Sulfoxide-Directed Metal-Free Aromatic C-H Functionalisation: Application to Heterocycle Synthesis and Derivatisation.

A thesis submitted to the University of Manchester for the degree of Doctor of Philosophy in the Faculty of Science and Engineering

2017

Harry J. Shrives

School of Chemistry

Contents

List of Abbreviations

Ac	acyl
AIBN	2,2'-azo *bisiso*butyronitrile
aq.	aqueous
Ar	aryl
BDT	benzodithiophene
BINAP	2,2'-*bis*(diphenylphosphino-1,1'-binaphthyl)
Bn	benzyl
Boc	*t*-butoxycarbonyl
br.	broad (NMR)
Bu	butyl
Bz	benzoyl
CAN	cerium(IV) ammonium nitrate
cat.	catalytic
CI	chemical ionisation
C	celsius
Cy	cyclohexyl
d	doublet (NMR)
δ	chemical shift (NMR)
DCE	1,2-dichloroethane
DDQ	2,3-dichloro-5,6-dicyano-*p*-benzoquinone
DMF	*N*,*N*-dimethylformamide
DMSO	dimethylsulfoxide
DMTSF	dimethyl(methylthio)sulfonium tetrafluoroborate
DPPE	ethylene*bis*(diphenylphosphine)
dr	diasteroisomeric ratio
DTBP	di-*tert*-butylpyridine
E	electrophile
ee	enantiomeric excess
EDG	electron donating group
EG	ethylene glycol
EI	electron ionisation
equiv	equivalent

ES+/ES-	positive/negative ion electrospray (MS)
Et	ethyl
EWG	electron withdrawing group
FSPE	fluorous solid phase extraction
g	gram
h	hour
HFIP	1,1,1,3,3,3-hexafluoro*iso*propanol
HMPA	hexamethylphosphoramide
HRMS	high resolution mass spectrometry
Hz	hertz
IBX	*o*-iodoxybenzoic acid
i-Pr	*iso*propyl
IR	infrared
J	coupling constant (NMR)
μ	electron mobility
M	Molar
m	multiplet (NMR)
m-CPBA	*m*-chloroperbenzoic acid
Me	methyl
mg	miligram
MHz	megahertz
min	minutes
ml	millilitre
mmol	millimole
MOM	methoxymethyl
mp	melting point
MS	mass spectrum
MW	micro wave
m/*z*	mass/charge ratio (MS)
NDT	naphthodithiophene
NCS	*N*-chlorosuccinimide
Nf	nonafluorobutanesulfonic
NMR	nuclear magnetic resonance

Nu	nucleophile
PCE	Power Conversion Efficiency
Ph	phenyl
PIFA	iodobenzene-*I*,*I*-*bis*(trifluoroacetate)
PMB	*p*-methoxybenzyl
ppm	parts per million
Pr	propyl
PTSA	*p*-toluenesulfonic acid
Pyr.	pyridine
q	quartet (NMR)
quin	quintet (NMR)
R^F	perfluoroalkyl
rt	room temperature
s	singlet (NMR)
sxt	sextet (NMR)
SEM	2-(trimethylsilyl)ethoxymethyl
t	triplet (NMR)
TBAF	tetrabutylammonium fluoride
TBS	*tert*-butyldimethylsilyl
TFA	trifluoroacetic acid
TFAA	trifluoroacetic anhydride
Tf	trifluoromethanesulfonic
THF	tetrahydrofuran
TIPS	tri*iso*propylsilyl
TMEDA	*N*,*N*,*N'*,*N'*-tetramethylethylenediamine
TMS	trimethylsilyl
Tol	tolyl
Ts	tosyl

Abstract.

University of Manchester

Harry J. Shrives

Degree of Doctor of Philosophy.

Sulfoxide-Directed Metal-Free Aromatic C-H Functionalisation: Application to Heterocycle Synthesis and Derivatisation.

March 2017.

Selective metal-free functionalisation of aromatic C-H bonds is a valuable goal in organic synthetic chemistry. Recently it has been shown that Pummerer-type reactions, for example interrupted Pummerer reactions, can be used to trap nucleophiles and deliver them selectively to aromatic rings via [3,3]-sigmatropic rearrangements.

This thesis investigates the utility of sulfoxide-directed metal-free C-H functionalisations in the synthesis and derivatisation of a range of benzothiophene scaffolds. Through a sequence involving metal-free aromatic propargylation reactions and novel, diversity introducing heterocyclisations, benzothiophenes possessing a range of functionality, namely ketone, alkane or alkene substituents, can be synthesised. The value of this new cyclisation protocol is demonstrated through the sysnthesis of different highly conjugated benzothiophene motifs, molecules of particular interest in organic electronics. Using alkene substituted benzothiophenes; a new, iodine-mediated route to highly conjugated benzodithiophene cores is reported along with the application of two-directional heterocyclisations allowing the synthesis of naphthodithiophene scaffolds.

Finally, selective C3 arylation and alkylation of benzothiophenes is reported through the use of benzothiophene *S*-oxides, an underexplored class of organic compound. Oxidation of the sulfur atom intrinsic to benzothiophene molecules allows the capture of phenol, propargyl silane and allyl silane coupling partners, which are delivered with complete regio-selectivity to the C3 position of the benzothiophene.

Declaration

No portion of the work referred to in the thesis has been submitted in support of an application for another degree or qualification of this or any other university or other institute of learning.

Portions of the work refered to in this thesis have been published in:

Eberhart, A. J.; Shrives, H. J.; Álvarez, E.; Carrër, A.; Zhang, Y.; Procter, D. J. *Chem. -Eur. J.,* **2015**, *21*, 7428.

Eberhart, A. J.; Shrives, H.; Zhang, Y.; Carrër, A.; Parry, A. V. S.; Tate, D. J.; Turner, M. L.; Procter, D. J. *Chem. Sci.,* **2016**, *7*, 1281.

Shrives, H. J.; Fernández-Salas, J. A.; Hedtke, C; Pulis, A. P.; Procter, D. J. *Nat. Commun.,* **2017**, *8*, 14801, doi: 10.1038/ncomms14801

Copyright Statement

Acknowledgments

I would like to thank, first and foremost, my supervisor Professor David J. Procter for the invaluable continued support and mentoring he has provided over the last four years. The chance to contribute to the chemistry going on in his group has been an irreplaceable experience in which I have learnt in incredible amount. Also, I must thank Novartis for funding my Ph.D studentship.

Thanks must also go to all the current and past members of the Procter group who have made my time so enjoyable; Craig, Irem, Miles, Matezeus, Nico, Becky, Huanming, Kay, Charlotte and the many others that have been a pleasure to work with. Special thanks should be given Andrew, Yuntong, Jose and Kristen all of whom, at one point or another, have been involved in my project and have therefore played a significant role in my development as a researcher, chemist and individual.

I would like to dedicate this thesis to my mother, Liz, for her unwavering support and encouragement throughout the duration of my undergraduate and Ph.D. studies, her experience and guidance has been unbelievably helpful over the years. Last, but not least, I would like to thank Amy for putting up with me day-to-day and for keeping me sane, happy and motivated throughout my studies.

"There is an art, it says, or rather, a knack to flying. The knack lies in learning how to throw yourself at the ground and miss."

Douglas Adams, The Hitchiker's Guide to the Galaxy

Chapter 1: Introduction

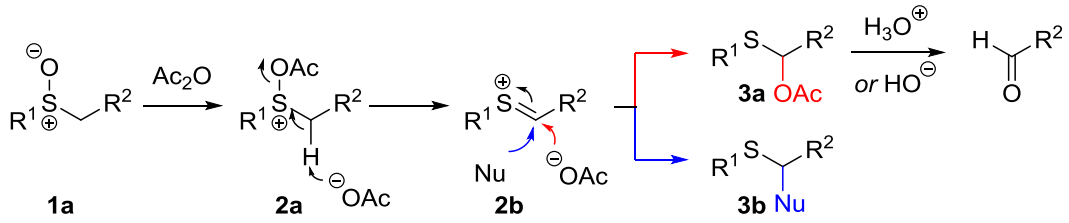
1.1 Pummerer and Pummerer-type Reactions

The selective introduction of carbon-carbon bonds into aryl and heteroaryl systems is one of the most sought after achievements in synthetic chemistry due to the abundance of these systems in pharmaceuticals, agrochemicals, and functional materials. The definitive end to this endeavour is a reaction that employs mild conditions, has wide functional group compatibility and avoids the use of expensive or toxic metals like palladium or ruthenium in achieving this crucial synthetic task. The Pummerer reaction, named after Rudolf Pummerer, was first reported in 1903, however, only relatively recently has it started to gain attention as a viable method for selectively functionalising aryl and heteroaryl systems.[1] It has now been subject to a wide range of synthetic studies which have fuelled the development of many intriguing methodologies.[2-5] This introduction will present the Pummerer reaction and recent developments within its various guises, before focusing on interrupted Pummerer reactions and their applications in the modification of aryl and heteroaryl systems.

1.1.1 The Classical Pummerer Rearrangement

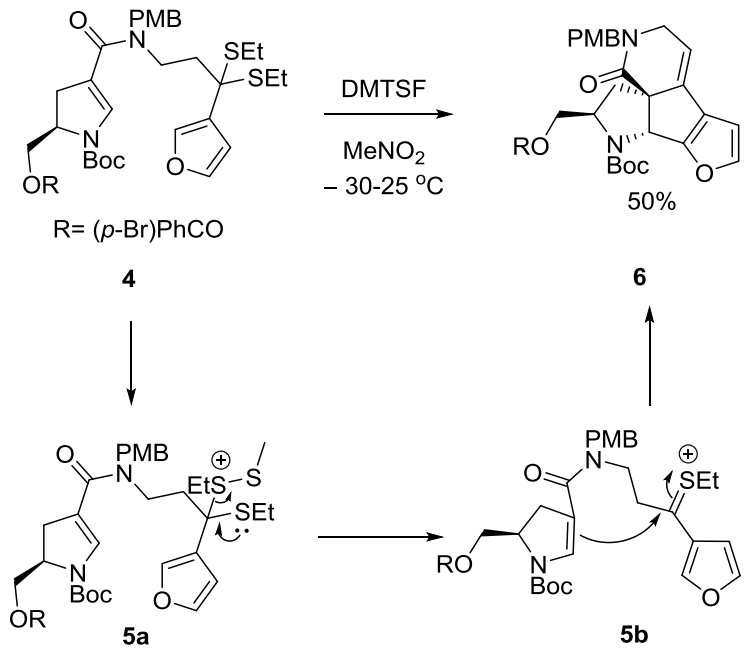
The Pummerer reaction initially involves *O*-activation of an alkyl sulfoxide by a suitable electrophile. Classically acetic anhydride was used (Ac_2O, see Scheme 1) yet more recently trifluoroacetic anhydride (TFAA), trifluoromethanesulfonic anhydride (Tf_2O), silyl chlorides or transition metal-derived Lewis acids have been developed as efficient activators.[3] Whilst these are the most common methods of initiating a Pummerer reaction, direct activation of sulfides is possible using oxidants like *N*-chlorosuccinamide (NCS) or hypervalent iodine compounds such as Stang's reagent (PhI(CN)OTf).[6, 7] The choice of activating agent depends on the reactivity and stability of both the sulfoxide/sulfide containing compound and the nucleophile; the activator must not lead to detrimental side reactions, for example capping of any hydroxyl groups in either the nucleophile or the sulfoxide partner when Tf_2O is used as an activator.

The classical Pummerer reaction is highlighted in Scheme 1. Activation of sulfoxide **1a** with Ac_2O and subsequent elimination of the resulting acyloxy group by loss of an α-proton affords thionium ion **2b.** Attack by a nucleophile generates thioether **3b**, whereas attack by acetate generates thioacetal **3a,** which can be hydrolysed to the corresponding aldehyde. Recent developments in Pummerer activation chemistry have allowed an expansion in the number of nucleophiles that can be used: amines, phenols, alkynes, arenes, alkenes and acetate nucleophiles are all compatible with Pummerer conditions.



Scheme 1

A recent example in target synthesis demonstrating the use of a classical Pummerer reaction is Winkler's route to the tetracyclic core of cytotoxic nakadomarin A **6** (Scheme 2).[8] In this synthesis, dimethyl(methylthio)sulfonium tetrafluoroborate, a sulfonium salt used for thionium ion generation, is thought to activate thioacetal **4** and directly produce **5a**, which then collapses to generate thionium species **5b**. Cyclisation followed by the elimination of thioethanol results in the stereoselective synthesis of **6** in a 50% yield.



Scheme 2

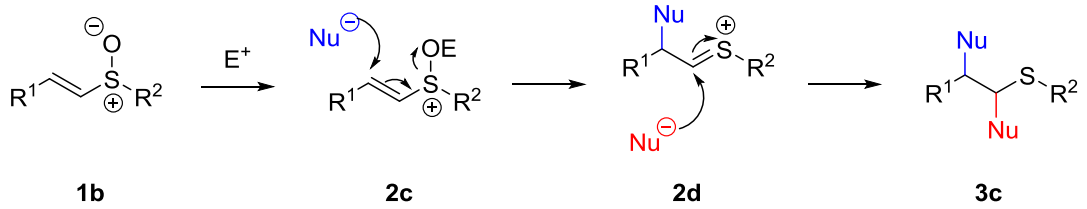
1.1.2 Additive and Vinylogous Pummerer Reactions

Using α,β-unsaturated sulfoxides as substrates in Pummerer-type chemistry allows for reaction by two different routes: additive or vinylogous. Timing of the acyloxy leaving group expulsion differentiates between these two mechanisms. In additive Pummerer reactions, nucleophilic attack and acyloxy expulsion occurs simultaneously, whereas in a vinylogous Pummerer reaction the leaving group is lost prior to nucleophilic attack. Often differentiation between these two mechanisms can be difficult as the reaction outcome for both can be the same, however, many examples exist that make a distinction between the two reaction pathways.

1.1.2.1 Additive Pummerer Reactions

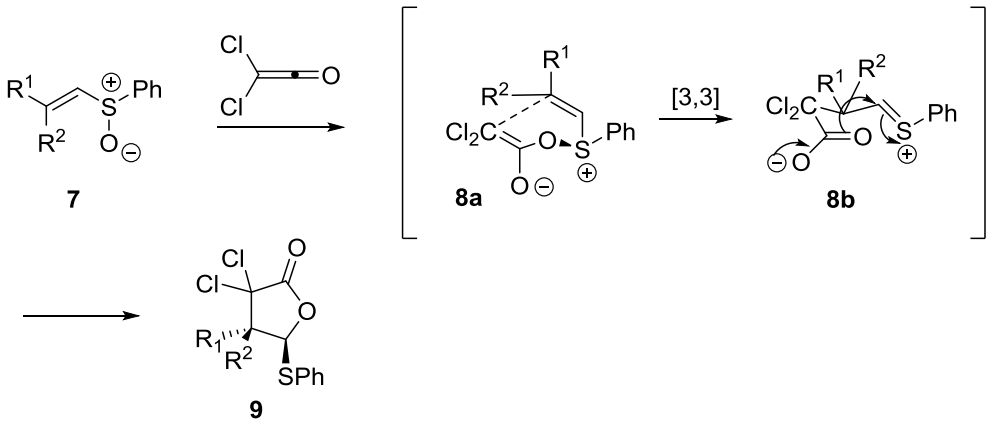
The mechanism of an additive Pummerer reaction, as outlined in Scheme 3, proceeds by activation of α,β-unsaturated sulfoxide **1b** which leads to nucleophilic attack at the β-carbon of **2c** and expulsion of the activated sulfoxide oxygen, thus generating thionium ion **2d**. This intermediate can then undergo attack from another nucleophile, be it the same or different to the first, to furnish the di-substituted

thioether **3c** (Scheme 3). The additive Pummerer reaction is arguably the quickest way to build molecular diversity within a molecule using Pummerer chemistry as it allows for the addition of two different nucleophiles to the parent α,β-unsaturated sulfoxide. The use of intramolecular nucleophiles also offers a powerful route for constructing ring systems (*vide infra*).



Scheme 3

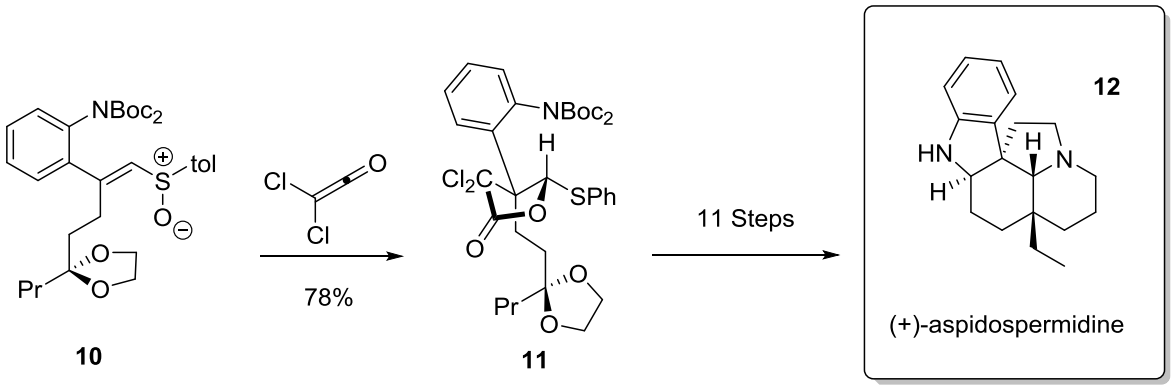
A seminal report concerning the additive Pummerer reaction described a sulfoxide/dichloroketene cyclocondensation and was disclosed by Marino and colleagues (Scheme 4).[9]



Scheme 4

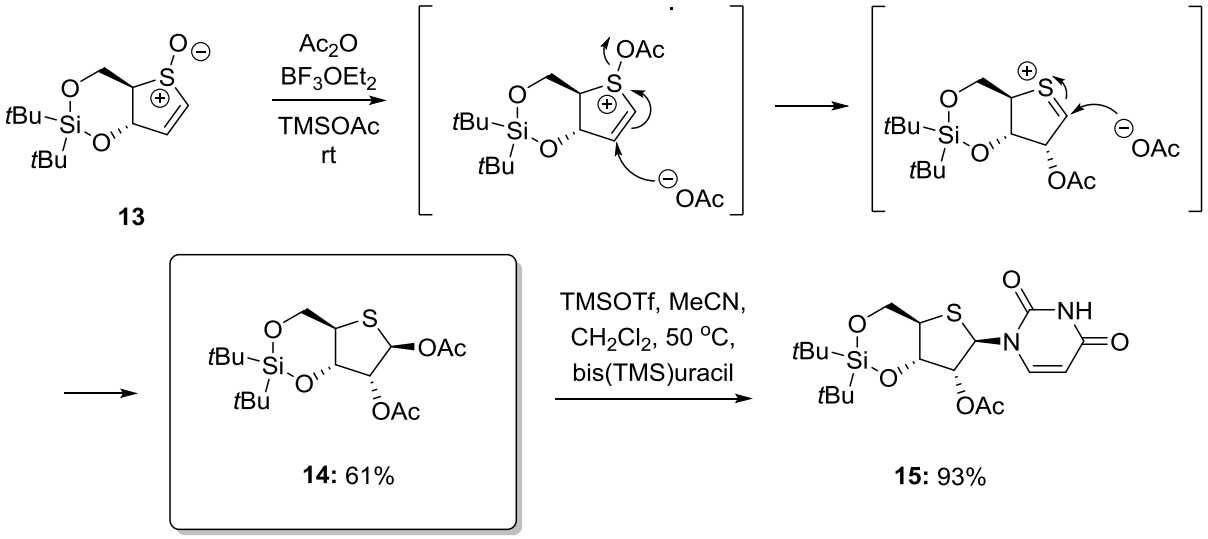
This mechanism is thought to proceed through the activation of α,β-unsaturated sulfoxide **7** by dichloroketene to give intermediate **8a**. The nucleophile in this example is tethered to the activated sulfoxide allowing **8a** to engage in a [3,3]-sigmatropic rearrangement to give thionium ion **8b**. A further intramolecular cyclisation gives butyrolactone **9** as a single stereoisomer. Marino advanced this methodology in his synthesis of (+)-aspidospermidine **12** (Scheme 5).[10] Readily available sulfoxide **10** was converted in good yield and with complete diastereocontrol to butyrolactone **11**, in the

process forming a crucial quaternary carbon centre. A further 11 steps afforded the natural product (+)-aspidospermidine.



