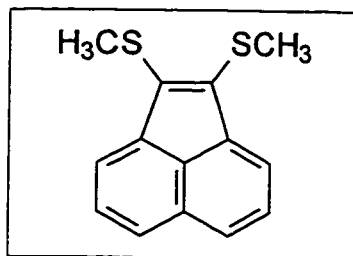
*Trans-1,2-bis(methylthio)acenaphthene.*



Acenaphthylene (3.81 g, 25 mmol) was added to a well-stirred mixture of clayzic (15.9 g) and DMDS (2.25 mL, 25 mmol) in 1,2-dichloroethane (50 mL). The reaction mixture was stirred overnight, was filtered and was washed with dichloromethane. After removal of the solvent, the crude product was re-dissolved in hexanes and the solution

was separated from a tar-like residue and placed in a  $-20^{\circ}\text{C}$  freezer to recrystallize overnight. 3.41 g (55%) of 1,2-*bis*(methylthio)-acenaphthene were isolated as pale yellow needles. The product was purified by flash chromatography (30%  $\text{CH}_2\text{Cl}_2$ /hexanes). M.p.  $61\text{--}62^{\circ}\text{C}$ ; IR (neat) 3043, 2975, 2913, 2828, 1601, 1493, 1424,  $1360\text{ cm}^{-1}$ ;  $\delta_{\text{H}}$  (200 MHz) 7.75 (d, 2H), 7.57 (m, 4H), 4.75 (s, 2H), 2.00 (s, 6H);  $\delta_{\text{C}}$  (50 MHz) 141.7 (qt.), 137.2 (qt.), 130.8 (qt.), 128.2 (CH), 124.0 (CH), 121.4 (CH), 55.9 (CH), 12.5 ( $\text{CH}_3$ );  $m/z$  246 ( $\text{M}^+$ , 10%); Analysis calculated for  $\text{C}_{14}\text{H}_{14}\text{S}_2$ : C 68.25%, H 5.73%; Found: C 68.51%, H 5.94%

*1,2-bis(methylthio)acenaphthylene*

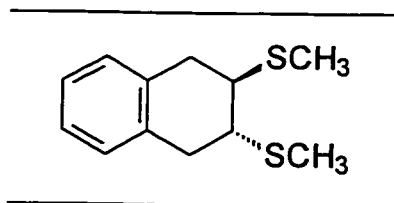


The sulfide (0.670 g, 2.72 mmol) was refluxed with DDQ (0.925 g, 4.08 eq) in toluene (5 mL) for 2 hours. After cooling, hexane was added (50 mL) and the reaction mixture was filtered. After removal of the solvent by rotary-evaporation from the filtrate, the remaining solid was purified by flash chromatography (30%  $\text{CH}_2\text{Cl}_2$ /hexane) to afford the product (0.439 g, 66%) as deep red solid; m.p.  $57\text{--}58^{\circ}\text{C}$ ; IR (neat) 3060, 3039, 2919, 1619,  $1427\text{ cm}^{-1}$ ;  $\delta_{\text{H}}$  (200 MHz) 7.79 (m, 4H), 7.56 (dd, 2H), 2.68 (s, 6H);  $\delta_{\text{C}}$  (50 MHz) 139.2 (qt.), 137.9 (qt.), 127.9 (qt.), 127.8 (qt.), 127.7 (CH), 127.4 (CH) 122.2



(CH), 18.3 (CH<sub>3</sub>);  $m/z$  244 ( $M^+$ , 100%); Analysis calculated for C<sub>14</sub>H<sub>12</sub>S<sub>2</sub>: C 68.81%, H 4.95%; Found: C 68.89%, H 5.03%

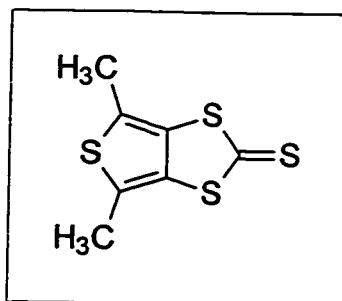
*Trans-2,3-bis(methylthio)-1,2,3,4-tetrahydronaphthalene.*



Clayzic (20 g) was added to a solution of 1,4-dihydronaphthalene (4.00 g, 30.7 mmol) and DMDS (5.7 mL, 63 mmol) in 1,2-dichloroethane (100 mL). The mixture was stirred at room temperature overnight, was filtered and the clay was washed with dichloroethane. After the solvents were removed by rotary evaporation, hexane was added to the residue and a white solid precipitated out immediately. The solid was filtered and washed with more hexane. 1.03 g (9.1%) of the ZnCl<sub>2</sub> complex was isolated. After evaporation of the hexane washings, the residue was distilled to give the product (3.00 g, 43.6%) as a white solid; m.p. 39-40°C; b.p. 140°C at 0.01 mm Hg; IR (KBr) 3022, 2916, 1581, 1494;  $\delta_H$  (200 MHz) 7.09 (m, 4H), 3.36 (m, 2H), 3.12 (m, 2H), 2.90 (m, 2H), 2.16 (s, 6H);  $\delta_C$  (50 MHz) 134.5 (qt.), 128.9 (CH), 126.3 (CH), 45.9 (CH), 34.0 (CH<sub>2</sub>), 13.9 (CH<sub>3</sub>);  $m/z$  224 ( $M^+$ , 100%); Analysis calculated for C<sub>12</sub>H<sub>16</sub>S<sub>2</sub>: C 64.24%, H 7.19%; Found: C 64.50%, H 7.33%

### 6.3 REACTIONS PERTAINING TO CHAPTERS 4 AND 5

#### *4,6-Dimethylthieno[3,4-d]-1,3-dithiole-2-thione*



*Method 1.* Liquid ammonia (200 mL) and 2,5-dimethyl-3,4-bis(methylthio)-thiophene (2.01 g, 9.83 mmol) were added to a 500 mL, flame-dried round-bottomed flask cooled to  $-40^{\circ}\text{C}$ . Sodium metal (0.904 g, 39.3 mmol) was cut into small pieces and was added to the ammonia mixture over 30 minutes. Stirring under nitrogen was continued until all the ammonia evaporated at which time the residue in the flask was dissolved in water (50 mL). The aqueous solution was washed with dichloromethane (2×50 mL) and then 2M HCl was added until the solution was acidic to litmus. The resulting emulsion was extracted with ether (4×20 mL) and the ether extracts were washed with brine (1×50 mL) and dried over  $\text{MgSO}_4$ . After removal of the solvent, 1.40 g of a foul-smelling oil were isolated (80.8% crude yield). GC-MS analysis resulted in a single-peaked chromatogram whose molecular ion had the correct mass to charge ratio for 2,5-dimethyl-3,4-thiophenedithiol.

The crude dithiol (1.40 g, 7.93 mmol) was dissolved in dichloromethane (100 mL) and the resulting solution was stirred vigorously under nitrogen for one hour.

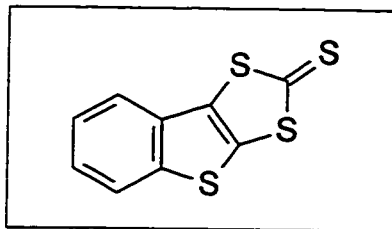
Diisopropylethylamine (1.02 g, 23.8 mmol) was added and the solution cooled to  $-78^{\circ}\text{C}$ . Thiophosgene (0.913 g, 7.94 mmol) was dissolved in dichloromethane (20 mL) and this solution was added dropwise over 20 minutes. The reaction mixture was permitted to warm to room temperature and was stirred overnight. The dichloromethane solution was washed with 1M  $\text{NH}_4\text{OH}$  ( $3 \times 50$  mL), water ( $1 \times 50$  mL) and was dried over  $\text{MgSO}_4$ . The solvent was evaporated *in vacuo* and the dark orange residue recrystallized from boiling 2-propanol (charcoal) to give the product (0.72 g, 33% from the *bis*-sulfide) as yellow-orange needles; m.p.  $110\text{--}111^{\circ}\text{C}$  (lit.<sup>104</sup>  $110\text{--}111^{\circ}\text{C}$ ); IR (KBr) 2907, 1551,  $1007\text{ cm}^{-1}$ ;  $\delta_{\text{H}}$  (200 MHz) 2.38 (s);  $\delta_{\text{C}}$  (50 MHz) 218.3, (qt.) 133.7 (qt.), 124.1 (qt.), 14.6 ( $\text{CH}_3$ );  $m/z$  218 ( $\text{M}^+$ , 100%)

*Method 2.* A solution of 5.23 g (25.6 mmol) of the *bis*-sulfide in 100 mL of pyridine was heated to  $105^{\circ}\text{C}$  under nitrogen and 2.35 g of sodium were slowly added taking care to prevent excessive heating of the mixture. The blue/purple solution was allowed to stir for an additional 3 hours, was cooled to room temperature and methanol (10 mL) was cautiously added *via* syringe. After removal of the majority of pyridine *in vacuo*, the remains were dissolved in 1M  $\text{NaOH}$  (100 mL), were washed with dichloromethane ( $3 \times 50$  mL), acidified with 2M  $\text{HCl}$  and were extracted with toluene ( $3 \times 50$  mL). The toluene extracts were dried over  $\text{MgSO}_4$  and the solvent was evaporated *in vacuo*. 3.77g of material were isolated (84% crude yield).