Scheme 5

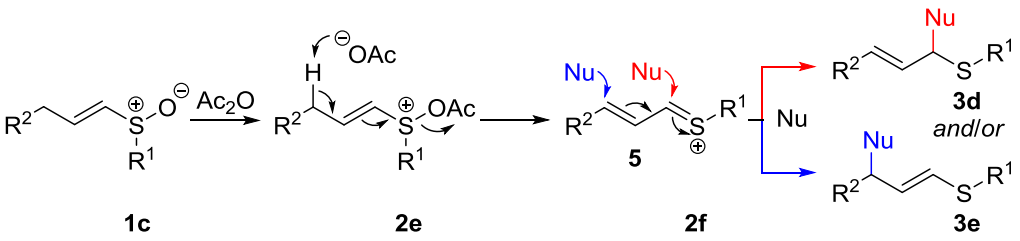
A more recent example of additive Pummerer chemistry can be seen in the synthesis of thionucleosides by Haraguchi (Scheme 6).[11] Upon activation with Ac_2O and $BF_3{\bullet}OEt_2$, cyclic sulfoxide **13** underwent an addition sequence that gave diacetate **14** in a 61% yield. It was found important for the survival of the silylene protecting group that the reaction was carried out in the presence of TMSOAc. Glycosyl donor **14** underwent nucleophilic addition of uracil, via another thionium ion, to give thionucleoside **15** in high yield.



Scheme 6

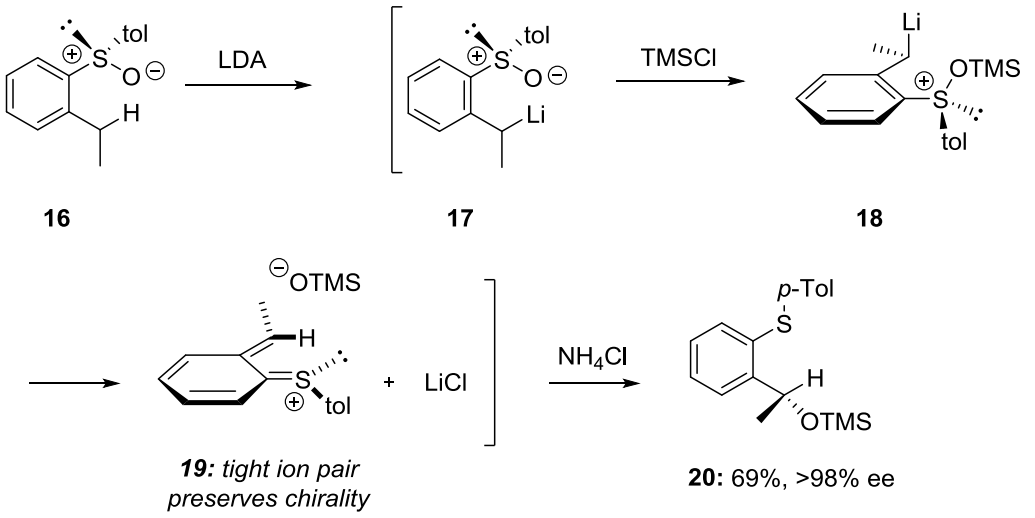
1.1.2.2 Vinylogous Pummerer reactions

In contrast to additive Pummerer reactions, α,β-unsaturated sulfoxides can react via a vinylogous pathway. The first step of a vinylogous Pummerer reaction is electrophilic activation of sulfoxide **1c** (Scheme 7). This is followed by expulsion of the activated sulfoxide oxygen to form an extended thionium ion **2f** through the loss of a γ-proton in **2e**. With the addition of a nucleophile to this intermediate there are two possible addition pathways; direct 1,2-addition to the thionium group (red nucleophile) gives allyl sulfides **3d**, whereas addition at the vinylogous site (blue nucleophile) affords unsaturated vinyl sulfides **3e**.



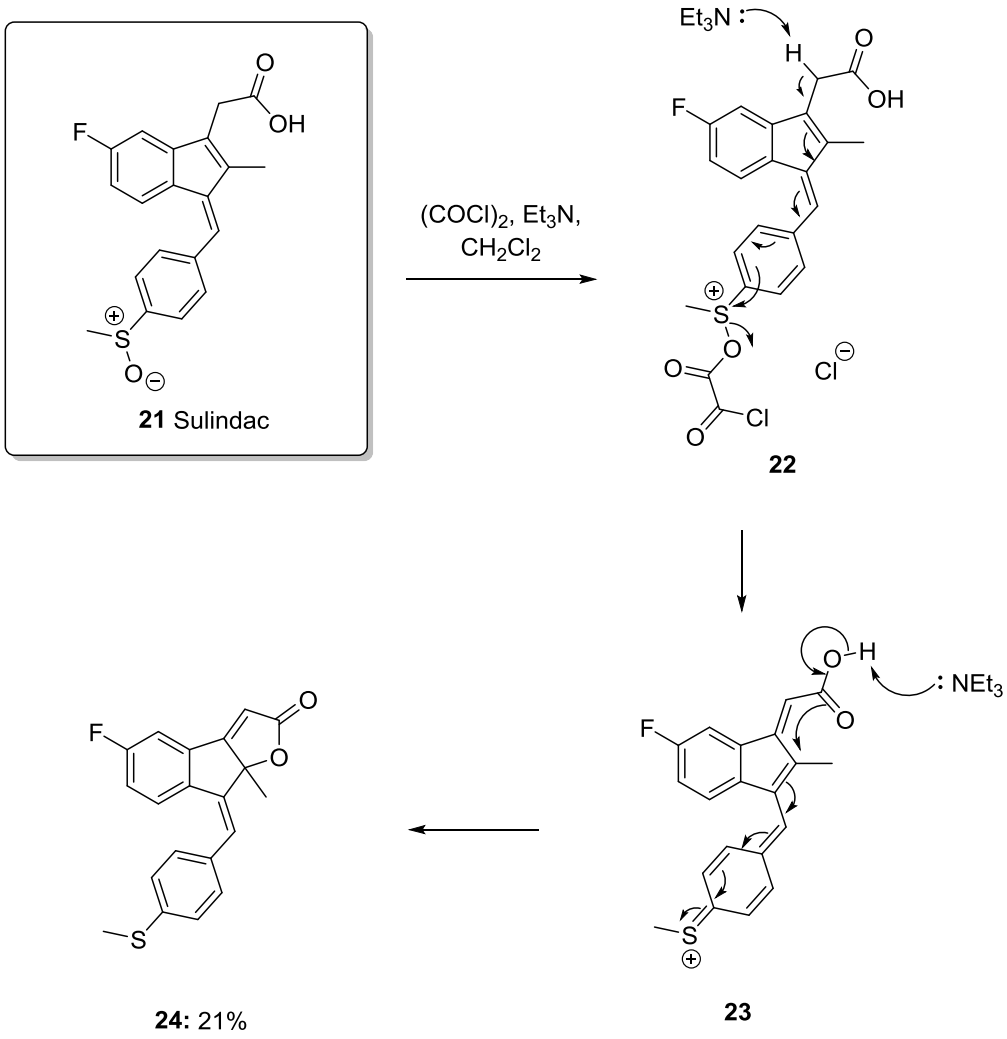
Scheme 7

Garcia Ruano and Padwa reported a vinylogous Pummerer reaction of *ortho*-sulfinyl alkyl benzenes that proceeded with high stereoselectivity (Scheme 8).[12] Treating sulfinyl benzene **16** with LDA is thought to give benzyllithium **17**. Further treatment with TMSCl is believed to activate the sulfinyl oxygen (**18**) and following the loss of lithium gives conjugate thionium salt **19**, believed to exist as a tight ion pair. The vinylogous Pummerer reaction that follows proceeds with efficient relay of stereochemical information from the parent sulfoxide to the enantiomerically enriched TMS protected benzyl alcohol **20**.



Scheme 8

Vinylogous Pummerer reactions may also occur via highly extended thionium ions. This has been demonstrated by Satyam and Halder who synthesised sulindac sulfide lactone, from the non-steroidal anti-inflammatory drug (NSAID) sulindac (**21**), via a long range vinylogous Pummerer-type reaction (Scheme 9).[13] It was thought that sulindac **21**, after activation with oxalyl chloride to give intermediate **22** and the addition of Et_3N, underwent elimination to give highly extended thionium ion **23**. Carboxylate cyclisation then furnished sulindac sulfide lactone **24** in 21% yield.

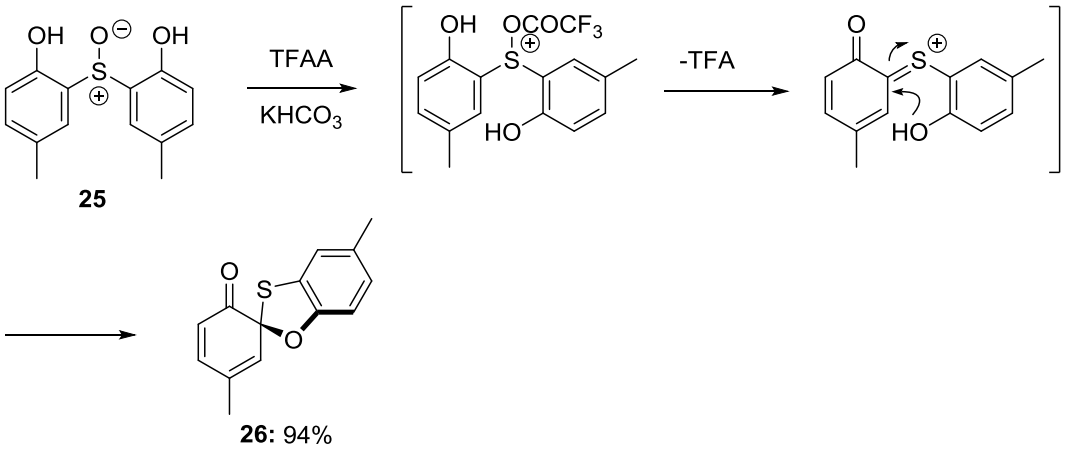


Scheme 9

The comparison between additive and vinylogous Pummerer pathways may not always be obvious, as both pathways can give the same product. However, it is interesting to consider both pathways when studying the reactivity aromatic sulfoxides, as is the case in much of this thesis, as the conjugation in these systems may mean that the products arising from either a vinylgous or additive pathway could be highly differentiated. Therefore, understanding the distinction between these two mechanisms will become increasingly important.

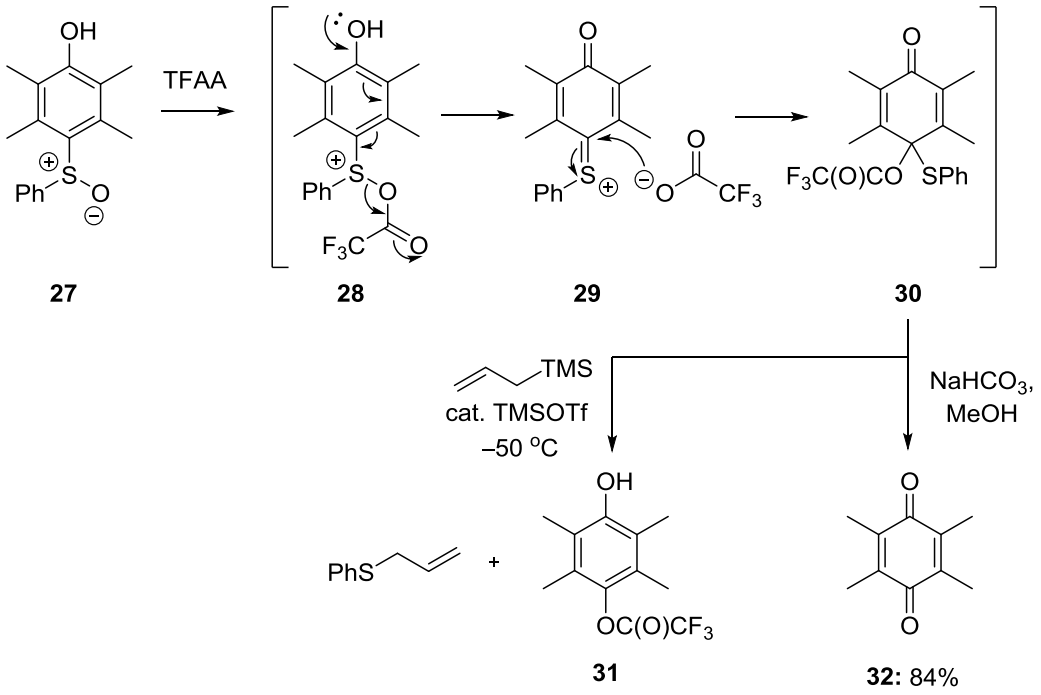
1.1.3 Aromatic and Hetero-aromatic Pummerer-type Reactions

Since the discovery by King that aromatic ring oxidation is possible by a Pummerer reaction, much effort has been invested in investigating the scope of aromatic Pummerer reactions and their application in synthesis.[14] For example, Jung has shown that upon activation with TFAA, bisphenolic sulfoxide **25** underwent an intramolecular Pummerer reaction, allowing access to spirocyclic hexadienone product **26** in high yield (Scheme 10).[15, 16]



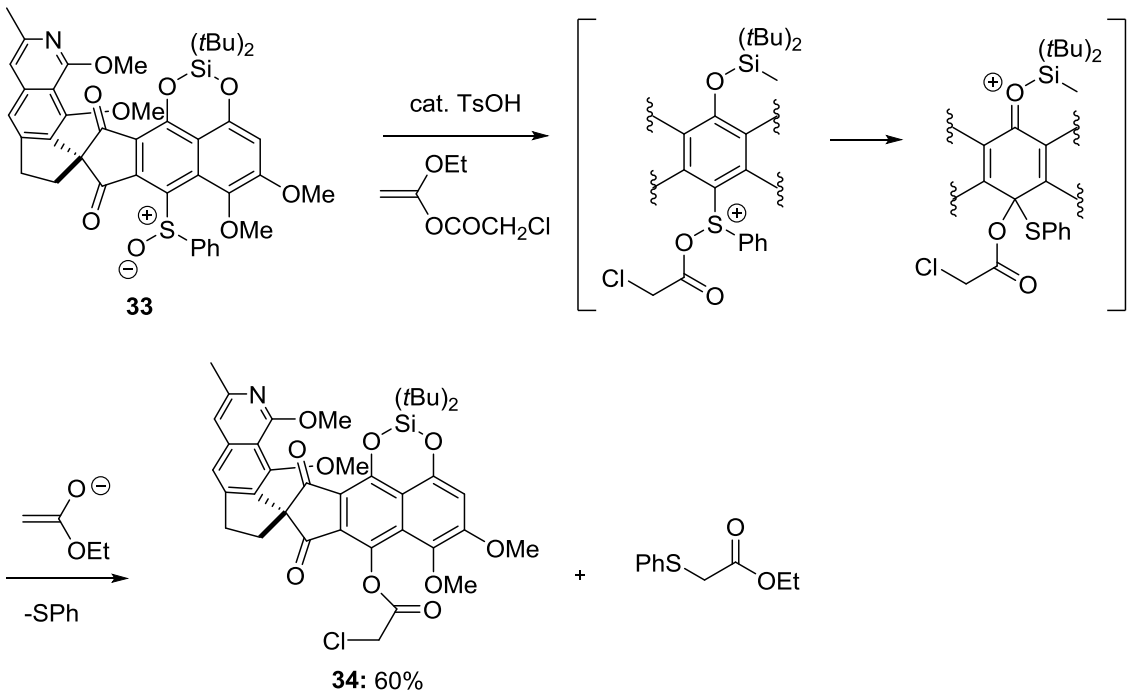
Scheme 10

Independent to Jung's development of this system, Kita et al. investigated the *ipso*-substitution of *para*-sulfinylphenols in an efficient synthsis of *para*-quinones (Scheme 11).[17-20]



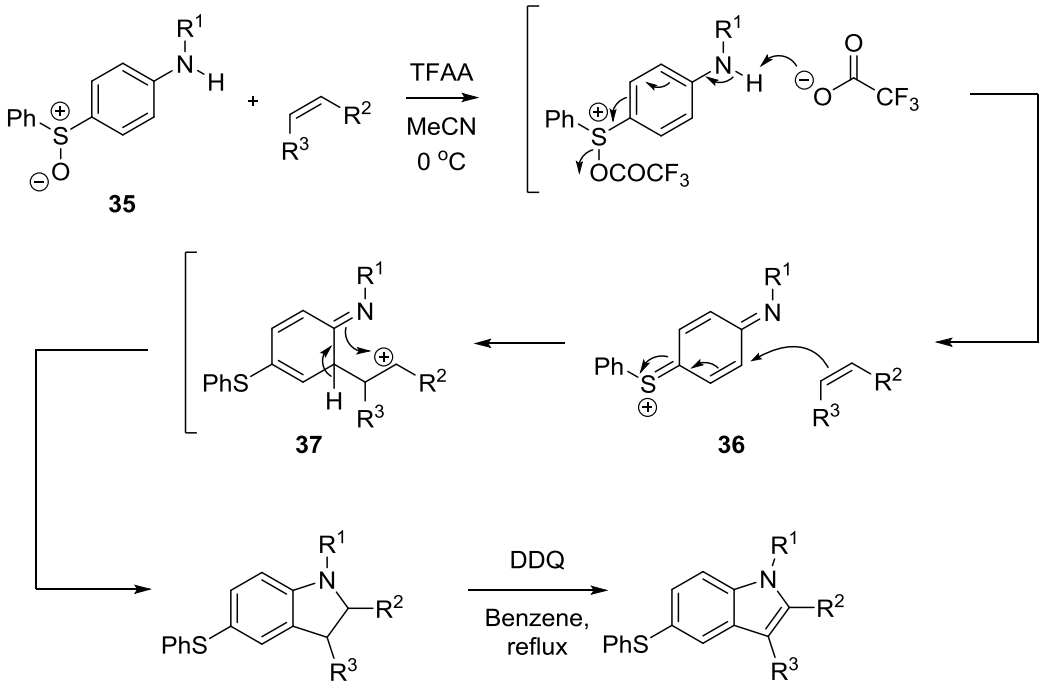
Scheme 11

Sulfinylphenols such as **27** are believed to undergo activation with TFAA to give sulfoxonium intermediate **28**. Thionium ion **29** is then formed through elimination of trifluoroacetate and attack by trifluoroacetate on thionium ion **29** is then believed to produce *S*,*O*-acetal intermediate **30**. Treatment of intermediate **30** with allyltrimethysilane and catalytic amounts of TMSOTf (5 mol%) gave mono(trifluoroacetyl) dihydroquinone **31** along with phenylallylsulfide as a side product. Under basic conditions intermediate **30** underwent hydrolysis of the trifluoroacetate and elimination of the phenylsulfanyl group, to give *para*-quinone **32** in high yield.[21] This methodology was applied to the synthesis of fredericamycin **34** through an *ipso*-substitution of sulfoxide **33**, executed in the presence of a quaternary β-dicarbonyl (sensitive to nucleophiles) and masked hydroquinones (sensitive to oxidation) with no undesired degradation and in good yield (Scheme 12).[19, 22]



Scheme 12

Kita has also demonstrated a synthesis of 2,3,5-substituted indoles that is thought to proceed via a 1,4-addition to an extended thionium ion (Scheme 13).[23] Protected sulfinyl anilines such as **35** were activated using TFAA and after deprotonation are believed to give intermediate **36**. A vinylogous Pummerer-type addition of the alkene nucleophile is then thought to generate carbocation **37** which, following rearomatisation and cyclisation, affords products **38** and **39** in good yields. Simple oxidation with DDQ in refluxing benzene then gave indoles as the sole products.

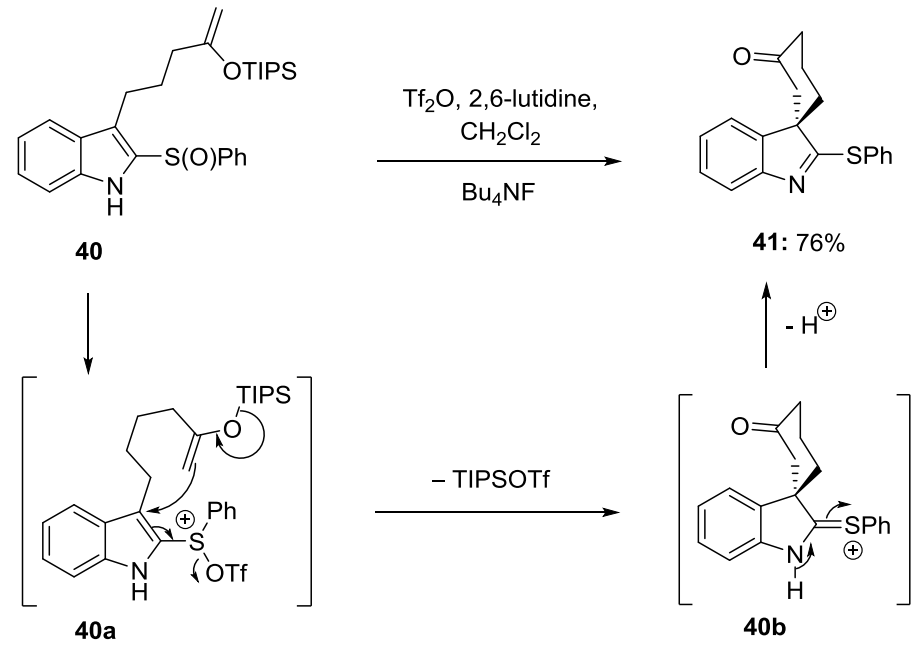


38: R^1 = Ts, R^2 = $C_6H_3(OMe)_2$, R^3 = Me, 75%

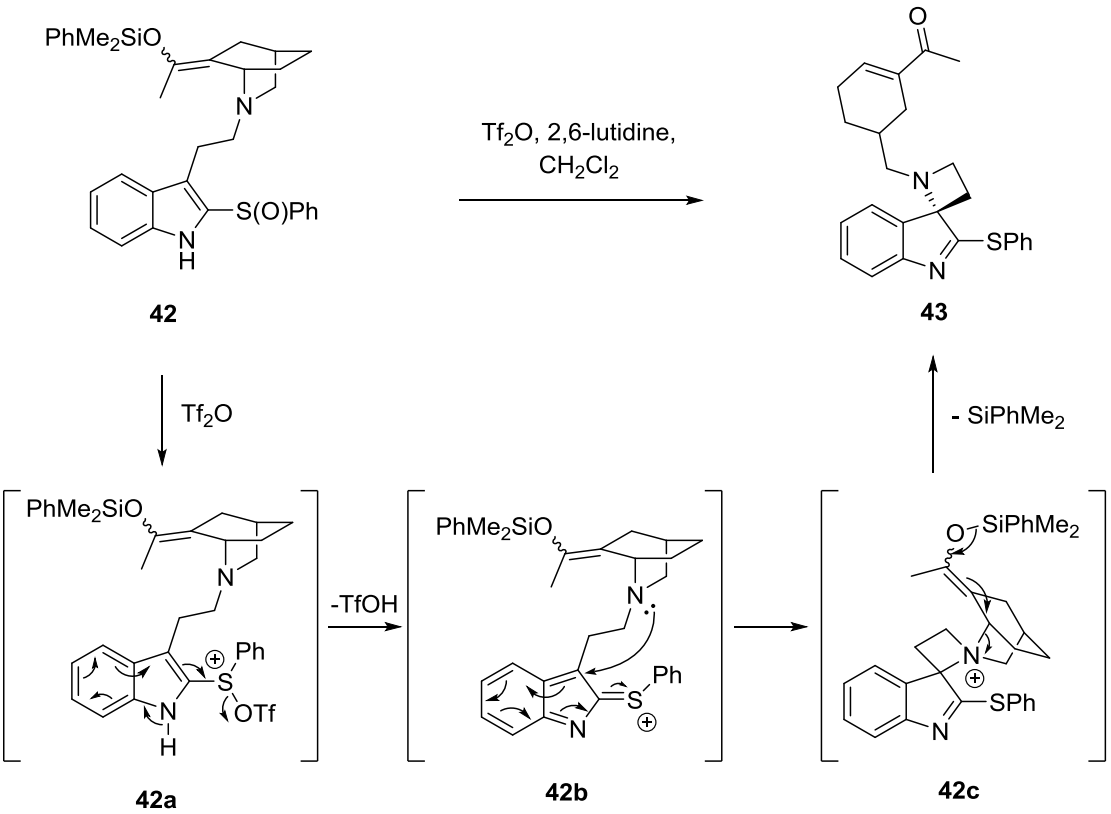
39: R^1 = Ns, R^2 = C_6H-4-OMe, R^4 = CO_2Et, 55%

Scheme 13

Feldman and co-workers have developed and demonstrated an aromatic Pummerer reaction on substrates containing a tethered silyl enol ether nucleophile (Scheme 14).[24, 25] Using Tf_2O to activate sulfoxide **40**, it is thought that an additive mechanism through intermediates **40a** and **40b** leads to spirocyclic product **41** in good yield. An interesting example of the comparison between additive and vinylogous mechanisms can be seen here when enol ether **42** was used as a substrate (Scheme 15). Expulsion of the activated oxygen of sulfoxide **42a** is thought to generate thionium ion **42b** which then undergoes nucleophilic attack by nitrogen to form ammonium ion **42c**. Collapse of **42c** ultimately generates spiroazetidine **43**. These reactions show the usefulness of aromatic Pummerer-type reactions and thionium ion intermediates in dearomatising C-C bond formations.

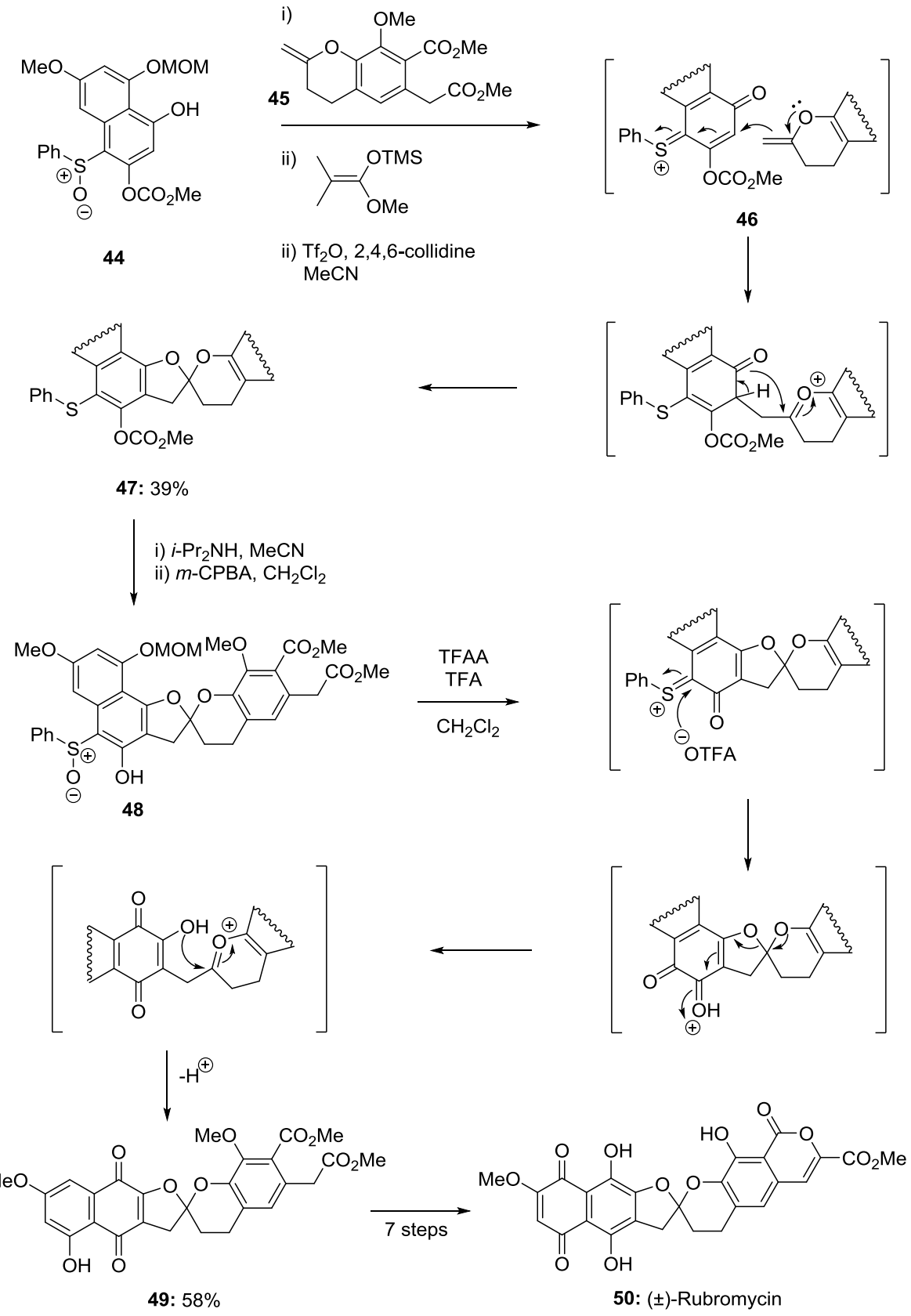


Scheme 14



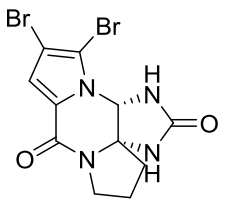
Scheme 15

The antibiotic (±)-γ-Rubromycin **50** was synthesised by Kita et al. in a sequence based on two aromatic Pummerer-type reactions (Scheme 16).[26] (±)-γ-Rubromycin exhibits activity against the reverse transcriptase of human immunodeficiency virus-1 and contains a highly oxygenated naphthoquinone, a 8-hydroxyisocoumarin moiety and a 5,6-spiroketal system. The first aromatic Pummerer reaction is thought to occur via 1,4-addition of enol ether **45** to thioquinone intermediate **46** after *in-situ* protection of the phenol in **44** with methyl trimethylsilyl dimethylketene acetal and activation of the sulfoxide. The resulting intermediate is then thought to cyclise to give spiroketal system **47** in moderate yield. Following deprotection and oxidation of sulfide **47**, sulfoxide **48** was subjected to a TFAA-mediated *ipso*-substitution of the sulfanyl group via the previously described Pummerer reaction. A successive acid-mediated ketal rearrangement furnishes spiroketal **49** in good yield which was then converted to (±)-γ-Rubromycin **50** in seven further steps.

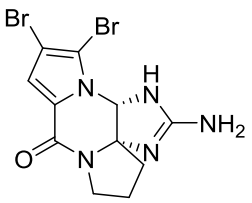

i)
ii)
45
44
ii) Tf2O, 2,4,6-collidine
MeCN
46
47: 39%
i) i-Pr2NH, MeCN
ii) m-CPBA, CH2Cl2
48
TFAA
TFA
CH2Cl2
OTFA
-H⊕
49: 58%
7 steps
50: (±)-Rubromycin

Scheme 16

Feldman has reported the synthesis of two natural products, dibromophakellstatin **51**, and dibromophakellin **52** (Figure 1) from a common intermediate **53** (Scheme 17).[27] The synthesis began with an intramolecular Pummerer reaction initiated by Stang's reagent. Again, the dichotomy of the additive/vinylogous Pummerer-type reaction is present here; the amide nitrogen could potentially attack in tandem with expulsion of the activated group, giving intermediate **54** or after simple loss of the activated group, giving intermediate **55**. In either case, this is followed by nucleophillic attack of the pyrolle nitrogen and with the loss of a proton funishes tetracycle **56**. Intermediate **56** was converted through a CAN mediated hydrolysis of the (phenylsulfanyl)amidine group to dibromophakellstatin **51** which was then converted to dibromophakellin **52** in 2 further steps.[28, 29]

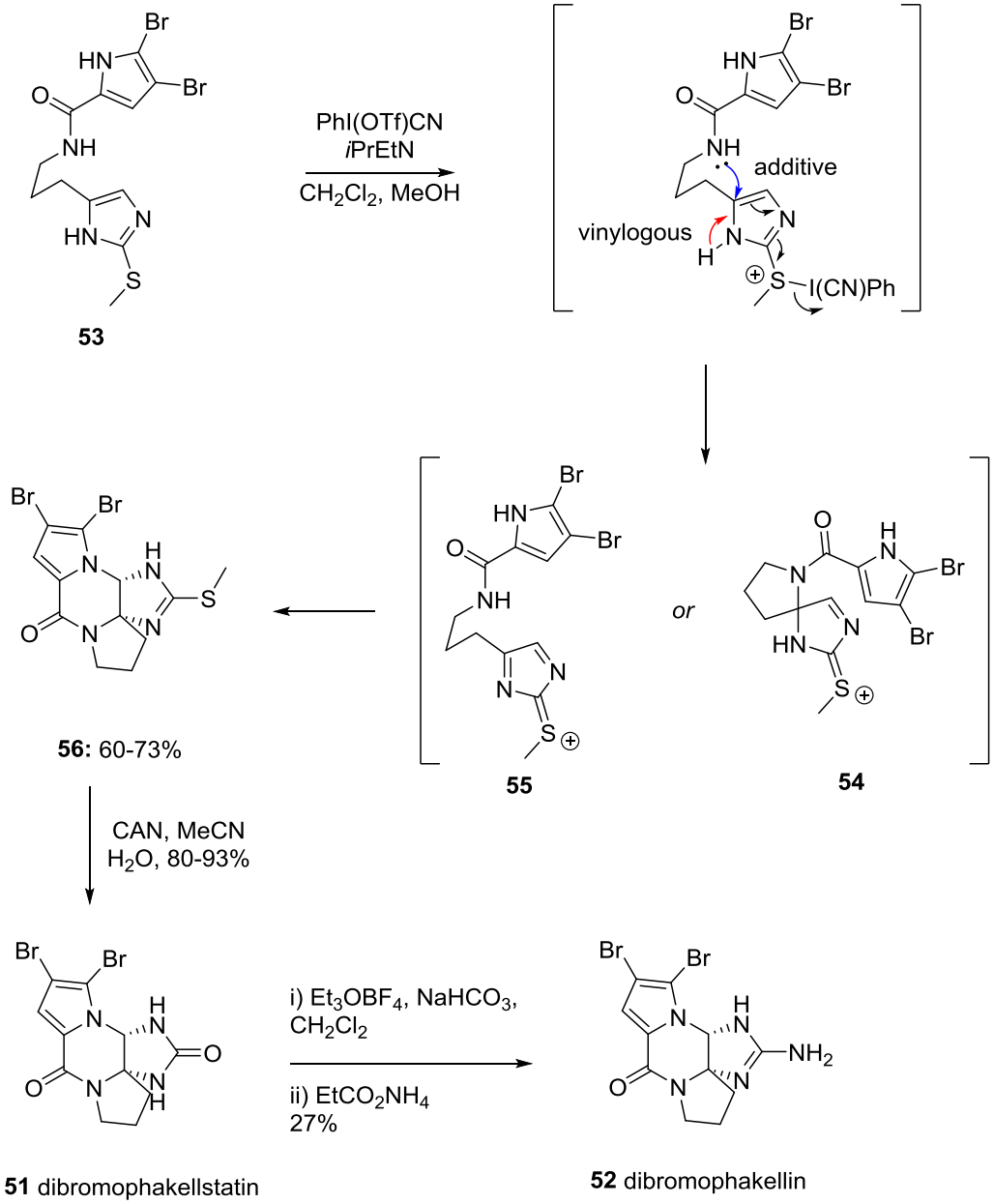


51 dibromophakellstatin



52 dibromophakellin

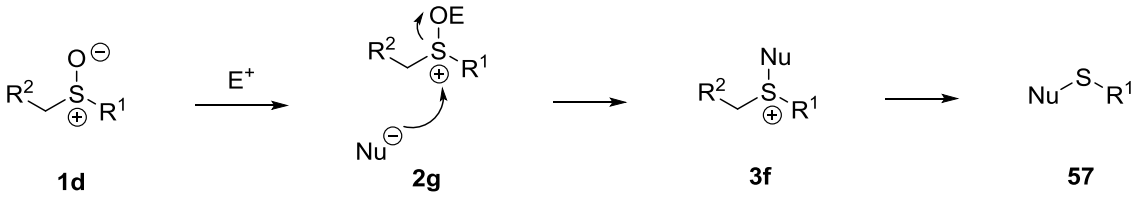
Figure 1


Br
HN
Br
O
NH
HN
N
S
53
PhI(OTf)CN
iPrEtN
CH2Cl2, MeOH
additive
vinylogous
I(CN)Ph
or
55
54
56: 60-73%
CAN, MeCN
H2O, 80-93%
i) Et3OBF4, NaHCO3,
CH2Cl2
ii) EtCO2NH4
27%
NH2
51 dibromophakellstatin
52 dibromophakellin