The crude dithiol (21.4 mmol) was dissolved in a 10:1 dichloromethane/acetic acid solution (100 mL) and was stirred under nitrogen. The solution was cooled to  $-78^{\circ}\text{C}$  and  $\text{N,N}$ -thiacarbonyldiimidazole (3.81 g, 21.4 mmol) was added. The reaction mixture was allowed to warm to room temperature and was stirred for 24 hours. The

dichloromethane solution was washed with water (1×100 mL), saturated NaHCO<sub>3</sub> (3×50 mL), brine (1×100 mL) and was dried over MgSO<sub>4</sub>. After removal of the solvent, the product was recrystallized from boiling 2-propanol (charcoal) to give 1.92 g (41%) of the dithiole product. Spectral and physical data were identical to those of the product from the previous experiment.

*Benzothieno[2,3-*d*]-1,3-dithiole-2-thione*

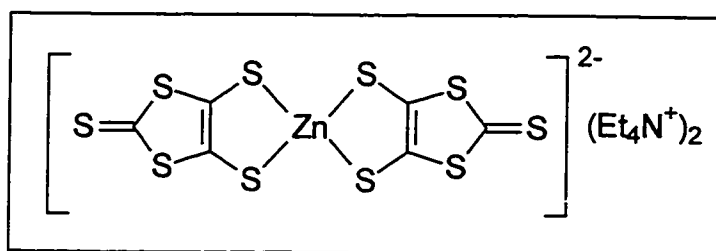


2,3-Bis(methylthio)benzo[*b*]thiophene (2.00 g, 8.83 mmol) was added to a 500 mL flame-dried round bottomed flask containing liq. NH<sub>3</sub> (250 mL) cooled to -40°C. Sodium metal (0.812 g, 35.3 mmol) was cut into small squares and added to the well-stirred liq. NH<sub>3</sub> mixture under N<sub>2</sub>. After addition of the sodium was complete, the ammonia was allowed to evaporate overnight. The following day, the solids were dissolved in 0.5 M NaOH (50 mL) and the solution was washed with toluene (2×25 mL). 2M HCl was added until the solution was acidic to litmus and was extracted with toluene (3×25 mL). The toluene extracts were washed with brine (1×50 mL) and were dried with MgSO<sub>4</sub>. After evaporation of the solvent, 1.74 g of crude dithiol were isolated (99%).

The crude dithiol (1.74 g, 8.77 mmol) was dissolved in dichloromethane (100 mL) and the resulting solution was stirred under N<sub>2</sub> for 1 h. Diisopropylethylamine

(3.40 g, 26.3 mmol) was added and the darkened solution was cooled to  $-78^{\circ}\text{C}$ . A solution of thiophosgene (1.21 g, 10.5 mmol) in dichloromethane (30 mL) was added dropwise after which the solution was allowed to warm to room temperature. The reaction mixture was washed with 1M  $\text{NH}_4\text{OH}$  ( $3 \times 50$  mL), water ( $1 \times 100$  mL), brine ( $1 \times 100$  mL) and was dried over  $\text{MgSO}_4$ . After evaporation of the solvent, the product was dissolved in boiling 2-propanol. This solution was decolourized with charcoal, and on cooling afforded the product (1.01 g, 47.6 % from the *bis*-sulfide) as yellow-orange needles; m.p.  $143\text{--}144^{\circ}\text{C}$ ; IR (KBr) 3046, 1449, 1409,  $1040\text{ cm}^{-1}$ ;  $\delta_{\text{H}}$  (200 MHz) 7.88 (m, 1H), 7.59 (m, 1H), 7.45 (m, 2H);  $\delta_{\text{C}}$  (50 MHz) 213.3 (qt.), 142.1 (qt.), 133.3 (qt.), 133.0 (qt.), 131.8 (qt.), 125.8 (CH), 125.4 (CH), 121.7 (CH);  $m/z$  240 ( $\text{M}^+$ , 100%); Analysis calculated for  $\text{C}_9\text{H}_4\text{S}_4$ : C 44.97%, H 1.68%; Found: C 44.96%, H 1.97%

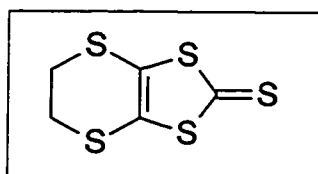
*Bis(tetraethylammonium)bis(1,3-dithiole-2-thione-4,5-dithiolato)zincate*



Sodium sand (23.0 g, 1.0 mol) was introduced into a 3-necked 3 L flask equipped with a mechanical stirrer, dropping funnel and a nitrogen inlet. Carbon disulfide (180 mL, 3 mol) was added and the flask placed in an ice-bath. DMF (200 mL) was added dropwise over 4 h taking care to maintain efficient stirring and cooling. After allowing the reaction to warm to room temperature overnight, any excess sodium was destroyed by

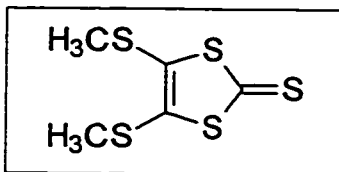
careful addition of methanol (50 mL). Once all traces of sodium were destroyed, a mixture of water and methanol (500 mL and 400 mL) was added in one portion. A zinc solution was prepared by dissolving zinc chloride (20 g, 0.15 mol) in concentrated aqueous ammonia (500 mL) followed by methanol (500 mL) and was added through the dropping funnel over 5 minutes. This was followed by the dropwise addition of a  $\text{NEt}_4\text{Br}$  solution (53 g, 0.25 mol) in water (250 mL) over 4 h. The mixture was stirred overnight and filtered on a large sintered funnel the following day. The crystals were washed with water (500 mL), 2-propanol (until the washings were colourless) and finally with ether (200 mL). Recrystallization from acetone/2-propanol afforded the product (58 g, 65%) as deep red crystals; m.p. 204-207°C (lit.<sup>50</sup> 206-208°C); IR (KBr) 2979, 14880, 1456, 1416, 1171, 1057, 1083, 995  $\text{cm}^{-1}$ ;  $\delta_{\text{C}}$  (50 MHz) 209.4 (qt.), 136.2 (qt.), 53.1 ( $\text{CH}_2$ ), 7.8 ( $\text{CH}_3$ ).

*4,5-Ethylenedithia-1,3-dithiole-2-thione*



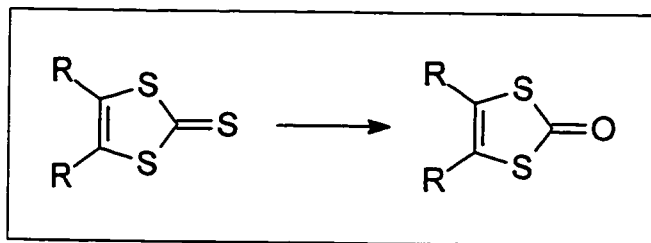
TEA-Zn[DMIT] (10 g, 13.9 mmol) was dissolved in 100 mL of acetonitrile. Dibromoethane (7.80 g, 41.8 mmol) was added and the mixture refluxed for 7 h. After evaporation of the solvent, the mixture was dissolved in toluene and filtered to remove any zinc salts. Recrystallization from 2-propanol (charcoal) yielded 3.60 g (58%) of 4,5-ethylenedithia-1,3-dithiole-2-thione; m.p. 116-120°C (lit.<sup>108</sup> 120-121°C); IR (KBr) 2951, 2919, 1480, 1060;  $^1\text{H-NMR}$  (200 MHz) 3.40 (s);  $m/z$  224 ( $\text{M}^+$ , 100%)

*4,5-Bis(methylthio)-1,3-dithiole-2-thione*



TEA-Zn[DMIT] (10 g, 13.9 mmol) was dissolved in acetone (100 mL) and stirred at room temperature in the presence of iodomethane (5.92 g, 41.7 mmol). After evaporation of the solvent, the product was dissolved in toluene and the mixture was filtered to remove any zinc salts. Recrystallization from 2-propanol (charcoal) yielded 4.82 g (77%) of 4,5-*bis*(methylthio)-1,3-dithiole-2-thione; m.p. 100-101°C (lit.<sup>108</sup> 100-101°C); IR (KBr) 2984, 2910, 1471, 1058;  $\delta_{\text{H}}$  (200 MHz) 2.42 (s);  $m/z$  226 ( $\text{M}^+$ , 100%)

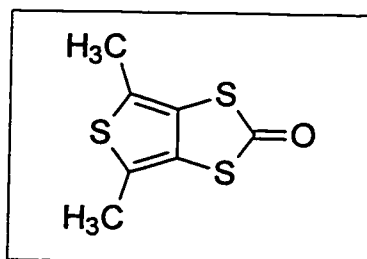
*General procedure for the transchalcogenation of 1,3-dithioles-2-thiones*



Mercuric acetate (*ca.* 3 eq) was added to a solution the 1,3-dithiole-2-thione in  $\text{CHCl}_3/\text{AcOH}$  (3:1, 10 mL per mmol of thione). The resulting white suspension was stirred overnight at room temperature after which time the white precipitate was filtered through a plug of Celite and washed with chloroform. The filtrate was sequentially

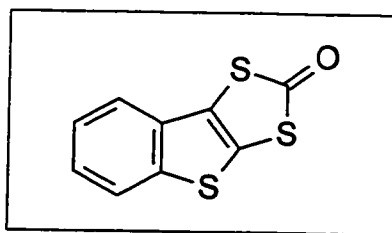
washed with water, saturated  $\text{NaHCO}_3$ , water and was dried over  $\text{MgSO}_4$ . Removal of the solvent *in vacuo* afforded the product which was be recrystallized from 2-propanol.