Scheme 17

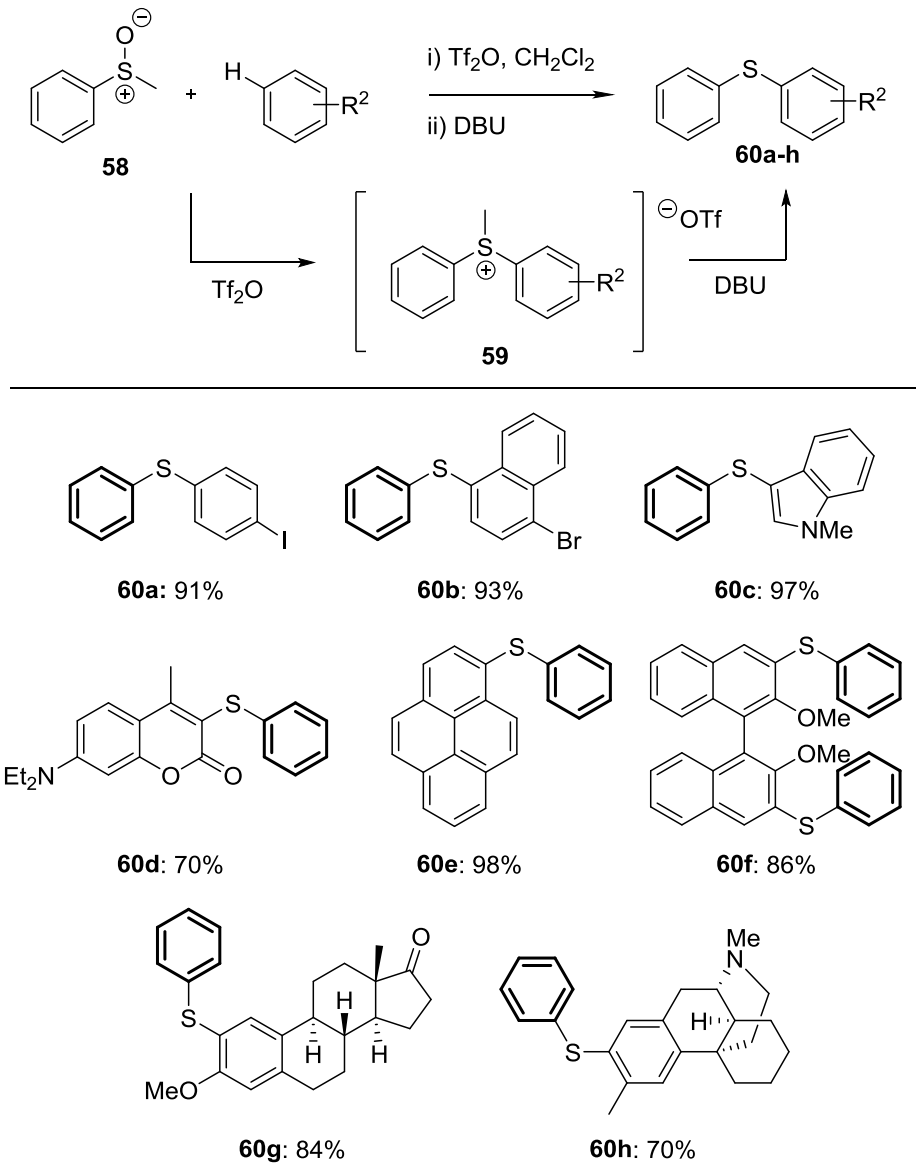
1.1.4 Interrupted Pummerer Reactions

Direct nucleophilic attack at the sulfur atom of an activated sulfoxide, usually caused by the lack of a sufficiently acidic α-proton for classical thionium ion formation, is known as an interrupted Pummerer reaction (Scheme 18). Attack by a nucleophile upon activated sulfoxide **2g** and expulsion of the activated oxygen gives sulfonium salt **3f**. Often these species can be isolated as reaction products however further reaction is also possible for example, cleavage of one C-S bond allows the formation of sulfide products (**57**).[30]



Scheme 18

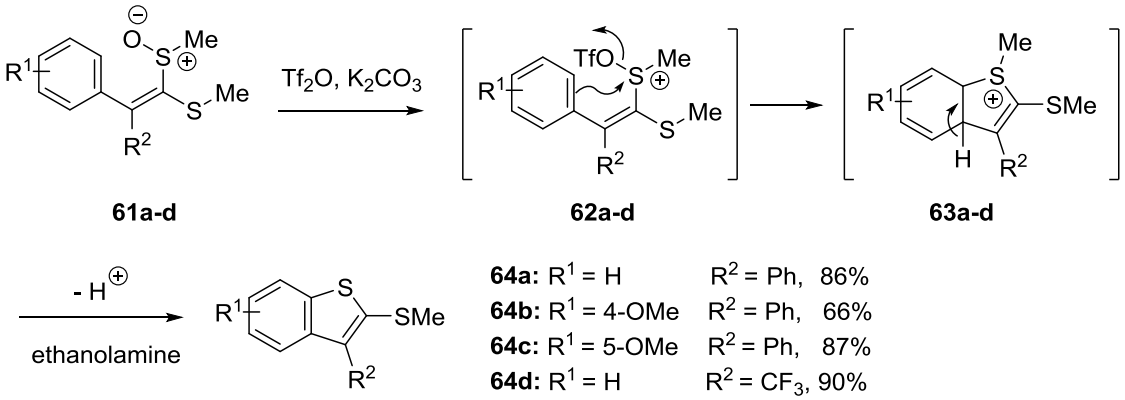
Recently, Procter and coworkers have demonstrated a simple use of an interrupted Pummerer reaction in the metal-free synthesis of a wide range of diaryl sulfides.[31] A general reaction is shown in Scheme 19**.** The reaction begins with the activation of arylmethylsulfoxide **58** by trifluoromethanesulfonic anhydride and is followed by the attack of an aryl nucleophile at the highly electrophilic sulfur of this species to form diarylsulfonium intermediates **59**. A simple demethylation with DBU then furnishes the final diarylsulfide products **60a-h**.



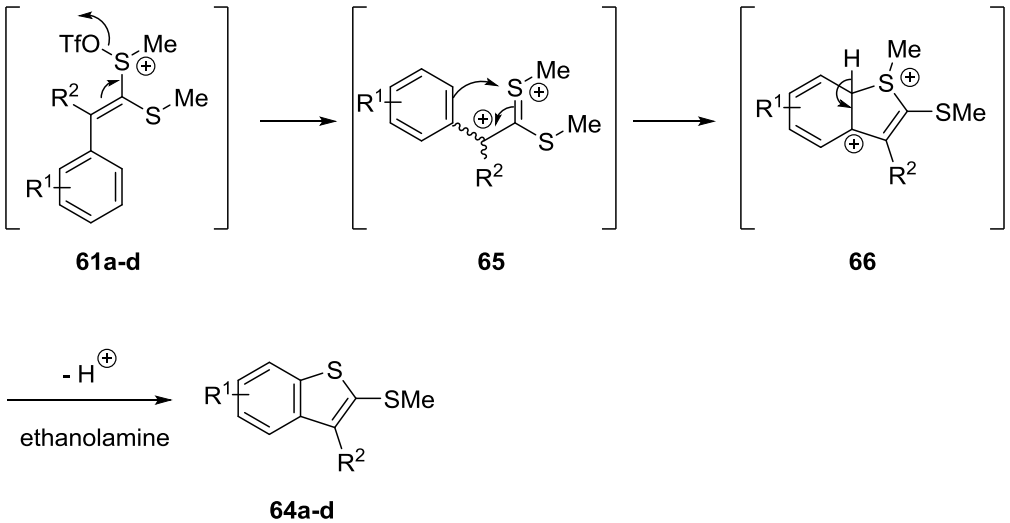
Scheme 19

Owing to the high electrophilicity of the activated sulfoxide a wide range of aryl nucleophiles and aryl sulfoxide starting materials were tolerated in this reaction. A high level of functional group tolerance was also observed, including halogen substituted arenes (**60a** and **60b**), a moiety that is often incompatible with metal catalysed diarylsulfide synthesis, and heteroaromatic substrates (**60c**). Of most interest was the application of this methodology to late stage diversification of a range of more complex molecular scaffolds. As shown in Scheme 19, coumarin based fluorophore **60d**, pyrene **60e**, dimethyl BINOL **60f**, estrone methyl ether **60g** and dextromethorphan **60h** all underwent smooth thioarylation, thus showcasing the utility of interrupted Pummerer chemistry in the modification of intricate structures.

Oshima and Yorimitsu have shown that the cyclisation of arylketene dithioacetal monoxides via an interrupted Pummerer reaction gives highly substituted benzothiophenes.[32] As shown in Scheme 20, activation of sulfoxides **61a-d** with Tf_2O is thought to lead to cyclised intermediates **63a-d** through direct attack of the aromatic ring onto sulfur. Following rearomatisation, these intermediates afforded highly substituted benzothiophenes **64a-d** in good yields. Interestingly, the choice of ketene dithioacetal monoxide isomer (*E*,*Z*) had little effect on the yield. This was rationalised by invoking dicationic intermediate **65** allowing bond rotation around the central C-C bond and attack of the aromatic ring onto the thionium once in the correct orientation (Scheme 21).

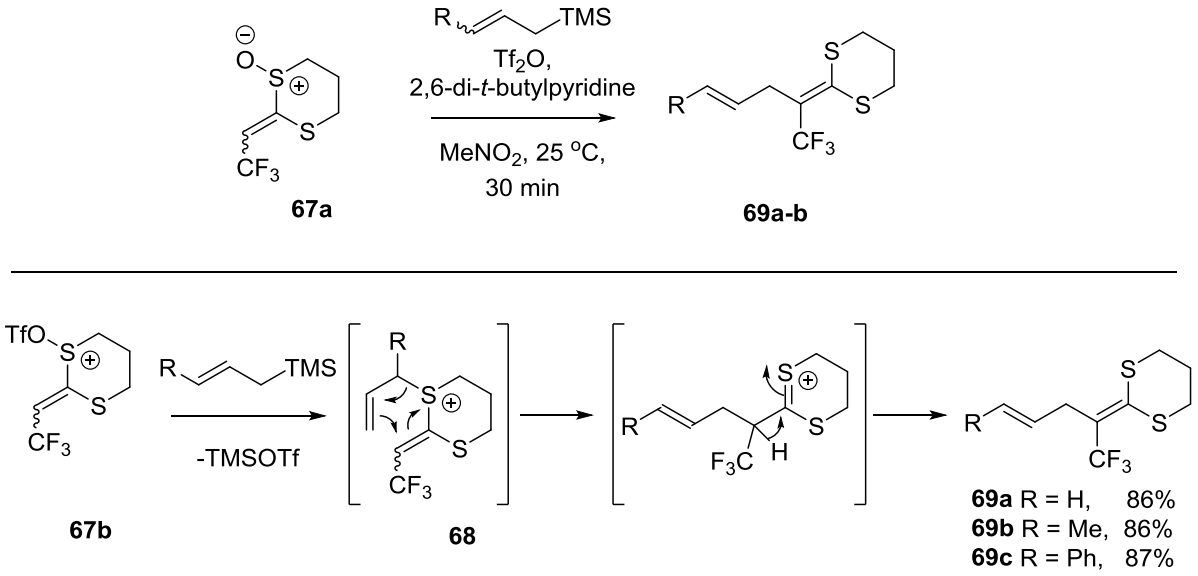


Scheme 20



Scheme 21

After identifying that **67a** could serve a as a trifluoromethylketene equivalent, Oshima and Yorimitsu developed a convenient synthesis of α-trifluoromethylated carbonyl compounds using an interrupted Pummerer reaction (Scheme 22).[33] Direct attack of an allylsilane upon activated sulfoxide **67b** is thought to produce sulfonium intermediate **68** which can undergo a [3,3]-sigmatropic rearrangement followed by deprotonation to provide dithioacetal products **69a-c** in high yields. Compounds such as **69a-c** are important intermediates in the approach to α-trifluoromethylketenes, a compound class that has proven useful in many biological studies.

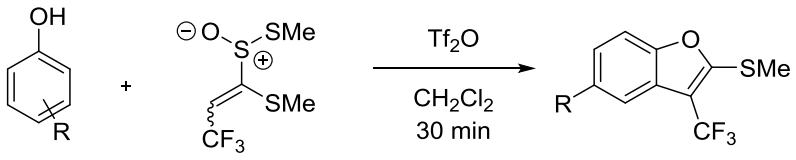


Scheme 22

1.2 Functionalisation of Aromatics Through Charge Accelerated Rearrangements

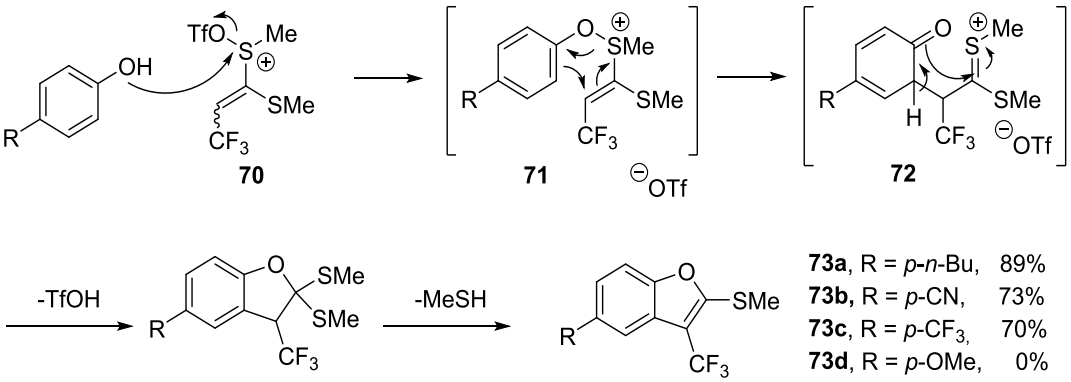
1.2.1 Charge Accelerated [3,3]-Sigmatropic Rearrangments

Interrupted Pummerer reactions always involve the formation of sulfonium or sulfoxonium intermediates, which have been demonstrated to be useful intermediates for use in charge-accelerated [3,3]-sigmatropic rearrangements. The 2-(2,2,2-trifluoroethylidene)-1,3-dithiane monoxide system (Scheme 22) was further employed by Oshima and Yorimitsu with phenolic nucleophiles to synthesize a range of substituted benzofurans (Scheme 23).[34]



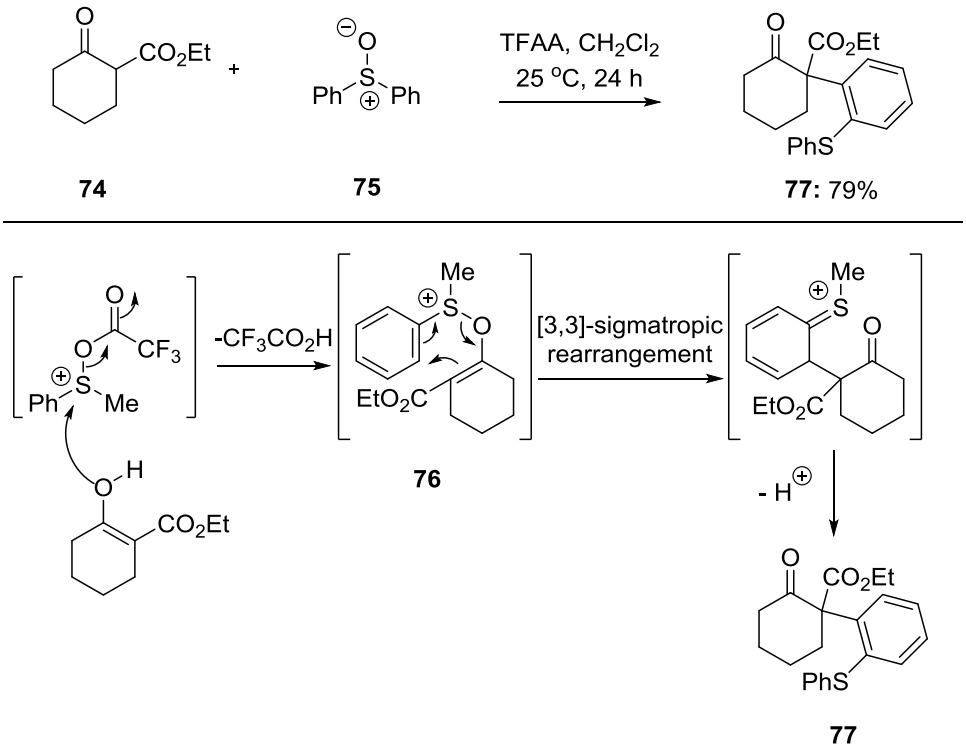
Scheme 23

This reaction is thought to proceed in a similar fashion to that of previous studies (shown in Scheme 22), beginning with attack of the phenolic oxygen at the electrophilic sulfur of activated 2-(2,2,2-trifluoroethylidene)-1,3-dithiane monoxide **70** to form sulfoxonium ion **71**. Following a [3,3]-sigmatropic rearrangement, **72** then smoothly cyclises and after rearomatisation, via the loss of methyl thiol, furnishes substituted benzofurans **73a-c** in good yields (Scheme 24). It must be noted that the use of *para*-methoxyphenol gave no reaction product due to triflation of the electron rich oxygen. This example demonstrates an interesting use of an sulfoxonium intermediate, generated through an interrupted Pummerer reaction, and subsequent charge accelerated [3,3]-sigmatropic rearrangement, to synthesise heteroaromatic scaffolds, all aspects of which are of interest in this report.



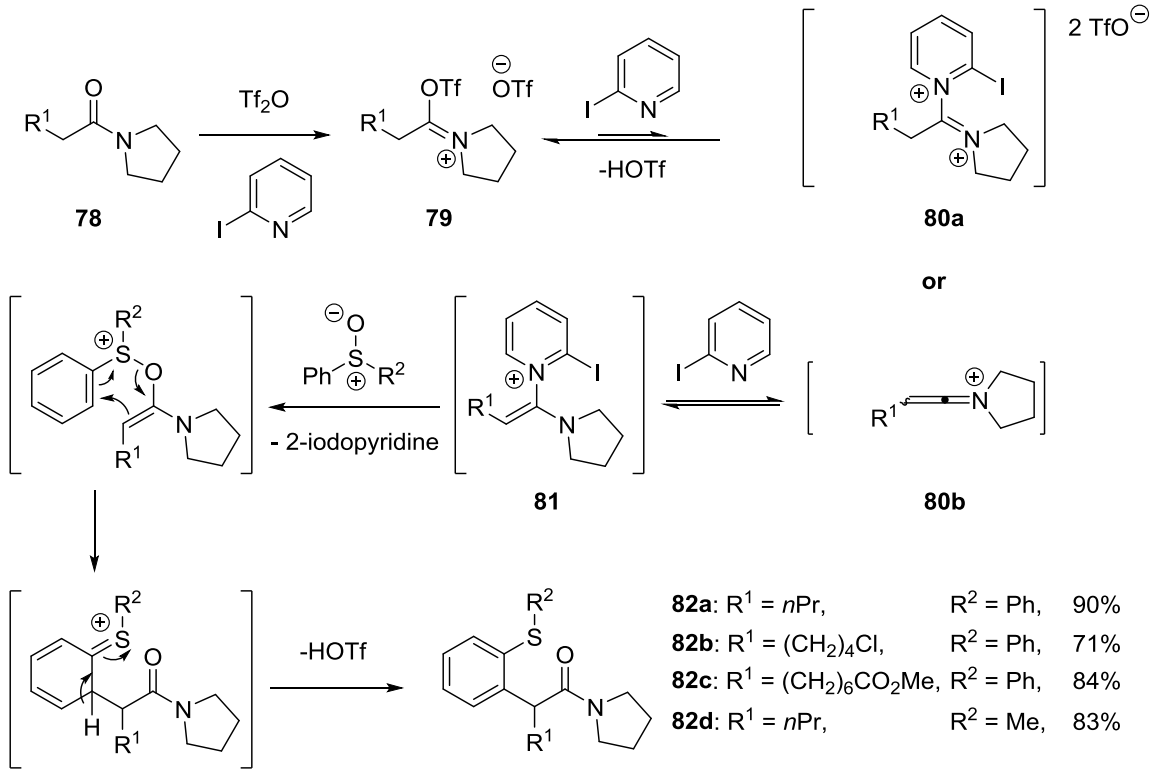
Scheme 24

Maulide has developed a sulfoxide mediated α-arylation of β-ketoesters; When TFAA was employed as an electrophilic activator of diphenylsulfoxide **75** in the presence of cyclic keto-ester **74**, arylated keto-ester **77** was isolated in high yields (Scheme 25).[35] This reaction is thought to proceed via an interrupted Pummerer/[3,3]-sigmatropic rearrangement sequence.[35, 36] Attack of the enol tautomer of keto-ester **74** on the activated sulfoxide is believed to produce sulfoxonium species **76**. A charge accelerated [3,3]-sigmatropic rearrangement followed by rearomatisation then furnished α-arylated keto-ester **77**.



Scheme 25

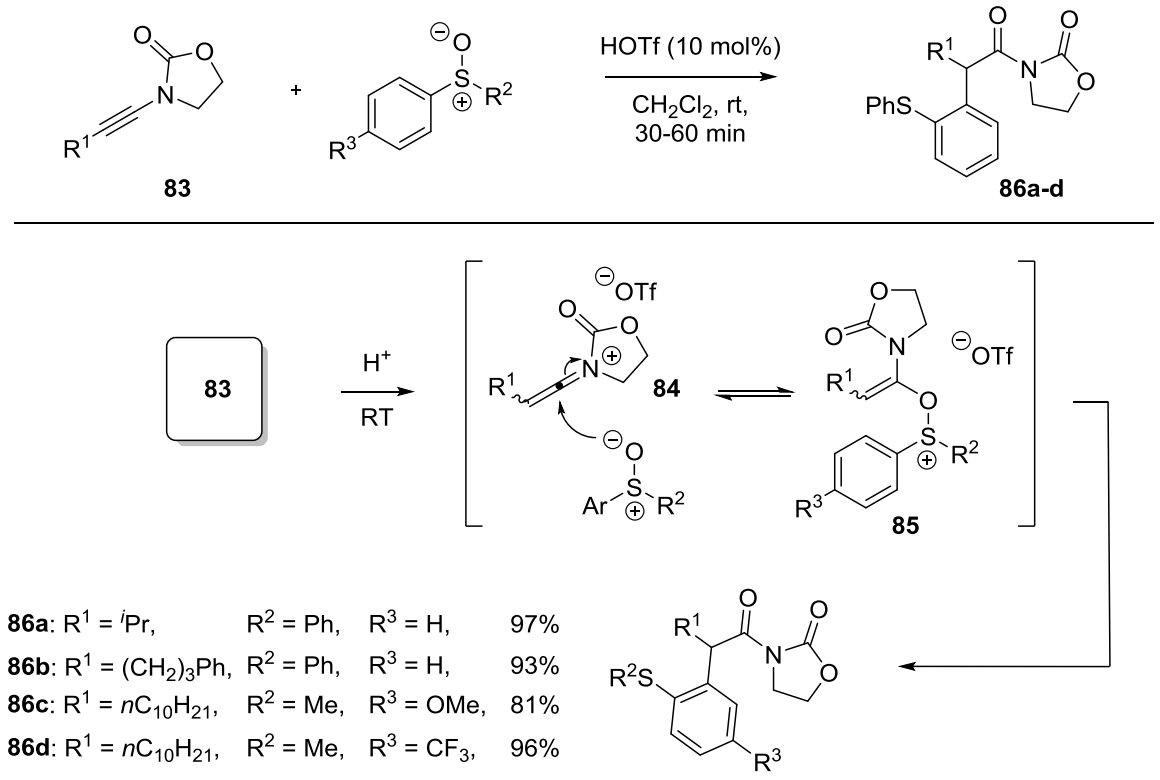
This methodology was later expanded by Maulide to include the α-arylation of amides (Scheme 26).[37] Competitive activation of the amide and sulfoxide proved to be a problem in this system. This was overcome by preactivation of the amide (**78**) to form intermediate **79**. In the presence of 2-iodopyridine, **79** was proposed to form either of the high energy intermediates **80a** or **80b** which can isomerise to form enamine type intermediate **81**. Subsequent reaction with diphenyl sulfoxide allows a charge accelerated [3,3]-sigmatropic rearrangement to take place. Rearomatisation then furnishes the α-arylated amides **82a-d** in high yields.



Scheme 26

This reaction shows an interesting difference from the previously considered interrupted Pummerer/[3,3]-sigmatropic rearrangement squences. In this case, the sulfoxide itself is not activated directly by triflic anhydride, rather it is activated by the activated coupling partner itself (**81**). In this way, the reaction reported in Scheme **26** does not represent an interrupted Pummerer reaction of any kind, however it does represent an interesting and relevant use of charge accelerated [3,3]-sigmatropic rearrangements in synthesis.

In a further modification to this reaction, Maulide and co-workers used oxazolidinone ynamides in a Bronsted acid-catalysed redox arylation (Scheme 27).[38] The reaction shows a good tolerance for a variety of sterically encumbered ynamides, providing a series of oxyarylated products at room temperature.

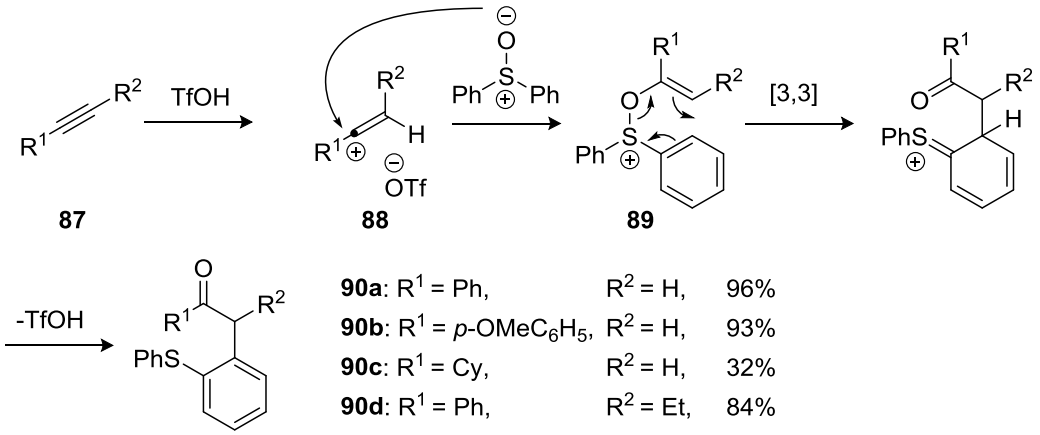


Scheme 27

This reaction proceeds via similar intermediates to that shown in Scheme 26. Preformation of intermediate ketiminiums **84**, from ynamide **83** and triflic acid, was follow by attack of the arylsulfoxide sulfinyl oxygen to form sulfoxonium intermediates **85**. A charge-accelerated [3,3]-sigmatropic rearrangement of these species formed products of hydrative arylation (**86a-d**), which were isolated high yields. It must be mentioned again that this mechanism does not represent an interrupted Pummerer reaction, only the use of sulfoxonium intermediates that could conceivably be formed by one.

From this study on acid catalysed redox arylations came two interesting elaborations on the usefulness of charge accelerated [3,3]-sigmatropic rearrangements in organic synthesis. Firstly, Maulide has shown that unactivated alkynes are convenient

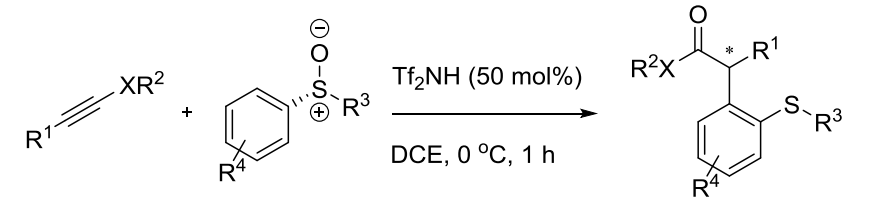
substrates for Bronsted acid mediated hydrative arylation (Scheme 28).[39] Protonation of unactivated alkyne **87** with TfOH gives vinyl cation intermediate **88** which can be trapped by diphenylsulfoxide to produce sulfoxonium intermediate **89**. This species is now primed for a charge accelerated [3,3]-sigmatropic rearrangement which furnishes products **90a-d** after rearomatisation.

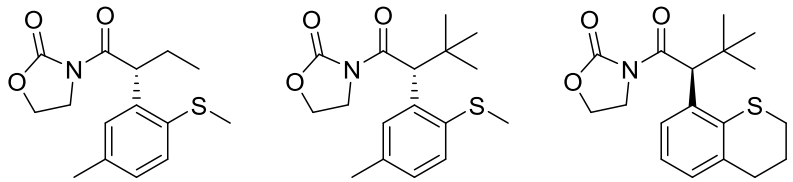


Scheme 28

DFT calculations provided evidence for the proposed mechanism of this reaction, indicating that overall the Scheme is thermodynamically favourable (ΔG = -65.0 kcal mol^{-1}). These calculations also agreed with the experimental observation that more electron rich sulfoxides (e.g. diphenylsulfoxide) outcompete less electron rich sulfoxides (e.g. methylphenylsulfoxide) for nucleophilic attack. Furthermore the stability of vinyl cation **88** was shown to be very important, with more electron rich alkynes producing a more stable intermediate and therefore a faster reaction.

Secondly, it has been demonstrated that the use of enantiomerically enriched sulfoxides, with slight changes of reaction conditions, results in an asymmetric equivalent of this redox arylation (Scheme 29).[40] This approach demonstrates an excellent use of chirality transfer from sulfur to carbon (see Marino's use of dichloroketenes for another reported example, Scheme 4). It was noticed that enantioselectivity increased with the steric bulk of alkynyl substituent R^1 (**91** to **92**)**.** Using cyclic sulfoxides a switch in enantioselectivty was observed, however the selectivity was still high (**93**) most likely due to a more rigid transition state. This reaction also tolerated different ynamides (**94**) and alkynylsulfides (**95**).

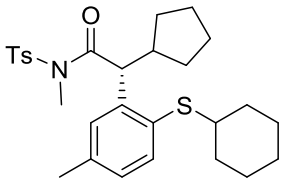




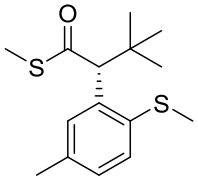
91: 76%
90:10 e.r.

92: 62%
97.5:2.5 e.r.

93: 79%
e.r. > 99.5:0.5



94: 83%
89.5:10.5 e.r.

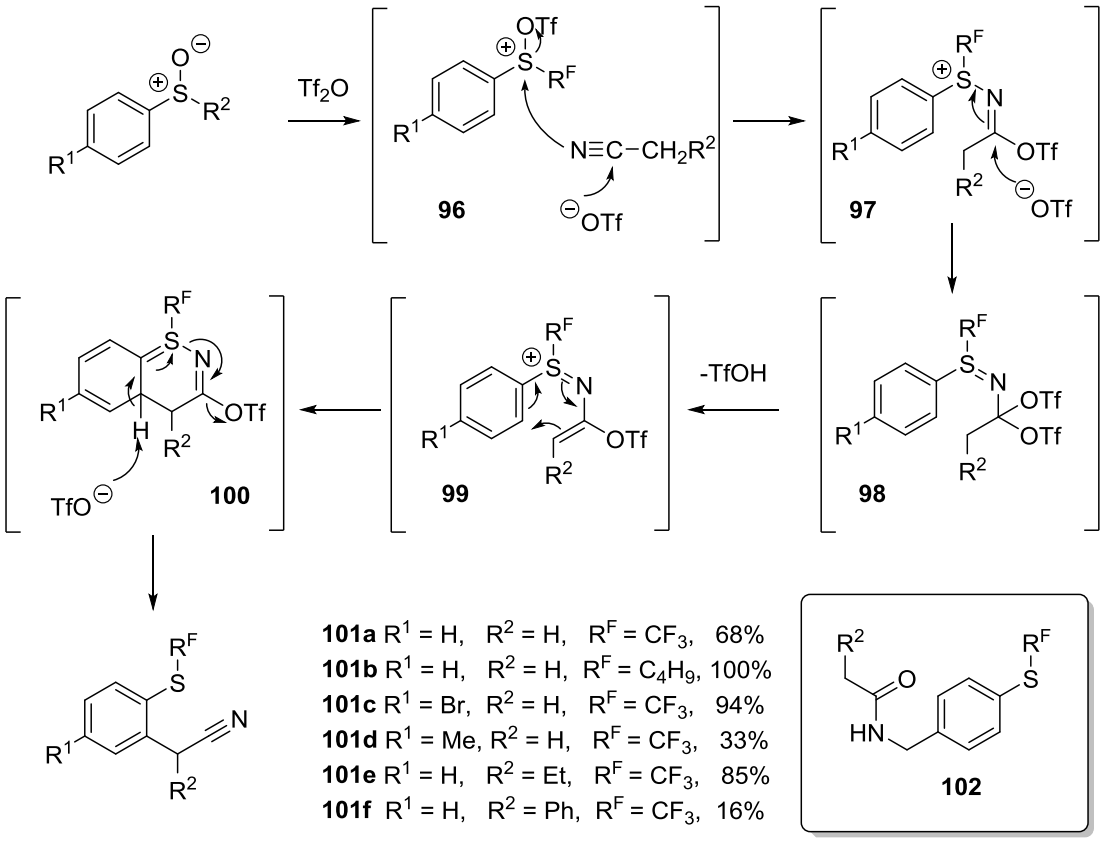


95: 73%
98.5:1.5 e.r.

Scheme 29

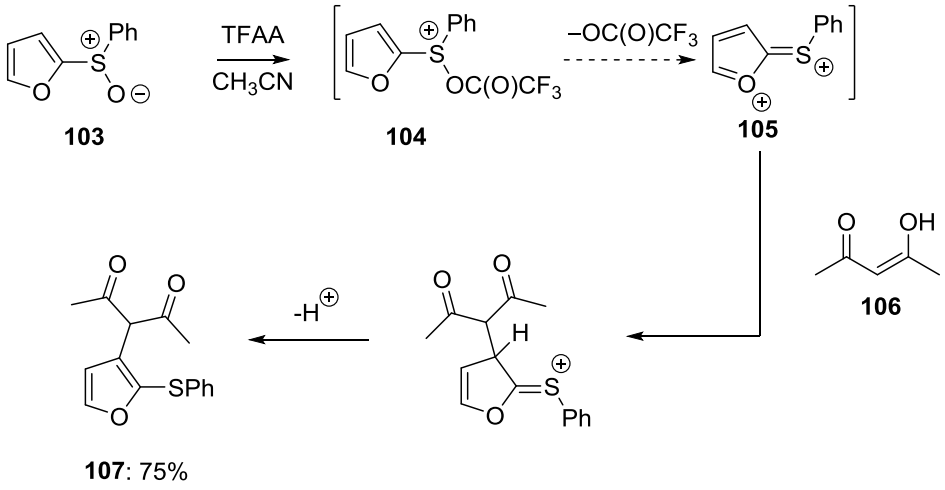
1.2.2 *Ortho* Alkylations of Aromatic and Heteroaromatic Systems

The use of Pummerer reactions to control selectivity, particularly in the *ortho* functionalisation of aromatic and heteroaromatic compounds, has recently been explored as a powerful alternative to traditional metal catalysed reactions. Magnier and co-workers, and more recently Peng[41], have demonstrated the formation of sulfilimines using a Tf_2O-activated Pummerer reaction of nitriles and perfluoroalkyl sulfoxides (Scheme 30).[42-45] The sulfilimine products are formed from the hydrolysis of intermediate **98**, the product of a Ritter-type, interrupted Pummerer reaction. Interestingly, when the reaction was carried out in the presence of a nitrile with a suitably acidic α-proton, elimination of TfOH is thought to have occurred to form sulfilimino ketenacetal **99** followed by an electrocyclic ring closure to give intermediate **100**. This intermediate presumably aromatises and opens the ring formed by the previous electrocyclic process, resulting in *ortho*-substituted aryl sulfides **101a-f**. The use of *p*-tolyl sulfoxide gave benzamide product **102** through an extended vinylogous Pummerer reaction triggered by the loss of a benzylic proton.



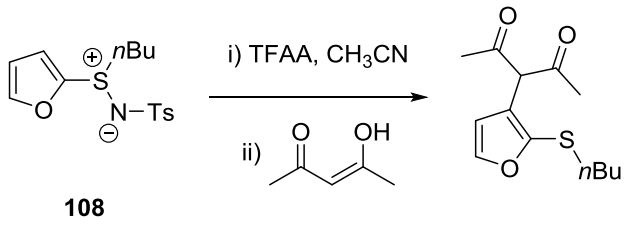
Scheme 30

Predating work reported by Maulide (Scheme 25), Kita and co-workers demonstrated an aromatic Pummerer reaction of C2-substituted thiophene and furan sulfoxides using carbon nucleophiles, shown in Scheme 31.[46] Furan sulfoxide system **103** was easily activated with TFAA to give sulfonium intermediate **104** which after explusion of trifluoroacetate gave thionium **105**. This was then trapped with carbon nucleophiles, such as 1,3 dicarbonyl **106**, to give C3 functionalised furan **107**. Reactions with furans bearing the sulfoxide moiety at the C3 postion proceeded with high *ortho* selectivity, giving the C2-substituted products in high yields. Although Kita proposed a vinylogous reaction pathway involving direct addition to the ring, an alternative mechanism involving an interrupted Pummerer process (attack at sulfur) cannot be ruled out.



Scheme 31

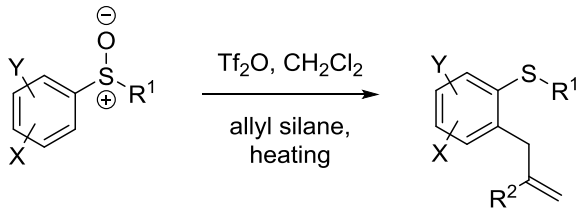
In a similar study Padwa et al. took advantage of an *N*-tosyl sulfilimine (the nitrogen analogue of a sulfoxide) to selectively *ortho* functionalise furan **111** in high yield (Scheme 32).[47]



108

Scheme 32

In recent years the Procter group have developed a methodology allowing the selective *ortho*-allylation and propargylation of a wide range of aromatic and heteroaromatic sulfoxides using allyl and propargyl silane nucleophiles. In the original studies, allylation of a range of aryl sulfoxides was investigated using Tf_2O as the electrophilic activating reagent and a variety of different allyl silane nucleophiles to give allylated aromatic sulfides **109a-e** (Scheme 33).[48] After activation with Tf_2O, aryl sulfoxide **110** underwent attack from the nucleophilic allyl silane coupling partner in an interrupted Pummerer-type reaction, giving sulfonium intermediate **111** which has been partially characterised by NMR. Upon heating, this intermediate then underwent a [3,3]-sigmatropic rearrangement to give *ortho*-allylated products **109f** with complete regioselectivity in both coupling partners.