*4,6-Dimethylthieno[3,4-*d*]-1,3-dithiole-2-one*



Mercuric acetate (4.38 g, 13.7 mmol) was added to a solution of 4,6-dimethylthieno[3,4-*d*]-1,3-dithiole-2-thione (1.00 g, 4.58 mmol) in 50 mL of the  $\text{CHCl}_3/\text{AcOH}$  solution and stirred overnight. Isolation of the product (as described in the general procedure) gave 0.707 g (76%) of 4,6-dimethylthieno[3,4-*d*]-1,3-dithiol-2-one; m.p 64-65°C; IR (KBr) 2941, 2910, 2846, 1745, 1680, 1376, 1144, 914, 830, 724  $\text{cm}^{-1}$ ;  $\delta_{\text{H}}$  (200 MHz) 2.42 (s);  $\delta_{\text{C}}$  (50 MHz) 193.3 (qt.), 126.2 (qt.), 124.3 (qt.), 14.8 ( $\text{CH}_3$ );  $m/z$  202 ( $\text{M}^+$ , 100%); Analysis calculated for  $\text{C}_7\text{H}_6\text{OS}_3$ : C 41.56%, 2.99%; Found: C 41.31%, H 2.98%

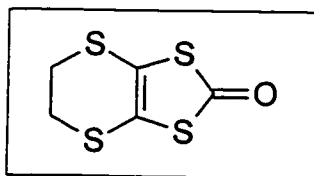
*Benzothieno[2,3-*d*]-1,3-dithiole-2-one*



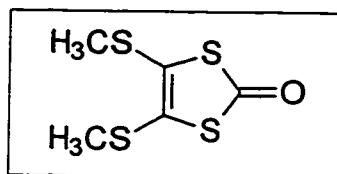


Mercuric acetate (1.44 g, 4.52 mmol) was added to a solution of benzothieno[2,3-*d*]-1,3-dithiole-2-thione (0.40 g, 1.67 mmol) in 13 mL of the CHCl<sub>3</sub>/AcOH solution and was stirred overnight. Isolation of the product (as described in the general procedure) gave 0.327 g (87%) of benzothieno[2,3-*d*]-1,3-dithiol-2-one; m.p. 98-99°C; IR (KBr) 3048, 1691, 1626; 1418, 741 cm<sup>-1</sup>;  $\delta_{\text{H}}$  (200 MHz), 7.82 (d, 1H), 7.48 (d, 1H), 7.38 (m, 2H);  $\delta_{\text{C}}$  (50 MHz) 192.6 (qt.), 139.2 (qt.), 133.1 (qt.), 125.4 (CH), 124.9 (CH), 123.5 (qt.), 122.7 (CH), 121.8 (qt.), 121.7 (CH);  $m/z$  224 ( $\text{M}^+$ , 45%); Analysis calculated for C<sub>9</sub>H<sub>4</sub>OS<sub>3</sub>: C 48.19%, H 1.80%; Found: C 47.78%, H 1.63%

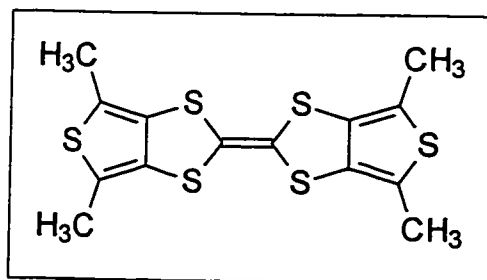
*4,5-Ethylenedithia-1,3-dithiole-2-one*



Mercuric acetate (5.75 g, 18.1 mmol) was added to solution of ET (1.50 g, 6.69 mmol) in the CHCl<sub>3</sub>/AcOH solution (70 mL). After stirring overnight, isolation of the product yielded 1.25 g (89%) of 4,5-ethylenedithia-1,3-dithiol-2-one; m.p. 122-124°C (lit.<sup>112</sup> 126-127°C); IR (KBr) 2971, 2924, 1636, 1603, 1500 cm<sup>-1</sup>;  $\delta_{\text{H}}$  (200 MHz) 3.41 (s);  $m/z$  208 ( $\text{M}^+$ , 100%).

*4,5-Bis(methylthio)-1,3-dithiole-2-one*

Mercuric acetate (4.78 g, 15 mmol) was added to a solution of 4,5-bis(methylthio)-1,3-dithiole-2-thione (1.13 g, 5.0 mmol) in 50 mL of the 3:1 CHCl<sub>3</sub>/AcOH solution. Isolation of the product (as described in the general procedure) gave 0.824 g (77%) of 4,5-bis(methylthio)-1,3-dithiole-2-one; m.p. 62-64°C (lit.<sup>113</sup> 63-64°C);  $\delta_{\text{H}}$  (200 MHz) 2.51 (s);  $m/z$  210 ( $\text{M}^+$ , 100%).

*(4,6-Dimethylthieno[3,4-d]-1,3-dithiole-2-ylidene)-4,6-dimethylthieno[3,4-d]-1,3-dithiole*

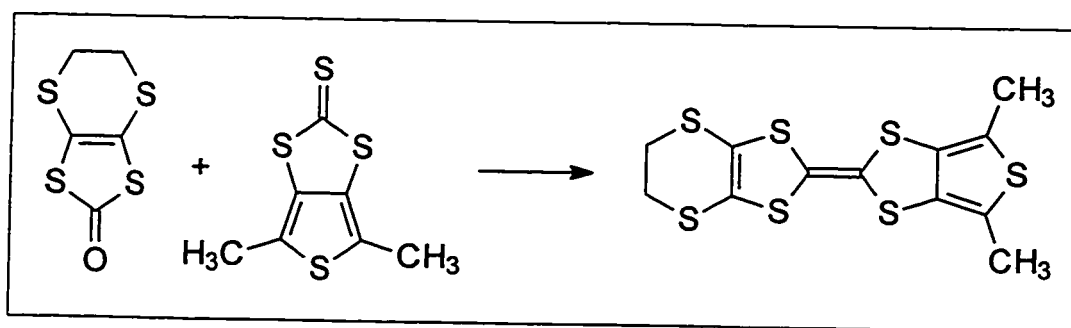
4,6-Dimethylthieno[3,4-*d*]-1,3-dithiole-2-one (0.202 g, 1.00 mmol) was added to a 10 mL round bottomed flask containing triethyl phosphite (10 mL). After stirring at 120°C for 8 hours, the mixture was allowed to cool and 5 mL of methanol were added. The resulting solid was filtered off and washed with ethanol to afford 0.015 g of yellow

crystals (8.8%); m.p 290-293°C (lit.<sup>104</sup> 295-297°C); IR (KBr) 2906, 2842, 1560;  $\delta_{\text{H}}$  (200 MHz) 2.30 (s);  $m/z$  372 ( $M^+$ , 100%).

*General procedure for the preparation of mixed TTF's*

A mixture consisting of the 1,3-dithiole-2-one (0.5 mmol), the 1,3-dithiole-2-thione (2 eq.) in 2 mL of triethyl phosphite were heated at 125°C under nitrogen. After the appropriate time had elapsed, the mixture was allowed to cool to room temperature and methanol (10 mL) was added under vigorous stirring. This mixture was cooled to 0°C for 1 h, filtered, and the solids were washed with cold methanol. The crude products were purified by flash chromatography (silica gel, 30%  $\text{CH}_2\text{Cl}_2$ /hexanes).

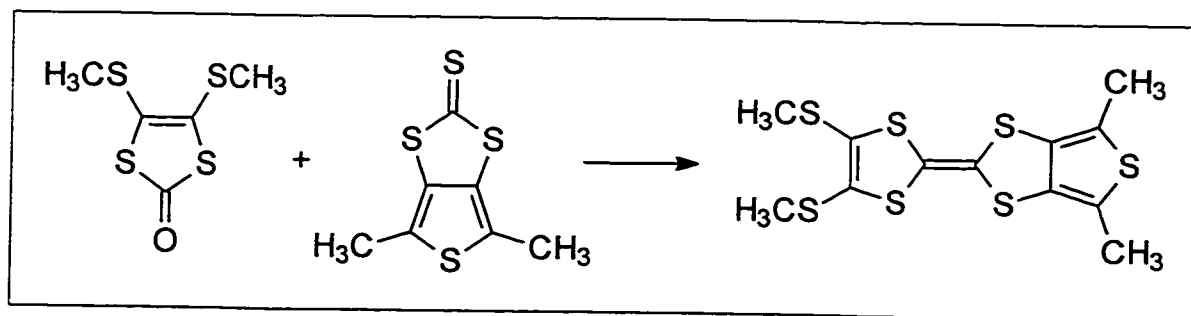
*(4,6-Dimethylthieno[3,4-d]-1,3-dithiole-2-ylidene)-4,5-ethylenedithia-1,3-dithiole*



The reaction mixture was heated at 125°C for 90 minutes. After cooling, a solid precipitated out of the deep red solution, which was then diluted with methanol. The solids were filtered, washed with methanol and purified by flash chromatography to afford a yellow-orange solid (0.142 g, 13%); m.p. 154-156°C; IR (KBr) 2954, 2907,

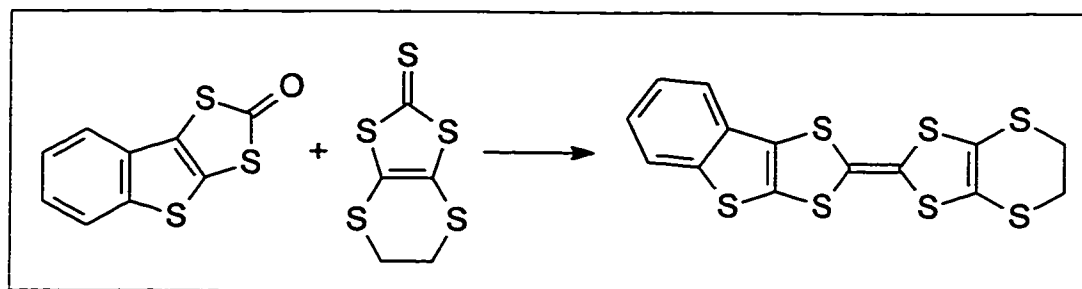
1561, 1421;  $\delta_{\text{H}}$  (200 MHz) 3.31 (s, 2H), 2.29 (s, 3H);  $\delta_{\text{C}}$  (50 MHz) 128.9 (qt.), 128.1 (qt.), 124.2 (qt.), 30.2 (CH<sub>2</sub>), 14.5 (CH<sub>3</sub>);  $m/z$  378 (M<sup>+</sup>, 100%); Analysis calculated for C<sub>12</sub>H<sub>10</sub>S<sub>7</sub>: C 38.07%, H 2.66%; Found: C 38.15%, H 2.69%