109a: 60% X = H, Y= H, R^1 = Ph, $R^2 = CH_2Cl$,

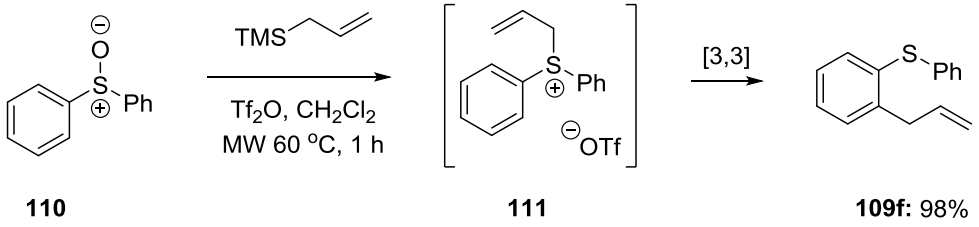
109b: 61% X = H, Y= H, R^1 = Ph, R^2 = Br,

109c: 72% X = *m*-MeO, Y= *m*-MeO, R^1 = Ph, $R^2 = CH_2Cl$,

109d: 67% X = H, Y= *m*-MeO, R^1 = Ph, R^2 = H,

109e: 94% X = *m*-Me, Y= m-Me, $R^1 = (CH_2)_2C_8F_{17}$ R^2 = Br,

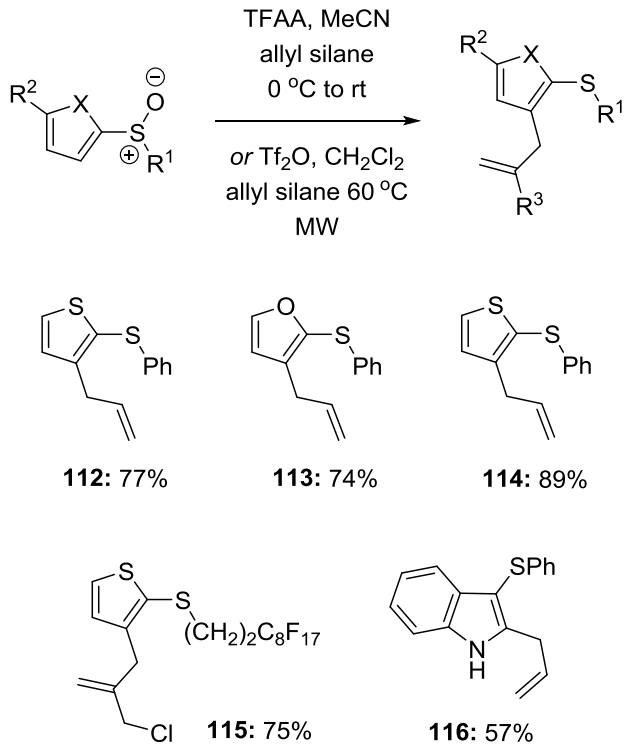
Scheme 33



110 **111** **109f:** 98%

Scheme 34

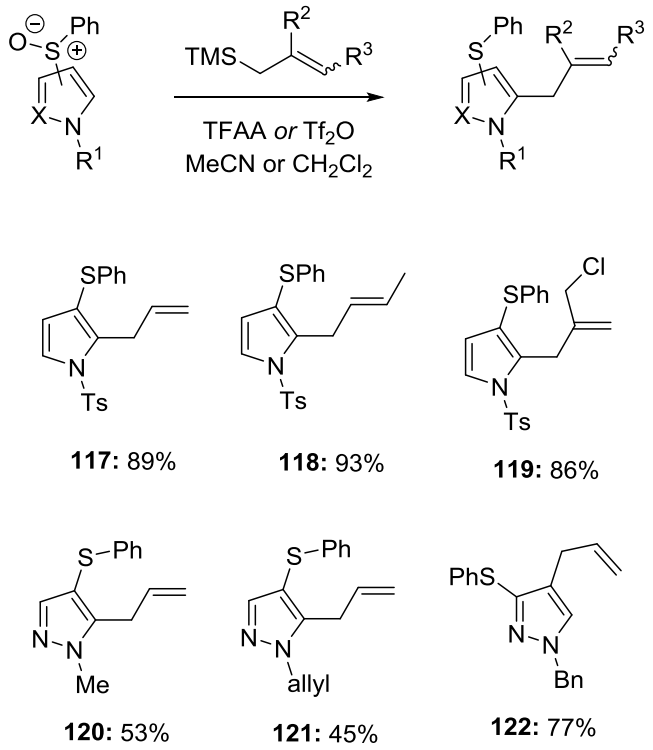
Looking to further elaborate the scope of this methodology, Procter et al. investigated the allylation of heteroaromatic systems shown in Scheme 35 and 36.[49] Under the optimal conditions, furans, thiophenes, indoles, pyrroles and pyrazoles were successfully allylated in good to high yields (**112-122**). These systems proved to be far more reactive than their aryl counterparts meaning less vigorous activating agents (TFAA) and lower temperatures were necessary for some substrates to avoid unwanted classical Pummerer chemistry.



112: 77% **113:** 74% **114:** 89%

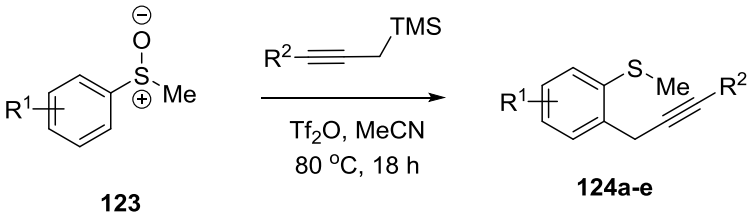
115: 75% **116:** 57%

Scheme 35



Scheme 36

On further investigation it was found that propargyl silanes could also be used as suitable nucleophilic coupling partners to give *ortho*-propargylated aromatic and heteroaromatic products.[50] Propargylation of aryl systems classically involves the use of stoichiometric amounts of metals and harsh conditions and often generates mixtures of allenyl and propargylic products.[51-54] This methodology allows for the facile propargylation of aromatic systems (**123**) using metal free conditions. No allenylation products were observed in any reaction. A variety of propargyl silanes and substituted aryl sulfoxides were screened and all provided the *ortho*-propargylation products in high yields (**124a-e**, Scheme 37).

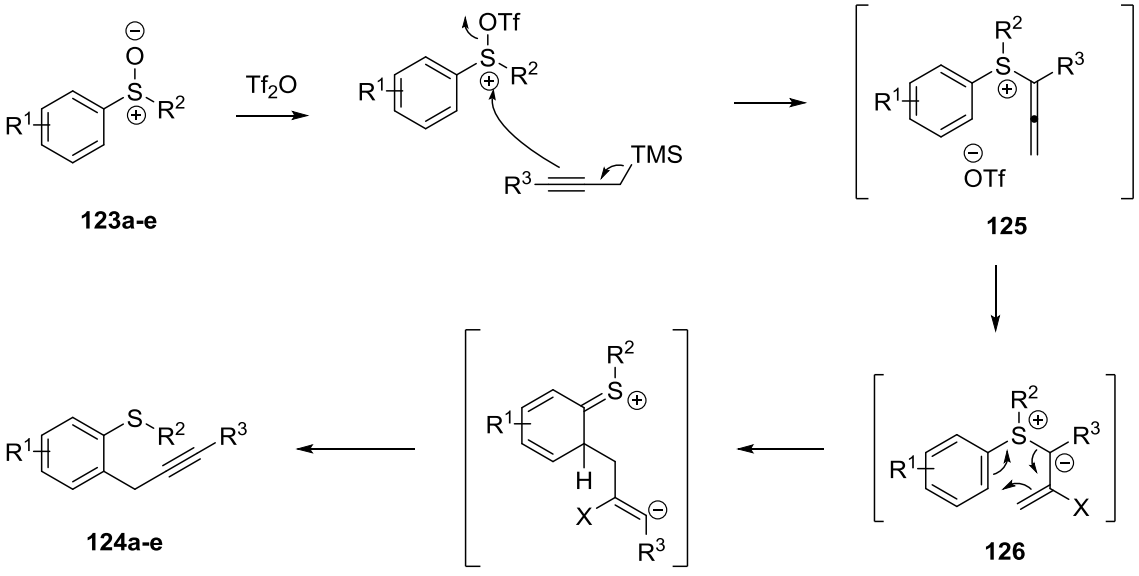


123 **124a-e**

124a	R^1 = H,	$R^2 = C_4H_9$,	91%
124b	R^1 = *p*-OMe,	$R^2 = C_4H_9$,	89%
124c	R^1 = *p*-CF_3,	$R^2 = C_4H_9$,	90%
124d	R^1 = H,	$R^2 = (CH_2)_2Ph$,	88%
124e	R^1 = H,	R^2 = Me,	96%

Scheme 37

Interestingly, the mechanism for this reaction proceeds through allenyl sulfonium salt **125**, which was stable and could be identified by NMR. Upon attack of a nucleophile, possibly triflate, and rearrangement to sulfur ylide **126**, a [3,3]-sigmatropic rearrangement and rearomatisation could be envisioned to occur. Further elimination of the triflate would then produce the *ortho*-propargylated products **124a-e** (Scheme 38).



123a-e **125** **126** **124a-e**

Scheme 38

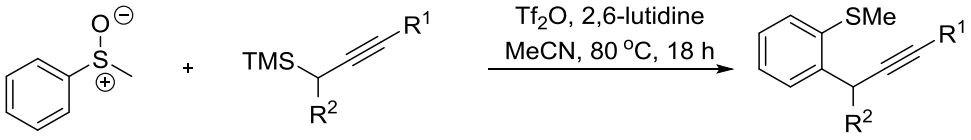
An interrupted Pummerer-type mechanism is supported in this instance by the observation of the exclusive formation of propargylated products. There is a possibility

that the propargyl silane coupling partner could add directly to the ring forming allenylated products, however, this was not observed. This concept will be of importance during this thesis when considering the mechanism of various sulfoxide-directed, metal-free, *ortho*-selective C-H functionalisations. Both the *ortho*-allylation and propargylation methodologies reported by Procter represent a potentially useful, metal-free course to selective aryl C-C bond formation. The products from *ortho*-propargylation reactions are of interest as carbon-carbon triple bonds are a functional group with high synthetic versatility.

As can be seen from this report, Pummerer reactions of all types represent a valuable methodology for many bond forming events. Amongst the most interesting of these are carbon-carbon bond forming reactions, especially when applied to aromatic and heteroaromatic systems. Recently, the ability of electrophilic sulfur to trap carbon nucleophiles by interrupted Pummerer reactions and selectively deliver that nucleophile to aromatic carbons at the expense of a C-H bond has shown the viability of this strategy for metal-free C-H functionalisation protocols.

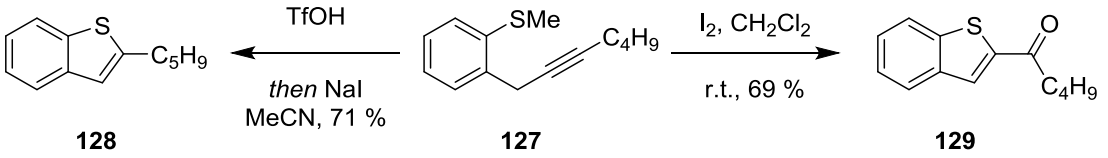
1.3 Proposed Work

The selective functionalisation of aromatic cores is an area of great interest in the field of organic chemistry and the ability to carry out carbon-carbon bond forming reactions on aromatic rings without the use of expensive, potentially contaminating and toxic metal catalysts is of particular interest in the synthesis of pharmaceuticals, agrochemicals and organic electronics. Henceforth, this project aims to further investigate scope for the metal-free propargylation of aryl and heteroaryl sulfoxide systems as described by Procter et al.[55] The use of branched propargyl silanes (Scheme 39) will allow the metal-free construction of sp^3 benzylic/propargylic centres, a novel bond to make using traditional metal catalysis, due to β-hydride elimation.

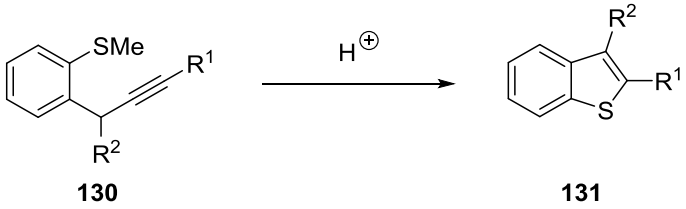


Scheme 39

This project will also aim to investigate the viability of these propargylation products as valuable intermediates in the synthesis of a wide range of privileged benzothiophene cores, molecules of wide interest in organic synthesis. As preliminary work has already shown (Scheme 40) activation of the alkyne moiety, with acid or molecular iodine, causes cyclisation of the arylsulfide and, following rearomatisation, affords substituted benzothiophene products (**128** and **129**). The use of branched propargyl compounds, such as **130**, in the synthesis of a range of di-substituted benzothiophene motifs (**131**) will initially be investigated (Scheme 41).

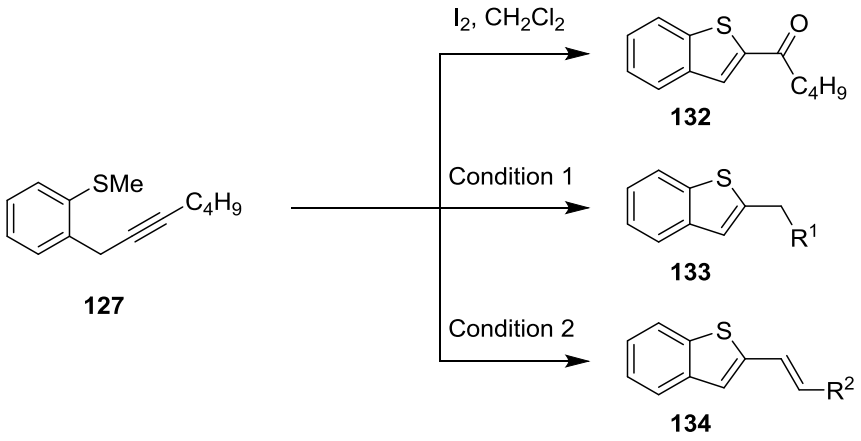


Scheme 40

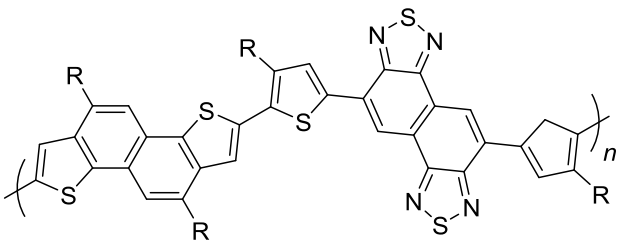


Scheme 41

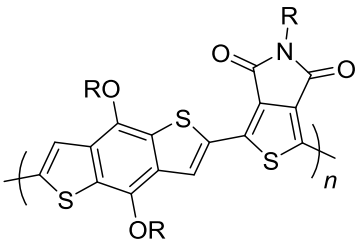
The ability to apply "tuneable" cyclisation conditions to the products of propargylation such as **127**, allowing the synthesis of a range of benzothiophene skeletons (**132-4**) from the same initial product, will be further investigated and expanded (Scheme 42). As diversity introducing heterocyclisations, these protocols will also be investigated in the synthesis of an assortment naphthodithophene (**135**) and benzodithiophene (**136**) scaffolds, molecules of much interest to organic materials scientists for their semi-conducting properties (Figure 2).[56-60]



Scheme 42



135: NDT
μ 0.5 cm^2/(V s); PCE 5%



136: BDT
PCE 6.6%

NDT = naphthodithiophene; BDT = benzodithiophene; μ = electron mobility; PCE = Power Conversion Efficiency

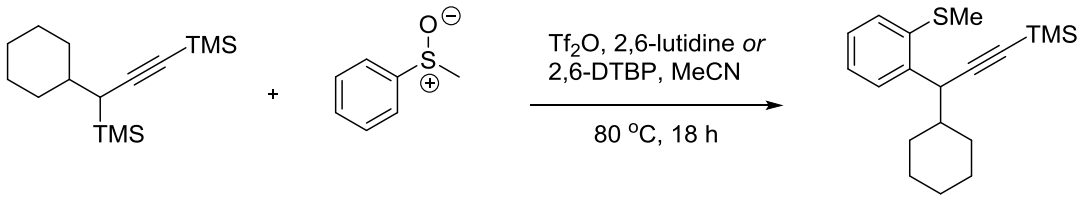
Figure 2

Overall, this project aims to develop the synthetic utility of sulfoxide-directed metal-free C-H functionalisation of aromatic and heteroaromatic systems and apply the the technology in the synthesis and functionalisation of a wide range of benzothiophene and highly conjugated benzothiophene scaffolds. In particular the development of simple, metal-free protocols involving propargylation and cyclisation will allow access to scaffolds of particular interest to society, for example NDT and BDT components of organic semiconductors.

Chapter 2: Results and Discussion

2.1 Propargylations with Branched Propargyl Silanes

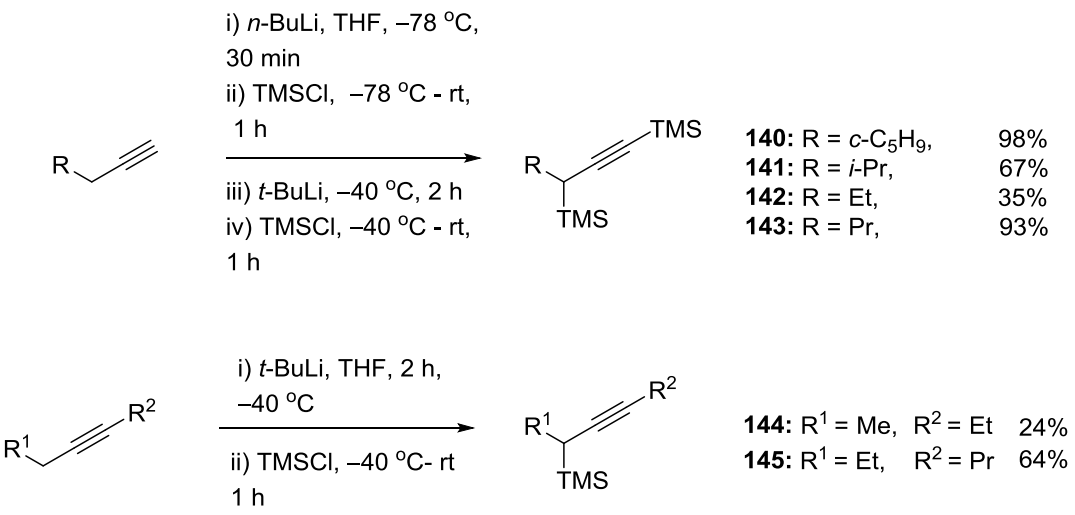
To begin this investigation, branched propargyl silane **137** was synthesised according to the procedure described by Rajagopalan and Zweifel.[61] Pleasingly, methylphenyl sulfoxide **138** underwent propargylation using branched silane **137** to give cyclohexyl substituted aryl sulfide **139** in good isolated yield (Scheme 43). The use of either 2,6-lutidine *or* 2,6-di-*tert*-butylpyridine as a base was found to give comparable yields in this case.