*(4,6-Dimethylthieno[3,4-d]-1,3-dithiole-2-ylidene)-4,5-bis(methylthio)-1,3-dithiole*



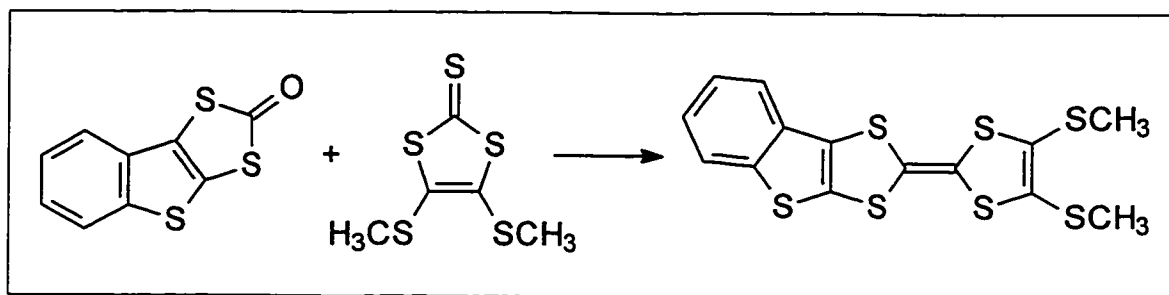
The reaction mixture was heated at 125°C for 90 minutes. After cooling, a solid precipitated out of the deep red solution, which was then diluted with methanol. The solids were filtered, washed with methanol and were purified by flash chromatography (30% CH<sub>2</sub>Cl<sub>2</sub>/hexane) to afford an orange solid (0.142 g, 5%); m.p. 128-130°C; IR (KBr) 2960, 2922, 1419, 1262, 1092, 1017, 803 cm<sup>-1</sup>;  $\delta_{\text{H}}$  (200 MHz) 2.44 (s, 6H), 2.28 (s, 6H);  $\delta_{\text{C}}$  (50 MHz, CS<sub>2</sub>/CDCl<sub>3</sub>) 129.3 (qt), 128.9 (qt), 125.8 (qt), 124.5 (qt), 18.3 (CH<sub>3</sub>), 14.7 (CH<sub>3</sub>)  $m/z$  380 (M<sup>+</sup>, 100%); Analysis calculated for C<sub>12</sub>H<sub>12</sub>S<sub>7</sub>: C 37.86%, H 3.18%; Found: C: 36.63%, H 3.92%

*(Benzothieno[2,3-d]-1,3-dithiole-2-ylidene)-4,5-ethylenedithio-1,3-dithiole*



The reagents were heated at 125°C for 90 minutes. Flash chromatography of the crude product gave 51 mg (26%) of the TTF; m.p. 156-157°C; IR (KBr) 3054, 2916, 1457, 1419, 753  $\text{cm}^{-1}$ ;  $\delta_{\text{H}}$  (200 MHz,  $\text{CS}_2/\text{C}_6\text{D}_6$ ) 8.30 (s, 1H) 7.60 (m, 3H), 3.71 (s, 4H);  $\delta_{\text{C}}$  (50 MHz,  $\text{CS}_2/\text{C}_6\text{D}_6$ ) 125.0 (CH), 124.6 (CH), 123.1 (CH), 121.5 (CH), 29.45 ( $\text{CH}_2$ ), 29.43 ( $\text{CH}_2$ );  $m/z$  400 ( $\text{M}^+$ , 100%); Analysis calculated for  $\text{C}_{14}\text{H}_8\text{S}_7$ : C 41.97%, H 2.01%; Found: C 41.84%, H 2.01%

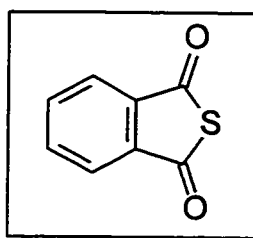
*(Benzothieno[2,3-d]-1,3-dithiole-2-ylidene)-4,5-bis(methylthio)-1,3-dithiole*



The reagents were heated at 125°C for 90 minutes. Flash chromatography of the crude product gave 35 mg (18%) of the TTF; m.p. 115-116°C; IR (KBr) 3067, 2985,

2922, 1488, 1457, 1419, 740  $\text{cm}^{-1}$ ;  $\delta_{\text{H}}$  (200 MHz,  $\text{CS}_2/\text{C}_6\text{D}_6$ ) 8.25 (s, 1H), 7.55 (m, 3H), 2.39 (s, 6H);  $\delta_{\text{C}}$  (50 MHz,  $\text{CS}_2/\text{C}_6\text{D}_6$ ) 124.5(CH), 123.9 (CH), 121.9 (CH), 121.0 (CH), 18.62 ( $\text{CH}_3$ );  $m/z$  402 ( $\text{M}^+$ , 100%); Analysis calculated for  $\text{C}_{14}\text{H}_{10}\text{S}_7$ : C 41.76%, H 2.50%; Found: C 41.67%, H 2.78%

*Thiophthalic anhydride*



Sodium sulfide nonahydrate (24 g, 0.1 mol) was dissolved in water (200 mL) and was added dropwise to a solution of phthaloyl chloride (23 g, 0.1 mol) and hexadecylphosphonium bromide (2.6 g, 5 mmol) in benzene (200 mL). The mixture was stirred vigorously for 1 h and then washed with 2M HCl (1×100 mL), water (1×100 mL), was dried over  $\text{MgSO}_4$ , and the solvent evaporated to give a yellow solid. Recrystallization from ethanol gave yellow plates (9.53g, 58%); m.p. 112-114°C (lit.<sup>109</sup> 112-113°C);  $\delta_{\text{H}}$  (200 MHz) 7.98 (m, 2H), 7.82 (m, 2H);  $m/z$  164 ( $\text{M}^+$ , 100%).

## REFERENCES

1. J. H. Clark. *Catalysis of Organic Reactions using Supported Inorganic Reagents*, VCH, New York, 1994.
2. N. N. Greenwood and A. Earnshaw. *Chemistry of the Elements*, Pergamon Press, Oxford, 1989.
3. I. V. Mitchell. *Pillared Layered Structures: Current Trends and Applications*, Elsevier, London, 1990.
4. S. J. Barlow, T. W. Bastock, J. H. Clark and S. R. Cullen. *J. Chem. Soc., Perkin Trans. 2*, **1994**, 1117.
5. Y. Izumi, M. Onaka and T. Shinoda. *Chem. Lett.* **1995**, 495.
6. D. R. Brown and J. Massam. *Catal. Lett.*, **1995**, 35, 335.
7. P. Laszlo, ed.. *Preparative Chemistry using Supported Reagents*, Academic Press, San Diego, 1987.
8. K. Smith, ed. *Solid Supports and Catalysts in Organic Synthesis*, Ellis Horwood, Chichester, 1992.
9. J. H. Clark, A. P. Kybett and D. J. Macquarrie. *Supported Reagents: Preparation, Analysis and Applications*, VCH, New York, 1992.
10. D. R. Brown, H. G. M. Edwards, D. W. Farwell and J. Massam. *J. Chem. Soc., Faraday Trans.*, **1996**, 92, 1027.
11. Mobil Research Corp., **USP 5057296/1991**; *Chem. Abs.* **115**:139158u.
12. M. Coudary and Y. Sudha. *Synth. Commun.*, **1990**, 26, 2993.
13. H. Horiuchi, J.-i. Tateiwa and S. Uemura. *J. Org. Chem.*, **1995**, 60, 4039.

14. E. C. L. Gautier, A. E. Graham, A. McKillop, S. P. Standen and R. J. K. Taylor. *Tetrahedron Lett.*, **1997**, 38, 1881.
15. A. Cornelis and P. Laszlo. *Synthesis*, **1985**, 909.
16. M. Balogh, A. Cornélis and P. Laszlo. *Tetrahedron Lett.*, **1984**, 25, 3313.
17. R. K. Saini and R. S. Varma. *Tetrahedron Lett.*, **1997**, 38, 2623.
18. A. Cornélis, B. Gigante, P. Laszlo, M. J. Marcelo-Curto and A. O. Prazeres. *J. Org. Chem.*, **1995**, 60, 3445.
19. J. H. Clark, A. P. Kybett, P. Landon, D. J. Macquarrie and K. Martin. *J. Chem. Soc., Chem. Commun.*, **1989**, 1355.
20. R. Dahiya and R. S. Varma. *Tetrahedron Lett.*, **1997**, 38, 2043.
21. H. Horiuchi, J.-i. Tateiwa and S. Uemura. *J. Chem. Soc., Chem. Commun.*, **1994**, 2567.
22. M. Fukami, M. Hirano, T. Morimoto and S. Yakabe. *Synth. Commun.*, **1997**, 27, 2783.
23. S. Békássy, E. Cseke, T. Cseri, R. Dutartre, F. Figueras and L-C de Menorval. *Appl. Catal. A.*, **1995**, 132, 141.
24. S. J. Barlow, J. H. Clark, K. Martin, A. J. Teasdale. *J. Chem. Soc., Chem. Commun.*, **1995**, 2037.
25. M. L. Kantam and P. L. Santhi. *Synth. Commun.*, **1996**, 26, 3075.
26. M. Matsui and H. Yamamoto. *Bull. Chem. Soc. Jpn.*, **1996**, 69, 137.
27. E. Hayama, T. Nishimura, J.-i. Tateiwa and S. Uemura. *Chem. Lett.*, **1996**, 59.
28. J. Lucchetti and P. Laszlo. *Tetrahedron Lett.*, **1984**, 25, 2147.
29. J. Lucchetti and P. Laszlo. *Tetrahedron Lett.*, **1984**, 25, 4387.



30. S. Patai and Z. Rapoport. *Supplement S; The Chemistry of Sulfur-containing Functional Groups*, J. Wiley, Chichester, 1993.
31. P. Metzner and A. Thuillier, *Sulfur Reagents in Organic Synthesis*, Academic Press, London, 1994.
32. C. M. Rayner. *Contemp. Org. Synth.*, **1996**, 3, 499.
33. J. S. Sawyer and E. A. Schmittling. *J. Org. Chem.*, **1993**, 58, 3229.
34. L. Testaferri, M. Tiecco and M. Tingoli. *J. Org. Chem.*, **1980**, 45, 4376.
35. D. Chianelli, M. Montanucci, L. Testaferri, M. Tiecco and M. Tingoli. *Tetrahedron*, **1982**, 38, 3687.
36. D. Chianelli, F. Maiolo, L. Testaferri, M. Tiecco and M. Tingoli. *Synthesis*, **1982**, 478.
37. J. E. Shaw. *J. Org. Chem.*, **1991**, 56, 3728.
38. J. C. Arnould, C. Cadilhac, M. Didelot and M. J. Pasquet. *Tetrahedron Lett.*, **1996**, 37, 4523.
39. E. Fleckerstein and S. Hünig. *Justus Liebigs Ann. Chem.*, **1970**, 738, 192.
40. J. R. Reddinger and J. R. Reynolds. *J. Org. Chem.*, **1996**, 61, 4833.
41. H. Inoue, H. Kojima, K. Nakamura and K. Yamamoto. *Synthesis*, **1996**, 1193.
42. V. De Stefano, I. W. J. Still and F. D. Toste. *Synth. Commun.*, **1995**, 24, 1277.
43. F. LaRonde, I. W. J. Still and F. D. Toste. *Tetrahedron Lett.*, **1995**, 36, 2949.
44. E. J. Hufnagel, D. Wobschall and F. Wudl. *J. Am. Chem. Soc.*, **1972**, 94, 670.
45. K. Bechgaard, C. S. Jacobsen, K. Mortensen, H. J. Pedersen and N. Thorup. *Solid State Commun.*, **1980**, 33, 1119.

46. E. M. Engler, R. L. Greene, R. Lagier, V. Y. Lee, S. S. P. Parkin, R. R. Schumaker and J. C. Scott. *Phys. Rev. Lett.*, **1983**, 50, 270.
47. H. D. Hartzler, L. R. Melby and W. A. Sheppard. *J. Org. Chem.*, **1974**, 39, 2456.
48. M. R. Bryce and A. J. Moore. *Synthesis*, **1997**, 407.
49. E. Hoyer, R. Kirmse, H. -J. Sieler and G. Steimecke. *Phosphorus and Sulfur*, **1979**, 7, 49.
50. J. Becher, M. P. Cava, T. K. Hansen, T. Jørgensen, R. Khedekar and K. S. Varma. *Org. Synth.*, **1996**, 73, 270.
51. J. Becher and N. Sventrup. *Synthesis*, **1995**, 215.
52. T. Nihira, K. Shibata, K. Takahashi and K. Takase. *Tetrahedron Lett.*, **1989**, 30, 3191.
53. H. Fujiwara, N. Higuchi, Y. Misaki, H. Mori, T. Mori, S. Tanaka and T. Yamabe. *Angew. Chem. Int. Ed. Engl.*, **1995**, 34, 1222.
54. M. Inaba, T. Kawase, S. Yoneda and Z.-i. Yoshida. *J. Org. Chem.*, **1978**, 43, 595.
55. M. Cava and K. Zong. *J. Org. Chem.*, **1997**, 62, 1903.
56. J. Cousseau, P. Frère, J. Garín, A. Gorgues, M. Jubault, T. Nozdryn, J. Orduna, M. Salle and Y. Siquot. *Tetrahedron Lett.*, **1997**, 38, 1919.
57. E. Aqad, J. Y. Becker, J. Bernstein, A. Ellern, V. Khodorkovsky and L. Shapiro. *J. Chem. Soc., Chem. Commun.*, **1994**, 2775.
58. J. D. Kilburn, R. P. Parg and T. G. Ryan. *Synthesis*, **1994**, 195.
59. W. Hartzler. *J. Am. Chem. Soc.*, **1970**, 92, 1412.
60. W. Hartzler. *J. Am. Chem. Soc.*, **1973**, 94, 4379.
61. F. Fleckenstein and S. Hunig. *Justus Liebigs Ann. Chem.*, **1970**, 738, 192.

62. K. Bechgaard, C. Jakobsen, J. Johannsen and K. Mortensen. *J. Chem. Soc., Chem. Commun.*, **1983**, 295.
63. R. A. Aitken, K. Carcas, L. Hill, T. Massil and S. V. Raut. *Tetrahedron*, **1997**, 53, 2261.
64. W. R. H. Hurlley and S. Smiles. *J. Chem. Soc.*, **1926**, 2263.
65. Y. Aso, F. Ogura, T. Otsubo, K. Takimiya. *Chem. Lett.*, **1995**, 735.
66. A. Belyasmin, A. Gorgues, M. Jubault, P. Leriche and M. Sallé. *Tetrahedron Lett.*, **1997**, 38, 1399.
67. K. D. Carlson, J. R. Ferraro, U. Geiser, A. M. Kini, R. J. Thorn, H. H. Wang, M. H. Whangbo and J. M. Williams. *Organic Superconductors (Including Fullerenes): Synthesis, Structure, Properties, and Theory*, Prentice Hall: Englewood Cliffs, New Jersey, 1992; and references therein.
68. M. A. Beno, K. D. Carlson, T. J. Emge, U. Geiser, A. J. Schultz, R. J. Thorn, H. H. Wang, M. -H. Whangbo and J. M. Williams. *Prog. Inorg. Chem.*, **1987**, 35, 51.
69. D. O. Cowan and F. M. Wiygui. *Chem. Eng. News*, **1986**, 64, 28.
70. T. Mukaiyama and K. Suzuki. *Chem. Lett.*, **1993**, 1.
71. T. Hiyama, N. Kamai, H. Ōya and H. Takeuchi. *J. Chem. Soc., Perkin Trans. 2*, **1997**, 2301.
72. A. Kirk, Ph.D. Thesis, University of Calgary, 1997.
73. P. D. Clark, A. J. Kirk and R. A. Kydd. *Catal. Lett.*, **1994**, 25, 163.
74. P. D. Clark, A. J. Kirk, R. A. Kydd, S. T. E. Mesher and J. Yee. *Phosphorus, Sulfur and Silicon*, **1994**, 95, 441.

75. Hewlett Packard NIST/EPA/NIH Mass Spectral Database Ver. C.00.00.
76. P. D. Clark, S. T. E. Mesher and A. Primak. *Phosphorus, Sulfur and Silicon*, **1996**, 114, 99.
77. P. D. Clark, S. T. E. Mesher, A. Primak and H. Yao. *Catal. Lett.*, **1997**, 48, 79.
78. F. A. Cotton and G. Wilkinson. *Advanced Inorganic Chemistry*, John Wiley & Sons, New York, 1988.
79. J. P. Collman, R. G. Finke, L. S. Hegedus, and J. R. Norton. *Principles and Applications of Organotransition Metal Chemistry*, University Science Books, Mill Valley, California, 1987.
80. N. Beye, V. Engels, E. Fanghänel and A. Richter. *Z. Chem.*, **1989**, 29, 444.
81. S. Gronowitz, A.-B. Hörnfeldt, and M. Temciuc. *J. Heterocyclic Chem.*, **1995**, 32, 791.
82. H. Yao, Ph.D. Thesis, University of Calgary, 1997.
83. E. Kühle. *Synthesis*, **1971**, 617; and references therein.
84. M. C. Caserio, C. L. Fisher and J. K. Kim. *J. Org. Chem.*, **1985**, 50, 4390.
85. G. W. Francis and K. Veland. *J. Chromatogr.*, **1981**, 219, 379.
86. J.-i. Matsuyuki, T. Kitamura and H. Taniguchi. *J. Chem. Soc., Perkin Trans. 1*, **1991**, 1607.
87. R. Obayashi, A. Ogawa, N. Sonoda, H. Tanaka and K. Yokoyama. *J. Org. Chem.*, **1992**, 57, 111.
88. P. D. Clark, S. T. E. Mesher and M. Parvez. *Catal. Lett.*, **1997**, 47, 73.
89. R. C. Larock. *Comprehensive Organic Transformations*, VCH, Medford, New York, 1989.