137 **138** **139**: 63%

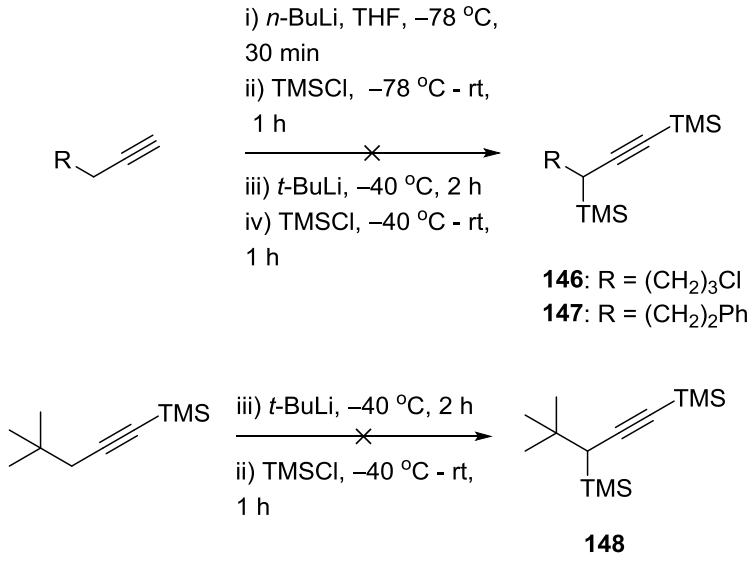
Scheme 43

This reaction represented the formation of a challenging carbon-carbon bond, particularly for metal catalysis. Encouraged by this initial finding, a collection of substituted propargyl silanes were synthesised in order to further investigate the substrate scope of this propargylation reaction. A range of different aliphatic alkynes were easily converted into the corresponding branched propargyl silanes (**140**-**145**) using the described methodology (Scheme 44).



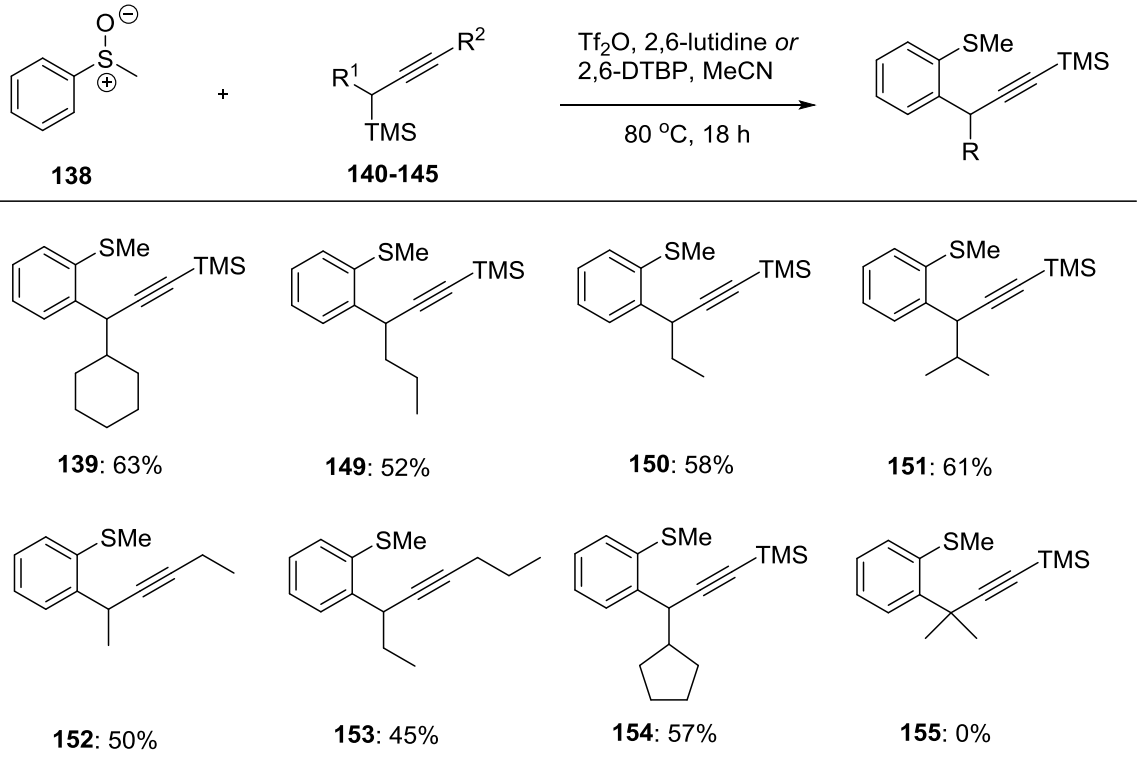
Scheme 44

It is worth mentioning that the forcing conditions needed for the synthesis of branched propargyl silanes (in particular the use of *t*-BuLi) caused problems when some alkynes bearing functionality were used. For example, the synthesis of chloro-substituted alkyne **146** and phenyl substituted alkyne **147** were incompatible with the reported conditions (Scheme 45). The second deprotonation of propargyl *tert*-butyl alkyne **148** was also not observed; this is easily rationalised by both the steric bulk and inductive effect of the *tert*-butyl group making deprotonation unfavourable.



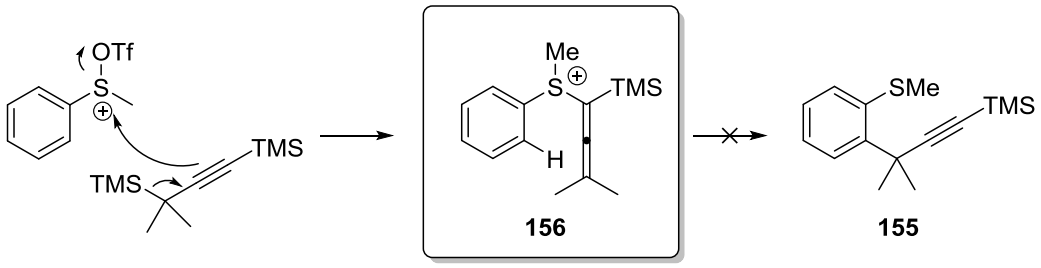
Scheme 45

Despite this, with branched propargyl silane library **140**-**145** in hand we were pleased to observe that propargylation occurred in good yields giving tertiary benzylic products **139**, **149–154** (Scheme 46). Primary alkyl (**149** and **150**) and secondary alkyl (**139**, **151** and **154**) branched propargyl silyl-protected silanes were well tolerated in the propargylation as were internal alkynes to that gave products **152** and **153**.[62] The propargyl silane nucleophile in all cases was delivered regiospecifically to the *ortho* postion on the aromatic ring; a specificity afforded to the reaction by the interrupted Pummerer/ rearrangement mechanism.



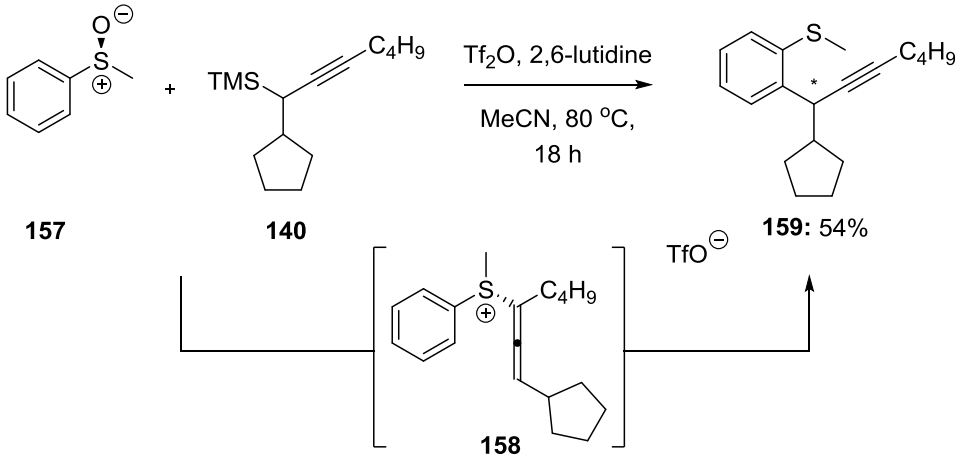
Scheme 46

Reaction with a propargyl silane at a tertiary carbon centre was also investigated however, unsurprisingly the reaction did not produce any of the expected gem-dimethyl product **155**. This may be rationalised if the sulfonium intermediate resulting from attack of *gem*-dimethyl propargyl silane onto the activated aryl sulfoxide is considered (Scheme 47). Rearrangement of dimethyl allenyl sulfonium salt **156** would involve overcoming large steric barriers.



Scheme 47

Now possessing the ability to construct benzylic tertiary carbon centres, we entertained the idea of using readily available enantiomerically enriched sulfoxide **157** in an attempt to induce asymmetric control in the contruction of the tertiary benzylic centre of the product **159** (Scheme 48). The idea of using enantioenriched propargyl silanes was considered, however these species were not readily available and involved lengthy syntheses.[63]

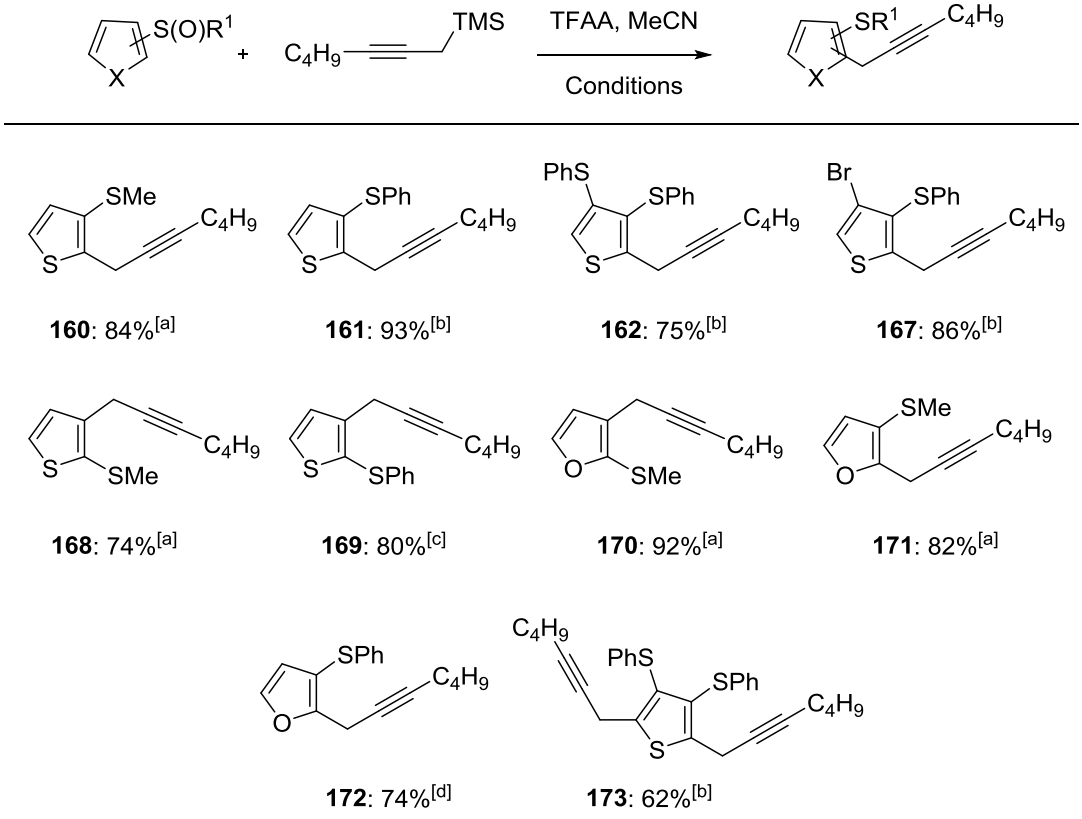


Scheme 48

The mechanistic rationale behind this hypothesis involved the formation of a stable enantiomerically and diasteromerically enriched allenyl sulfonium intermediate **158**. During rearrangement this intermediate could relay stereochemical information when forming the new carbon-carbon bond and establishing the new carbon stereocentre. Whilst this reaction gave a yield comparable to that when using the racemic sulfoxide, unfortunately no enantiomeric excess was observed in **159** (chiral

HPLC versus racemic standard). This is perhaps not surprising when considering the configurational stability of the activated sulfoxide: triflate exchange could very easily scramble any stereochemical information at sulfur, a conclusion supported by Maulide's recent findings in the unsuccessful asymmetric α-arylation of β-ketoesters.[40]

During this investigation into the use of branched propargyl silanes in propargylation reactions, further advances were made in the group regarding the scope and applications of our metal-free reactions. The methodology was expanded to include a range of heteroaromatic systems that were previously unexplored (Scheme 49).[62] A variety of furan and thiophene sulfoxides gave high yields of propargylated heterocyclic systems (**160**-**173**). Interestingly, *bis*-propargylation product **173** could be prepared from the corresponding *bis*-sulfoxide, the first report of a two-directional propargylation reaction.



[a] –40 °C to RT, 18 h; [b] RT, 1 h; [c] –78 °C, 2 h; [d] –20 °C to RT, 2 h

Scheme 49

When propargylation of 3-methylsulfinylthiophene was attempted with a branched propargyl silane nucleophile, the corresponding propargylated product **174** was isolated in good yield (Figure 3). Unfortunately, branched silanes containing cycloalkyl substitution performed poorly (**175** and **176**).

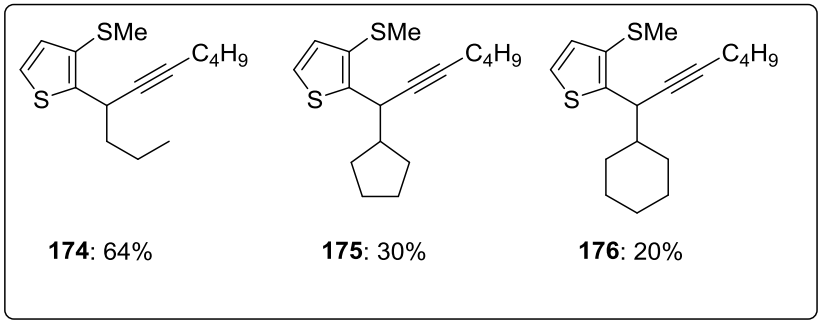
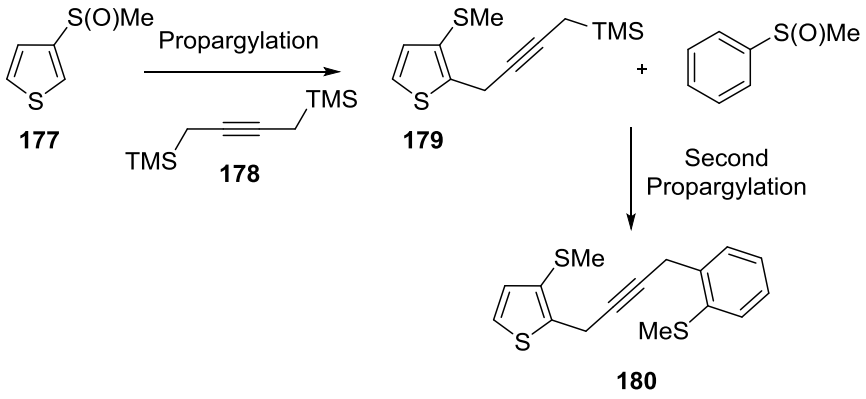


Figure 3

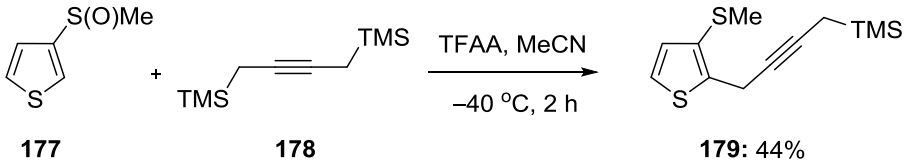
After the discovery of the ease at which a variety of different aromatic and heteroaromatic sulfoxides could be propargylated, we were intrigued by the idea of using *bis*-propargyl silane **178** and selectively couple this nucleophilic partner with different sulfoxides to give alkynes such as **180** (Scheme 50).



Scheme 50

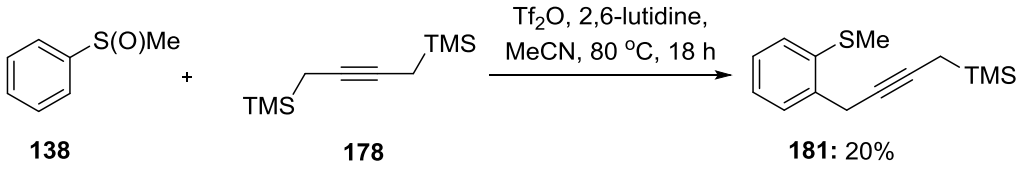
To probe the viability of this idea, we began by investigating the propargylation of methylthienyl sulfoxide **177** with *bis*-propargyl silane **178**. Satisfyingly, with a slight adjustment to conventional propargylation conditions for heteroaromatic sulfoxides, **177** could be propargylated to give **179** in 44% yield (Scheme 51). However, during optimisation, it proved difficult to improve the yield above this level and so it was

decided to shift focus to the propargylation of methylphenyl sulfoxide **138** with *bis*-propargyl silane **178** (Scheme 52).



177 **178** **179:** 44%

Scheme 51

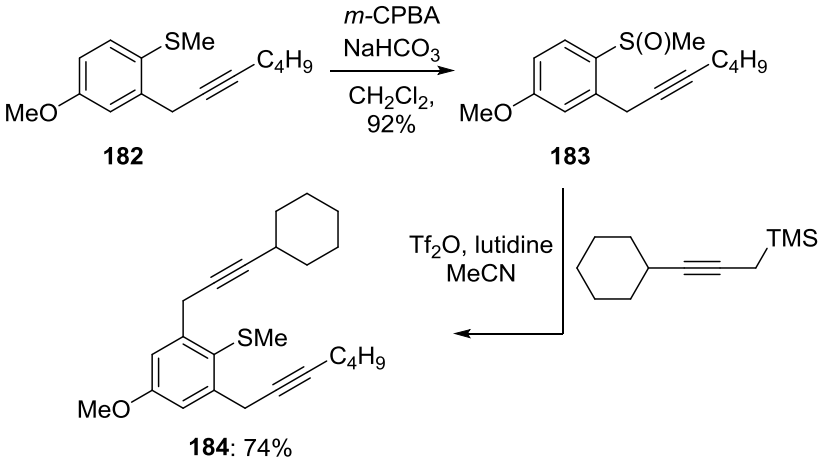


138 **178** **181:** 20%

Scheme 52

Unfortunately, the yield of this reaction was similar and the process proved resistant to optimisation, and often produced a mixture of inseparable products. Interestingly, however, neither reaction shown in Scheme 51 or 52 showed any evidence of double arylation, suggesting that a second propargylation is less facile than the first. Due to time constraints and other emerging work this investigation was unfortunately set aside.

Inspired by the versatility of our propargylation reactions, further investigation in the group proved that propargylation products, such as **182**, could be easily re-oxidised (**183**) and propargylated once more using different propargyl silanes to give unsymmetrical propargylation products, such as **184** (Scheme 53). This approach demonstrates the 'safety-catch' nature of the sulfoxide directing group as functionalisation is only possible once the sulfide has been reactivated by oxidation and over alkylation is therefore not possible.