90. A. J. Birch, G. Subba Rao. *Adv. Org. Chem.*, **1972**, 8, 1.
91. F. Maiolo, L. Testaferri, M. Tiecco and M. Tingoli. *J. Org. Chem.*, **1981**, 46, 3070.
92. D. N. Burdge, D. P. Tate and W. E. Truce. *J. Am. Chem. Soc.*, **1960**, 82, 2872.
93. P. A. Odorisio, S. D. Pastor and J. D. Spivack. *Phosphorus and Sulfur*, **1982**, 13, 309.
94. K. Müllen, M. Przybylski and P. Wolf. *Chimia*, **1986**, 40, 200.
95. E. Breitmeier, G. Haas, W. Voelter. *Atlas of Carbon-13 NMR Data*, Heyden & Son Ltd., London, 1979.
96. E. D. Shtefan, V. Yu. Vvedenskii. *Russ. Chem. Rev.*, **1996**, 65, 307.
97. C. N. Habecker, S. M. Pitzenberger, G. S. Ponticello and S. L. Varga. *J. Org. Chem.*, **1989**, 54, 3223.
98. T. W. Greene and P. G. M. Wuts. *Protective Groups in Organic Synthesis*, J. Wiley, New York, 1991.
99. U. Azzena, T. Denurra and G. Melloni. *J. Org. Chem.*, **1992**, 57, 1444.
100. J. J. Breiter and W. E. Truce. *J. Am. Chem. Soc.*, **1962**, 82, 1623.
101. N. Beye, E. Fanghänel and A. M. Richter. *Sulfur Lett.*, **1987**, 6, 135.
102. N. Beye, E. Fanghänel and A. M. Richter. *Z. Chem.*, **1988**, 28, 284.
103. N. Beye, E. Fanghänel and A. M. Richter. *Synthesis*, **1990**, 1149.
104. D. Cowan, T. Kistenmacher, M. Lee and K. Lerstrup. *Mol. Cryst. Liq. Cryst.*, **1985**, 120, 295.
105. R. Ketcham. *J. Org. Chem.*, **1984**, 49, 1117.

106. A. Block, L. Chiang, D. Cowan, T. Emge, D. Holt, T. Kistenmacher, M. Lee, T. Poehler, P. Shu and T. Poehler. *J. Chem. Soc., Chem. Commun.*, **1981**, 920.
107. L.-Y. Chiang, D. Cowan, D. Holt and P. Shu. *J. Org. Chem.*, **1983**, 48, 4713.
108. J. Becher, G. J. Kristensen, P. Mørk, J. Lau, K. B. Simonsen, O. Simonsen and N. Svenstrup. *Synthesis*, **1996**, 407.
109. M. Fukuda, M. Kodomar and S. Yoshitomi. *Synthesis*, **1981**, 637.
110. S. Gronowitz, A.-B. Hörnfeldt and M. Temciuc. *J. Heterocyclic Chem.*, **1993**, 30, 1111.
111. M. A. Andreeva, V. P. Perevalov, V. Ya. Rodionov and B. I. Stepanov. *J. Org. Chem. USSR*, **1974**, 10, 1242.
112. J. Larsen and C. Lenoir. *Org. Synth.*, **1995**, 72, 265.
113. K. Hartke, T. Kissel, R. Matusch and J. Quante. *Chem. Ber.*, **1980**, 113, 1898.

## APPENDIX: X-RAY STRUCTURE REPORT FOR 1,2-BIS(METHYLTHIO)INDAN

### EXPERIMENTAL

#### DATA COLLECTION

A colourless plate crystal of  $C_{11}H_{14}O_4S_2$  having approximate dimensions of  $0.40 \times 0.30 \times 0.07$  mm was mounted on a glass fiber. All measurements were made on a Rigaku AFC6S diffractometer with graphite monochromated Mo-K $\alpha$  radiation.

Cell constants and an orientation matrix for data collection, obtained from a least-squares refinement using the setting angles of 12 carefully centered reflections in the range  $15.0 < 2\theta < 30.0^\circ$  corresponded to a primitive monoclinic cell with dimensions:

$$\begin{aligned} a &= 11.138(6) \text{ \AA} \\ b &= 8.102(2) \text{ \AA} \\ c &= 13.307(2) \text{ \AA} \\ V &= 1200.2(6) \text{ \AA}^3 \end{aligned} \quad \beta = 91.82(2)^\circ$$

For  $Z = 4$  and F.W. = 274.35, the calculated density is  $1.52 \text{ g/cm}^3$ . The systematic absences of:

$$0k0: k \neq 2n$$

uniquely determine the space group to be:

$$P2_1 \text{ (\#14)}$$

The data were collected at a temperature of  $-103 \pm 1^\circ\text{C}$  using the  $\omega$ - $2\theta$  scan technique to a maximum  $2\theta$  value of  $50.2^\circ$ . Omega scans of several intense reflections, made prior to data collection, had an average width at half-height of  $0.39^\circ$  with a take-off angle of  $6.0^\circ$ . Scans of  $(1.31 + 0.34 \tan \theta)^\circ$  were made at a speed of  $4.0^\circ/\text{min}$  (in omega).

The weak reflections ( $I < 10.0\sigma(I)$ ) were rescanned (maximum of 4 scans) and the counts were accumulated to ensure good counting statistics. Stationary background counts were recorded on each side of the reflection. The ratio of peak counting time to background counting time was 2:1. The diameter of the incident beam collimator was 1.0 mm, the crystal to detector distance was 400 mm, and the detector aperture was  $9.0 \times 13.0$  mm (horizontal  $\times$  vertical).

## DATA REDUCTION

Of the 2418 reflections which were collected, 2297 were unique ( $R_{int} = 0.041$ ). The intensities of three representative reflection were measured after every 200 reflections. Over the course of data collection, the standards decreased by 1.4 %. A linear correction factor was applied to the data to account for this phenomenon.

The linear absorption coefficient,  $\mu$ , for Mo-K $\alpha$  radiation is  $4.4 \text{ cm}^{-1}$ . An empirical absorption correction based on azimuthal scans of several reflections was applied which resulted in transmission factors ranging from 0.92 to 1.00. The data were corrected for Lorentz and polarization effects.

## STRUCTURE SOLUTION AND REFINEMENT

The structure was solved by direct methods<sup>1</sup> and expanded using Fourier techniques.<sup>2</sup> The non-hydrogen atoms were refined anisotropically. Hydrogen atoms were included but not refined. The final cycle of full-matrix least-squares refinement<sup>3</sup>



was based on 1000 observed reflections ( $I > 3.00\sigma(I)$ ) and 154 variable parameters and converged (largest parameter shift was 0.04 times its esd) with unweighted and weighted agreement factors of:

$$R = \sum ||F_o| - |F_c|| / \sum |F_o| = 0.041$$

$$R_w = \sqrt{\left( \sum w(|F_o| - |F_c|)^2 / \sum wF_o^2 \right)} = 0.038$$

The standard deviation of an observation of unit weight<sup>4</sup> was 1.42. The weighting scheme was based on counting statistics and included a factor ( $p = 0.015$ ) to downweight the intense reflections. Plots of  $\sum w(|F_o| - |F_c|)^2$  versus  $|F_o|$ , reflection order in data collection,  $\sin\theta/\lambda$  and various classes of indices showed no unusual trends. The maximum and minimum peaks on the final difference Fourier map corresponded to 0.29 and  $-0.30 \text{ e}^-/\text{\AA}^3$ , respectively.

Neutral atom scattering factors were taken from Cromer and Waber.<sup>5</sup> Anomalous dispersion effects were included in  $F_{\text{calc}}$ ;<sup>6</sup> the values for  $\Delta f'$  and  $\Delta f''$  were those of Creagh and McAuley.<sup>7</sup> The values for the mass attenuation coefficients are those of Creagh and Hubbel.<sup>8</sup> All calculations were performed using the teXsan<sup>9</sup> crystallographic software package of Molecular Structure Corporation.

## REFERENCES

- (1) SAPI91: Fan Hai-Fu (1991). Structure Analysis Programs with Intelligent Control, Rigaku Corporation, Tokyo, Japan.
- (2) DIRDIF94: Beurskens, P.T., Admiraal, G., Beurskens, G., Bosman, W.P., de Gelder, R., Israel, R. and Smits, J.M.M. (1994). The DIRDIF-94 program system, Technical Report of the Crystallography Laboratory, University of Nijmegen, The Netherlands.
- (3) Least-Squares:

Function minimized:  $\sum w(|F_o| - |F_c|)^2$

$$\text{where } w = \frac{1}{\sigma^2(F_o)} = \frac{4F_o^2}{\sigma^2(F_o^2)}$$

$$\sigma^2(F_o^2) = \frac{S^2(C + R^2 B) + (pF_o^2)^2}{L_p^2}$$

$S$  = Scan rate

$C$  = Total integrated peak count

$R$  = Ratio of scan time to background counting time

$B$  = Total background count

$Lp$  = Lorentz-polarization factor

$p$  = p-factor

- (4) Standard deviation of an observation of unit weight:

$$\sqrt{\sum w(|F_o| - |F_c|)^2 / (N_o - N_v)}$$

where:  $N_o$  = number of observations

$N_v$  = number of variables

- (5) Cromer, D. T. & Waber, J. T.; "International Tables for X-ray Crystallography", Vol. IV, The Kynoch Press, Birmingham, England, Table 2.2 A (1974).
- (6) Ibers, J. A. & Hamilton, W. C.; *Acta Crystallogr.*, **17**, 781 (1964).
- (7) Creagh, D. C. \& McAuley, W.J. ; "International Tables for Crystallography", Vol C, (A.J.C. Wilson, ed.), Kluwer Academic Publishers, Boston, Table 4.2.6.8, pages 219-222 (1992).
- (8) Creagh, D. C. \& Hubbell, J.H.; "International Tables for Crystallography", Vol C, (A.J.C. Wilson, ed.), Kluwer Academic Publishers, Boston, Table 4.2.4.3, pages 200-206 (1992).
- (9) teXsan: Crystal Structure Analysis Package, Molecular Structure Corporation (1985 & 1992).

## EXPERIMENTAL DETAILS

### A. CRYSTAL DATA

Empirical Formula	$C_{11}H_{14}O_4S_2$
Formula Weight	274.35
Crystal Color, Habit	colourless, plate
Crystal Dimensions	$0.40 \times 0.30 \times 0.07$ mm
Crystal System	monoclinic
No. of Reflections Used for Unit	
Cell Determination ( $2\theta$ range)	12 (15.0 - 30.0°)
Omega Scan Peak Width	
at Half-height	0.39°
Lattice Parameters	$a = 11.138(6)$ Å $b = 8.102(2)$ Å $c = 13.307(2)$ Å $\beta = 91.82(2)^\circ$ $V = 1200.2(6)$ Å <sup>3</sup>
Space Group	P2 <sub>1</sub> (#14)
Z value	4
$D_{calc}$	1.518 g/cm <sup>3</sup>
$F_{000}$	576.00
$\mu(\text{MoK}\alpha)$	4.43 cm <sup>-1</sup>

## B. INTENSITY MEASUREMENTS

Diffractometer	Rigaku AFC6S
Radiation	MoK $\alpha$ ( $\lambda = 0.71069$ Å) graphite monochromated
Temperature	-103.0°C
Scan Type	$\omega$ - $2\theta$
Scan Rate	4.0°/min (in $\omega$ ) (up to 4 scans)
Scan Width	$(1.31 + 0.34 \tan\theta)^\circ$
$2\theta_{max}$	50.2°
No. of Reflections Measured	Total: 2418 Unique: 2297 ( $R_{int} = 0.041$ )
Corrections	Lorentz-polarization Absorption (trans. factors: 0.9205 - 1.0000) Decay (1.38%)

## C. STRUCTURE SOLUTION AND REFINEMENT

Structure Solution	Direct Methods (SAPI91)
Refinement	Full-matrix least-squares
Anomalous Dispersion	All non-hydrogen atoms
No. Observations ( $I > 3.00\sigma(I)$ )	1000
No. Variables	154
Reflection/Parameter Ratio	6.49

Residuals: R; Rw	0.041; 0.038
Goodness of Fit Indicator	1.42
Max Shift/Error in Final Cycle	0.04
Maximum peak in Final Diff. Map	$0.29\ e^{-}/\text{\AA}^3$
Minimum peak in Final Diff. Map	$-0.30\ e^{-}/\text{\AA}^3$

Table 1. Atomic coordinates and  $B_{iso}/B_{eq}$ 

Atom	X	Y	Z	$B_{eq}$
S(1)	0.7532(1)	0.3567(2)	0.1336(1)	2.05(3)
S(2)	0.4937(1)	0.6988(2)	0.2088(1)	2.03(3)
O(1)	0.8827(3)	0.3601(5)	0.1466(3)	2.57(10)
O(2)	0.7027(3)	0.4030(5)	0.0360(3)	2.9(1)
O(3)	0.5510(3)	0.7967(5)	0.2866(3)	2.9(1)
O(4)	0.3641(3)	0.6855(5)	0.2072(3)	2.8(1)
C(1)	0.6909(5)	0.4931(7)	0.2245(4)	1.7(1)
C(2)	0.5519(5)	0.4932(7)	0.2165(4)	1.7(1)
C(3)	0.5073(5)	0.4075(7)	0.3124(4)	2.2(1)
C(4)	0.6173(5)	0.3995(7)	0.3813(4)	1.9(1)
C(5)	0.6243(5)	0.3532(8)	0.4811(4)	2.3(1)
C(6)	0.7346(5)	0.3580(8)	0.5327(4)	2.3(1)
C(7)	0.8372(5)	0.4070(7)	0.4845(4)	2.3(1)
C(8)	0.8310(5)	0.4523(7)	0.3836(4)	2.2(1)
C(9)	0.7201(4)	0.4473(7)	0.3332(4)	1.7(1)
C(10)	0.7017(5)	0.1594(7)	0.1644(4)	2.8(1)
C(11)	0.5370(5)	0.7708(8)	0.0909(4)	2.9(2)
H(1)	0.7190	0.6018	0.2127	2.0339
H(2)	0.5258	0.4323	0.1589	2.0705
H(3)	0.4458	0.4703	0.3421	2.6137
H(4)	0.4782	0.2997	0.2975	2.6137
H(5)	0.5543	0.3184	0.55140	2.8124
H(6)	0.7398	0.3274	0.6016	2.7336
H(7)	0.9122	0.4099	0.5205	2.7378
H(8)	0.9010	0.4858	0.3501	2.6195
H(9)	0.6166	0.1561	0.1565	3.3312
H(10)	0.7359	0.0802	0.1210	3.3312
H(11)	0.7244	0.1347	0.2321	3.3312
H(12)	0.6219	0.7811	0.0905	3.4722
H(13)	0.5112	0.6949	0.0402	3.4722
H(14)	0.5012	0.8754	0.0778	3.4722

$$B_{eq} = \frac{8}{3} \pi^2 \left( U_{11} (aa^*)^2 + U_{22} (bb^*)^2 + U_{33} (cc^*)^2 + 2U_{12} aa^* bb^* \cos \gamma + 2U_{13} aa^* cc^* \cos \beta + 2U_{23} bb^* cc^* \cos \alpha \right)$$

Table 2. Anisotropic Displacement Parameters

Atom	$U_{11}$	$U_{22}$	$U_{33}$	$U_{12}$	$U_{13}$	$U_{23}$
S(1)	0.0230(8)	0.0296(9)	0.0255(9)	0.0014(8)	0.0031(7)	0.0035(8)
S(2)	0.0233(9)	0.0259(9)	0.0279(9)	0.0028(7)	0.0005(7)	0.0031(8)
O(1)	0.014(2)	0.044(3)	0.040(2)	0.002(2)	0.004(2)	-0.005(2)
O(2)	0.035(3)	0.053(3)	0.024(2)	0.008(2)	0.000(2)	-0.3001(2)
O(3)	0.035(3)	0.036(3)	0.037(2)	0.004(2)	-0.006(2)	-0.0315(2)
O(4)	0.019(2)	0.040(3)	0.047(3)	0.007(2)	0.003(2)	0.0023(2)
C(1)	0.023(3)	0.017(3)	0.024(3)	-0.001(3)	0.000(2)	0.001(3)
C(2)	0.020(3)	0.023(3)	0.023(3)	-0.001(3)	0.001(3)	-0.003(3)
C(3)	0.023(3)	0.029(4)	0.032(4)	-0.002(3)	0.003(3)	0.005(3)
C(4)	0.022(3)	0.025(4)	0.027(3)	0.003(3)	0.000(3)	0.000(3)
C(5)	0.035(4)	0.027(4)	0.028(4)	-0.004(3)	0.007(3)	0.002(3)
C(6)	0.038(4)	0.025(4)	0.023(3)	0.004(3)	-0.006(3)	0.005(3)
C(7)	0.029(4)	0.029(4)	0.028(4)	0.004(3)	-0.009(3)	-0.003(3)
C(8)	0.023(3)	0.026(4)	0.034(4)	-0.002(3)	0.003(3)	-0.006(3)
C(9)	0.020(3)	0.021(3)	0.022(3)	0.001(3)	0.001(3)	-0.005(3)
C(10)	0.029(3)	0.027(4)	0.049(4)	-0.001(3)	0.008(3)	-0.1010(3)
C(11)	0.042(4)	0.032(4)	0.036(4)	0.000(3)	0.004(3)	0.007(3)

The general temperature factor expression

$$\exp\left(-2\pi^2(a^{*2}U_{11}h^2 + b^{*2}U_{22}k^2 + c^{*2}U_{33}l^2 + 2a^*b^*U_{12}hk + 2a^*c^*U_{13}hl + 2b^*c^*U_{23}kl)\right)$$



Table 3. Bond Lengths (Å)

atom	atom	distance	atom	atom	distance
S(1)	O(1)	1.448(4)	S(1)	O(2)	1.449(4)
S(1)	C(1)	1.795(6)	S(1)	C(10)	1.751(6)
S(2)	O(3)	1.438(4)	S(2)	O(4)	1.446(4)
S(2)	C(2)	1.789(6)	S(2)	C(11)	1.755(6)
C(1)	C(2)	1.549(7)	C(1)	C(9)	1.519(7)
C(2)	C(3)	1.548(7)	C(3)	C(4)	1.508(7)
C(4)	C(5)	1.380(7)	C(4)	C(9)	1.384(7)
C(5)	C(6)	1.389(7)	C(6)	C(7)	1.386(8)
C(7)	C(8)	1.391(7)	C(8)	C(9)	1.387(7)

Table 4. Bond Angles (°)

atom	atom	atom	angle	atom	atom	atom	angle
O(1)	S(1)	O(2)	117.3(2)	O(1)	S(1)	C(2)	108.2(2)
O(1)	S(1)	C(10)	108.8(3)	O(2)	S(1)	C(2)	107.3(2)
O(2)	S(1)	C(10)	109.0(3)	C(1)	S(1)	C(3)	105.5(3)
O(3)	S(2)	O(4)	118.2(2)	O(3)	S(2)	C(2)	108.7(2)
O(3)	S(2)	C(11)	109.4(3)	O(4)	S(2)	C(3)	106.9(3)
O(4)	S(2)	C(11)	108.3(3)	C(2)	S(2)	C(3)	104.5(3)
S(1)	C(1)	C(2)	111.2(4)	S(1)	C(1)	C(4)	114.6(4)
C(2)	C(1)	C(9)	104.4(4)	S(2)	C(2)	C(4)	111.4(4)
S(2)	C(2)	C(3)	109.9(4)	C(1)	C(2)	C(4)	106.8(4)
C(2)	C(3)	C(4)	104.1(4)	C(3)	C(4)	C(5)	128.1(5)
C(3)	C(4)	C(9)	112.1(5)	C(5)	C(4)	C(5)	119.9(5)
C(4)	C(5)	C(6)	119.4(5)	C(5)	C(6)	C(5)	120.5(5)
C(6)	C(7)	C(8)	120.4(5)	C(7)	C(8)	C(5)	118.3(5)
C(1)	C(9)	C(4)	110.7(4)	C(1)	C(9)	C(5)	127.9(5)
C(4)	C(9)	C(8)	121.5(5)				

Table 5. Torsion Angles (°)

atom	atom	atom	atom	angle	atom	atom	atom	atom	angle
S(1)	C(1)	C(2)	S(2)	-129.3(3)	S(1)	C(1)	C(2)	C(3)	110.7(4)
S(1)	C(1)	C(9)	C(4)	-113.2(5)	S(1)	C(1)	C(9)	C(8)	68.0(7)
S(2)	C(2)	C(1)	C(9)	106.6(4)	S(2)	C(2)	C(3)	C(4)	-107.7(4)
O(1)	S(1)	C(1)	C(2)	-178.9(4)	O(1)	S(1)	C(1)	C(9)	-60.8(4)
O(2)	S(1)	C(1)	C(2)	53.6(4)	O(2)	S(1)	C(1)	C(9)	171.7(4)
O(3)	S(2)	C(2)	C(1)	-48.4(4)	O(3)	S(2)	C(2)	C(3)	69.8(4)
O(4)	S(2)	C(2)	C(1)	-176.9(4)	O(4)	S(2)	C(2)	C(3)	-58.8(4)
C(1)	C(2)	S(2)	C(11)	68.4(4)	C(1)	C(2)	C(3)	C(4)	13.2(6)
C(1)	C(9)	C(4)	C(3)	-0.2(7)	C(1)	C(9)	C(4)	C(5)	-179.8(5)
C(1)	C(9)	C(8)	C(7)	179.0(5)	C(2)	C(1)	S(1)	C(10)	-62.5(5)
C(2)	C(1)	C(9)	C(4)	8.6(6)	C(2)	C(1)	C(9)	C(8)	-170.2(6)
C(2)	C(3)	C(4)	C(5)	171.36(6)	C(2)	C(3)	C(4)	C(9)	-8.3(7)
C(3)	C(2)	S(2)	C(11)	-173.5(4)	C(3)	C(2)	C(1)	C(9)	-13.4(6)
C(3)	C(4)	C(5)	C(6)	-178.4(6)	C(3)	C(4)	C(9)	C(8)	178.7(5)
C(4)	C(5)	C(6)	C(7)	-0.7(10)	C(4)	C(9)	C(8)	C(7)	0.3(9)
C(5)	C(4)	C(9)	C(8)	-1.0(9)	C(5)	C(6)	C(7)	C(8)	0.1(10)
C(6)	C(5)	C(4)	C(9)	1.1(9)	C(6)	C(7)	C(8)	C(9)	0.1(9)
C(9)	C(1)	S(1)	C(10)	55.6(4)					

Table 6. Non-bonded Contacts out to 3.60 Å

atom	atom	distance	ADC	atom	atom	distance	ADC
O(1)	C(3)	3.361(7)	4	O(1)	C(11)	3.390(7)	64502
O(1)	C(2)	3.535(7)	4	O(1)	C(11)	3.539(7)	56504
O(1)	C(10)	3.557(7)	4	O(2)	O(4)	3.375(5)	66503
O(2)	C(11)	3.417(7)	66503	O(2)	C(11)	3.566(7)	64502
O(2)	C(10)	3.570(7)	65502	O(3)	C(6)	3.370(7)	65602
O(3)	C(7)	3.374(7)	65602	O(3)	C(8)	3.465(7)	46504
O(4)	C(1)	3.253(7)	46504	O(4)	C(10)	3.368(7)	45504
C(6)	C(8)	3.553(8)	64602				

The ADC (atom designator code) specifies the position of an atom in a crystal. The 5-digit number shown in the table is a composite of three one-digit numbers and one two-digit number: TA (first digit) + TB (second digit) + TC (third digit) + SN (last two digits). TA, TB and TC are the crystal lattice translation digits along cell edges a, b and c. A translation digit of 5 indicates the origin unit cell. If TA = 4, this indicates a translation of one unit cell length along the a-axis in the negative direction. Each translation digit can range in value from 1 to 9 and thus  $\pm 4$  lattice translations from the origin (TA=5, TB=5, TC=5) can be represented.

The SN, or symmetry operator number, refers to the number of the symmetry operator used to generate the coordinates of the target atom. A list of symmetry operators relevant to this structure are given below.

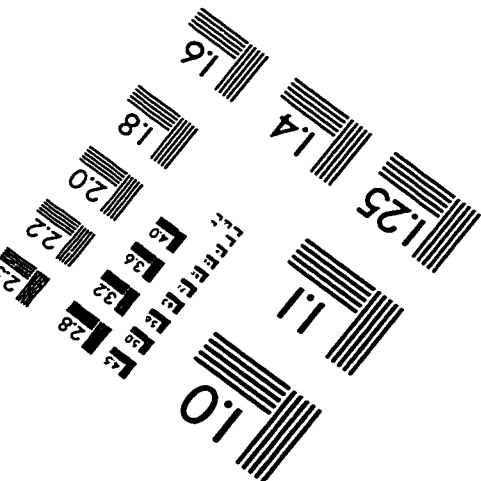
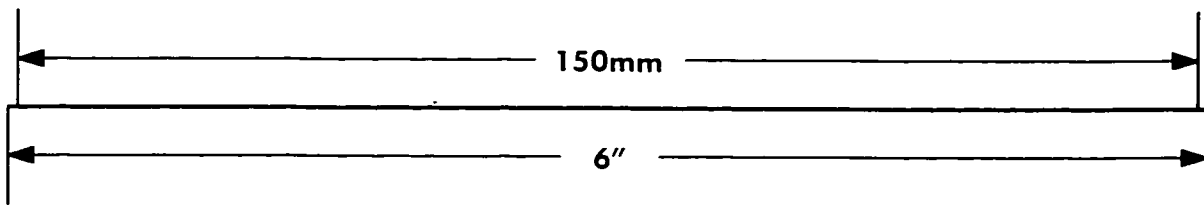
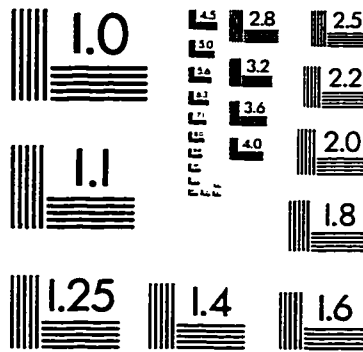
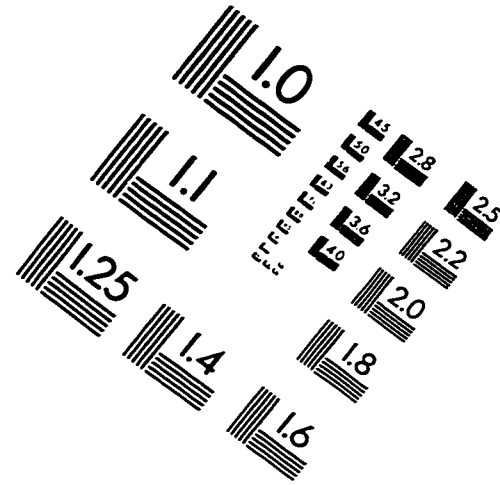
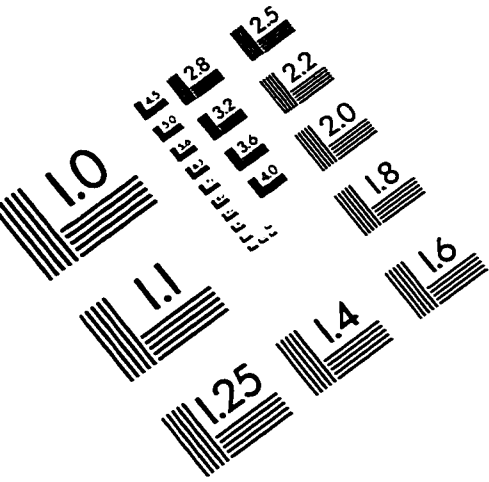
For a given intermolecular contact, the first atom (origin atom) is located in the origin unit cell and its position can be generated using the identity operator (SN=1). Thus, the ADC for an origin atom is always 55501. The position of the second atom (target atom) can be generated using the ADC and the coordinates of the atom in the parameter table. For example, an ADC of 47502 refers to the target atom moved through symmetry operator two, then translated -1 cell translations along the a axis, +2 cell translations along the b axis, and 0 cell translations along the c axis.

An ADC of 1 indicates an intermolecular contact between two fragments (eg. cation and anion) that reside in the same asymmetric unit.

#### Symmetry Operators:

(1)	X,	Y,	Z	(2)	$1/2-X,$	$1/2+Y,$	-Z
(3)	-X,	-Y,	-Z	(4)	$1/2+X,$	$1/2-Y,$	Z

# IMAGE EVALUATION TEST TARGET (QA-3)



APPLIED IMAGE, Inc  
1653 East Main Street  
Rochester, NY 14609 USA  
Phone: 716/482-0300  
Fax: 716/288-5989

© 1993, Applied Image, Inc., All Rights Reserved