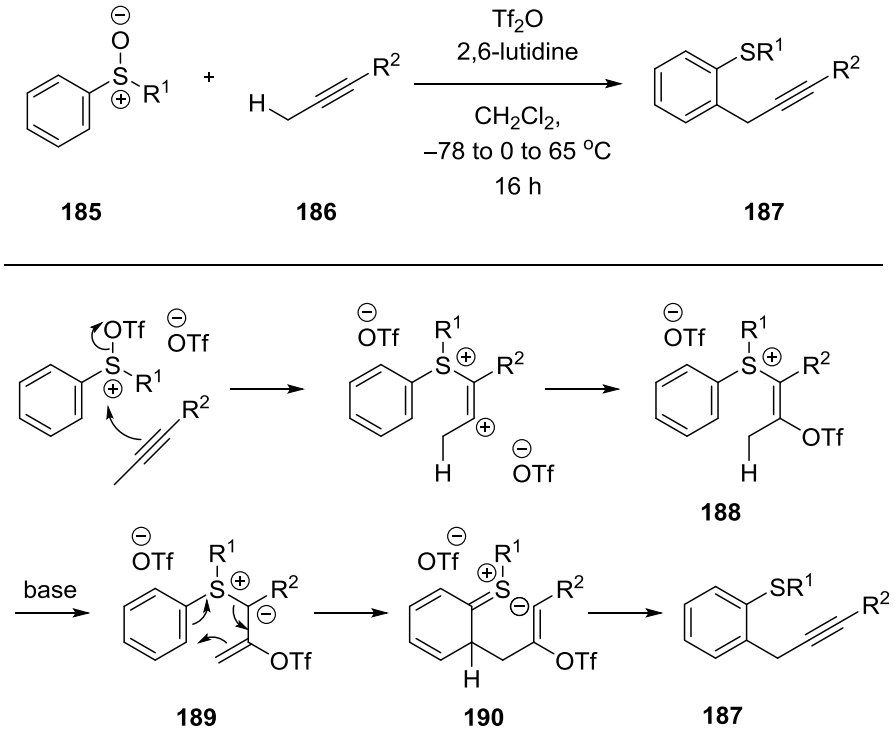
182 **183**

184: 74%

Work by Dr. Amandinen Carrer

Scheme 53

More recently, elaborating on this *ortho*-propargylation reaction, our group reported the metal-free CH-CH-type cross-coupling of arenes and alkynes.[64] Through the careful control of temperature and choice of base, alkynes rather than propargyl silanes proved to be effective coupling partners with activated sulfoxides. Scheme 54 shows the proposed mechanism for this metal-free CH-CH coupling reaction. Notice in this case (compared to couplings with propargyl silanes) that the addition of base is of the utmost importance for the deprotonation of sulfonium intermediate **188**. The resulting sulfonium ylide **189** can undergo a [3,3]-sigmatropic rearrangement, elimination of TfOH and aromatisation to give the final propargylated products **187**.



Work by Dr. Jose Fernandes-Salas

Scheme 54

During the investigation of this reaction it was observed that the incorporation of large R^2 groups (for example triisopropylsilyl) in the alkyne starting material had a large positive effect on the reaction yield. This effect was rationalised by the steric protection that large groups provide towards unwanted deprotonation or nucleophilic demethylation or arylation of the sulfide group, encouraging ylide formation.

2.2 Synthesis of Benzothiophenes

Sulfur-containing heterocycles, especially benzothiophene-based architectures, are recognised as important structures in small molecule and polymeric organic materials (Figure 4).[58] These types of materials are typically prepared using Pd-mediated cross-couplings[65, 66] and C-H activation using platinum group metals.[67] Crucially, traces of platinum group metals are known to have detrimental effects on the physical properties of the materials.[68] Naphthodithiophenes **191** and **192**, and benzodithiophenes **193** and **194**, in particular, have shown great promise in semi-conducting materials and solar cells.[60, 69-71]

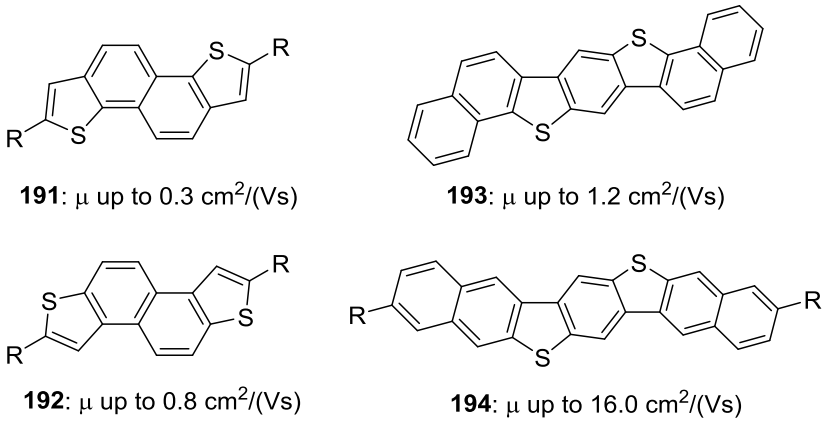
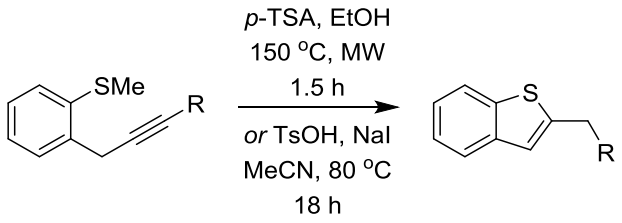


Figure 4

Thus, the conversion of our propargylation products to such architectures would be of significant synthetic interest and would provide quick, metal-free access to a number of small molecule components of benzothiophene-based materials. The propargylation products obtained constituted a library of new compounds perfect for testing in new methodology for the synthesis of substituted benzothiophene motifs.

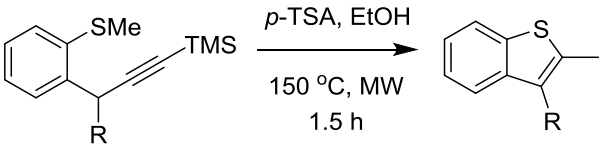
2.2.1 Acid-Mediated Cyclisations to Give Alkyl Benzothiophenes

Two sets of conditions had been provisionally developed for the synthesis of substituted benzothiophenes from products of propargylation. The first involved acid-mediated cyclisations that furnished C2-alkyl substituted benzothiophenes (Scheme 55).



Scheme 55

Branched products of propargylation were an obvious choice of substrate for this acid-mediated cyclisation strategy and so compounds **138**, **141** and **142** were heated to 150 °C for 1.5 h in a microwave reactor with 1 equivalent of *p*-TSA in EtOH (Scheme 56). There was no need for initial deprotection of the TMS protected alkynes and deprotection/cyclisation occurred in all cases to give 2,3-disubstituted benzothiophenes **195**-**197** in moderate to high yield.

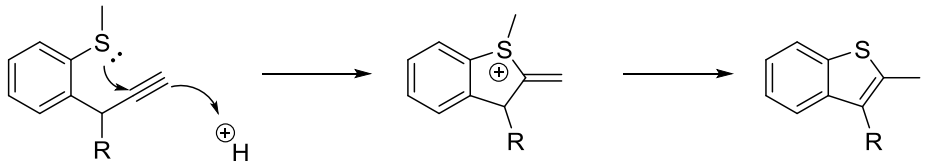


138: R= Cyh
141: R= Et
142: R= ^{i}Pr

195: 81%
196: 56%
197: 42%

Scheme 56

The proposed mechanism for this acid mediated cyclisation is presented in Scheme 57. Following initial acid-mediated deprotection of the starting material, the reaction proceeds through intramolecular attack of the sulfide moiety of **198** onto the acid-activated alkyne, furnishing sulfonium intermediate **199**. A sequence of tautomerisation and demethylation then occurs, providing the final 2-methyl-substituted benzothiophene **200**.

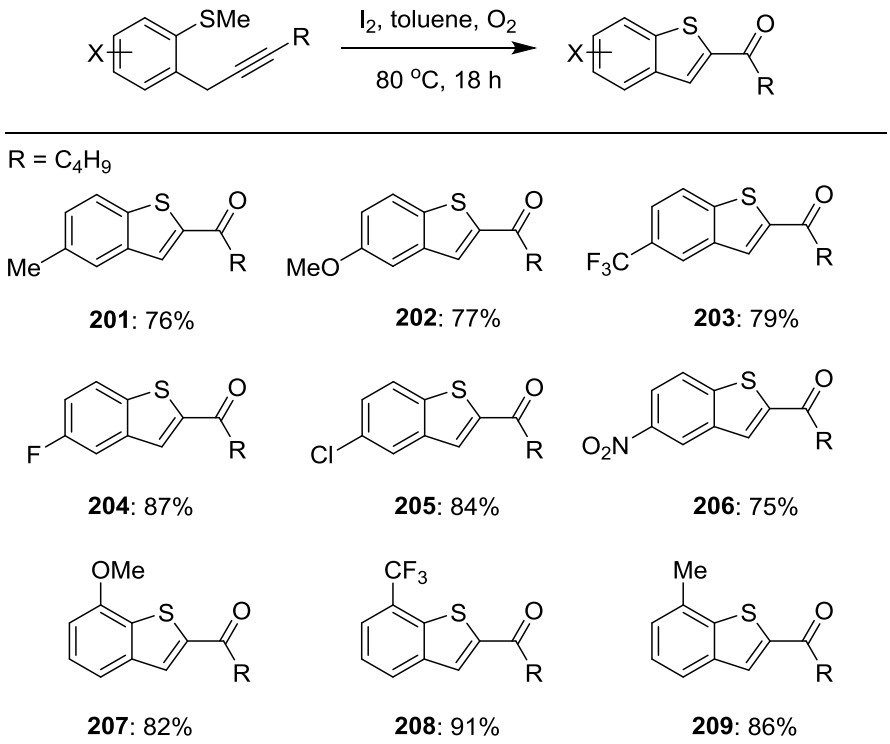


Scheme 57

Although this cyclisation approach constitutes a quick, metal-free method that allows access to substituted benzothiophene scaffolds, the alkyl group produced lacks functionality. To address this concern, a second cyclisation protocol was found to be particularly useful.

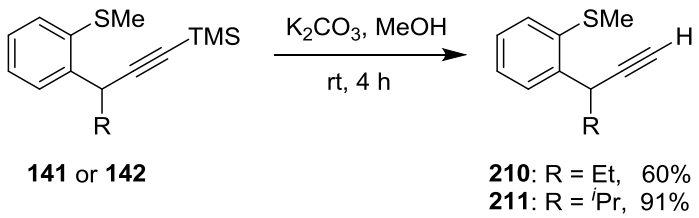
2.2.2 Iodine-Mediated Cyclisations to Give Carbonyl-Substituted Benzothiophenes

A related procedure using molecular iodine,[72, 73] rather than acid, produced 2-acyl substituted benzothiophenes from the propargyl products of metal-free coupling reactions (**201**-**209**, Scheme 58). This reaction had already shown great functional group tolerance, for example, tolerating an NO_2 group (to form **206**) and a methoxy group (to form **202** and **207**).



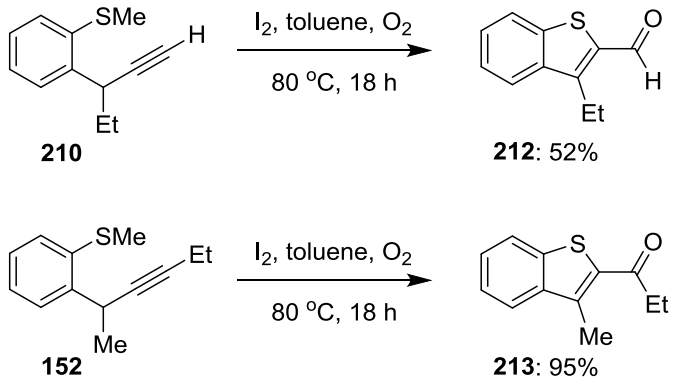
Scheme 58

Again, branched products of propargylation presented the possibility of increasing molecular complexity in benzothiophene synthesis. However, it was quickly found that alkynyl-TMS compounds required an additional deprotection step before they could take part in these oxidative, iodine-mediated cyclisations. TMS protected alkynes, such as **141** and **142**, could easily be deprotected under basic conditions in MeOH to give terminal alkynes **210** and **211** in good yield (Scheme 59).



Scheme 59

In order to demonstrate the effectiveness of the previously described cyclisation conditions in building molecular complexity, deprotected alkyne **210** and internal alkyne **152** were selected as suitable substrates to undergo cyclisation. Terminal alkyne **210** gave the previously unreported aldehyde-substituted benzothiophene **212** and internal alkyne **152** gave benzothiophene **213** in high yield (Scheme 60).



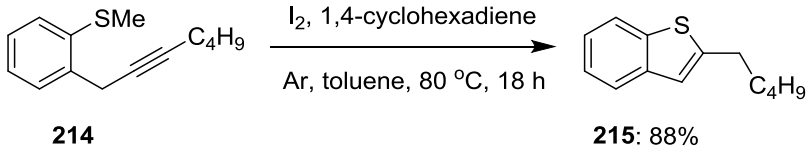
Scheme 60

With the development of these two cyclisation techniques, we recognised the potential of propargylation products as crucial synthetic precursors to a wide array of functionalised benzothiophene cores. An approach that has the ability to introduce different functionalities on a benzothiophene scaffold, thereby tuning the electronics of the system, is of great interest to any scientist synthesising drug candidates or organic materials, especially if this approach can avoid the use of expensive catalysts and the potential of metal contamination.[74] With this in mind, we set out to further diversify the benzothiophene scaffolds available to us through the use of iodine-mediated cyclisations.

2.2.3 Iodine-Mediated Cyclisations to Give Alkyl-Substituted Benzothiophenes

In parallel to the development of oxidative cyclisations to give 2-acyl substituted benzothiophenes (*vide supra*), a complementary iodine-mediated cyclisation was developed allowing access to 2-alkylbenzothiophene structures (complementary to the acid-mediated cyclisations in Scheme 55). Similar to the above cyclisation, this method involved heating propargyl substrate **72** with molecular iodine in toluene, however it

was critical that the reaction be conducted under an inert atmosphere (argon) to avoid production of the corresponding carbonyl substituted benzothiophene and to isolate alkyl benzothiophene **214** in high yield. 1,4-Cyclohexadiene is known to act as a hydrogen atom donor and its inclusion was found to be important for the formation of **215** (Scheme 61).

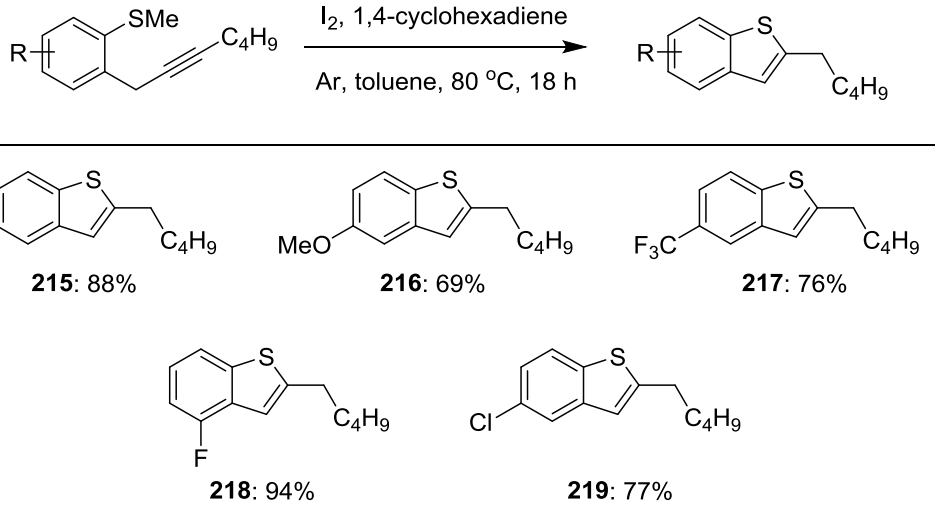


214 **215**: 88%

Work by Dr. Andrew J. Eberhart

Scheme 61

With these conditions, previously optimised by Dr Andrew J. Eberhart, in hand, the scope of this reductive cyclisation reaction was investigated (Scheme 62). From propargyl starting materials, 2-alkylbenzothiophenes **215**-**219** could be isolated in high yields. Propargylation products bearing electron donating groups (**216**) and electron withdrawing groups (**217**) were well tolerated in this reaction along with halide-substituted rings (**218** and **219**).



215: 88% **216**: 69% **217**: 76%

218: 94% **219**: 77%

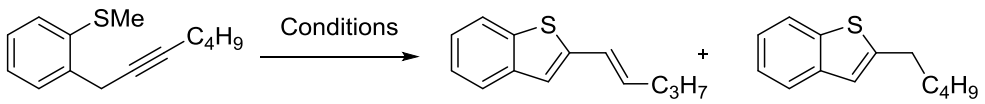
Scheme 62

Having now identified three separate sets of metal-free conditions allowing access to functionalised benzothiophene cores, we set out to investigate if any further conditions could be found that would diversify the benzothiophene products available to us, and possibly provide an approach to NDT or BDT structures.

2.2.4 Iodine-Mediated Cyclisations to Give Alkenes

During optimisation of iodine-mediated cyclisations of propargylation products, small amounts of 2-alkenylbenzothiophene **79** were observed as a side product under certain conditions. The ability to synthesise another decorated benzothiophene scaffold with only small adjustment to the iodine-mediated conditions described above was an attractive prospect and so optimisation studies were carried out in order to selectively synthesise alkene **79**. A summary and discussion of the optimisation process is presented below (Table 1):

Table 1



214 **220** **215**

Entry	I_2 eq.	Base	Additive	Solv.	Conc. (M)	Temp (^oC)	Yield (%) **220**	Yield (%) **215**
1	1.1	Cs_2CO_3 (1.2 eq)	-	Tol.	0.01	80	53	32
2	2	2,6-DTBP (2.5 eq)	-	Tol.	0.01	80	31 (34 [a])	12 [a]
3	2	Et_3N (2.5 eq)	-	Tol.	0.01	80	58 [a]	29 [a]
5	4	Et_3N (2.5 eq)	-	Tol.	0.01	80	45 [a]	20 [a]
6	2	Et_3N (2.5 eq)	-	DCE	0.01	80	49 [a]	30 [a]
7	2	2,6-DTBP (2.5 eq)	-	DCE	0.01	80	52 [a]	34 [a]
8	2	Et_3N (2.5 eq)	-	DCE	0.01	rt	-	-
9	2	-	-	DCE	0.01	80	-	40 [a]
10	2	-	MeOH (50 eq.)	DCE	0.01	80	72 [a]	-
11	1.1	-	MeOH (50 eq.)	DCE	0.01	80	75 [a]	-
12	**1.1**	**-**	**MeOH (100 eq.)**	**DCE**	**0.01**	**80**	**92**	**-**
13	1.1	-	^iPrOH (100 eq.)	DCE	0.01	80	77 [a]	-
14	1.1	Et_3N (1.5 eq)	MeOH (100 eq.)	DCE	0.01	80	-	-

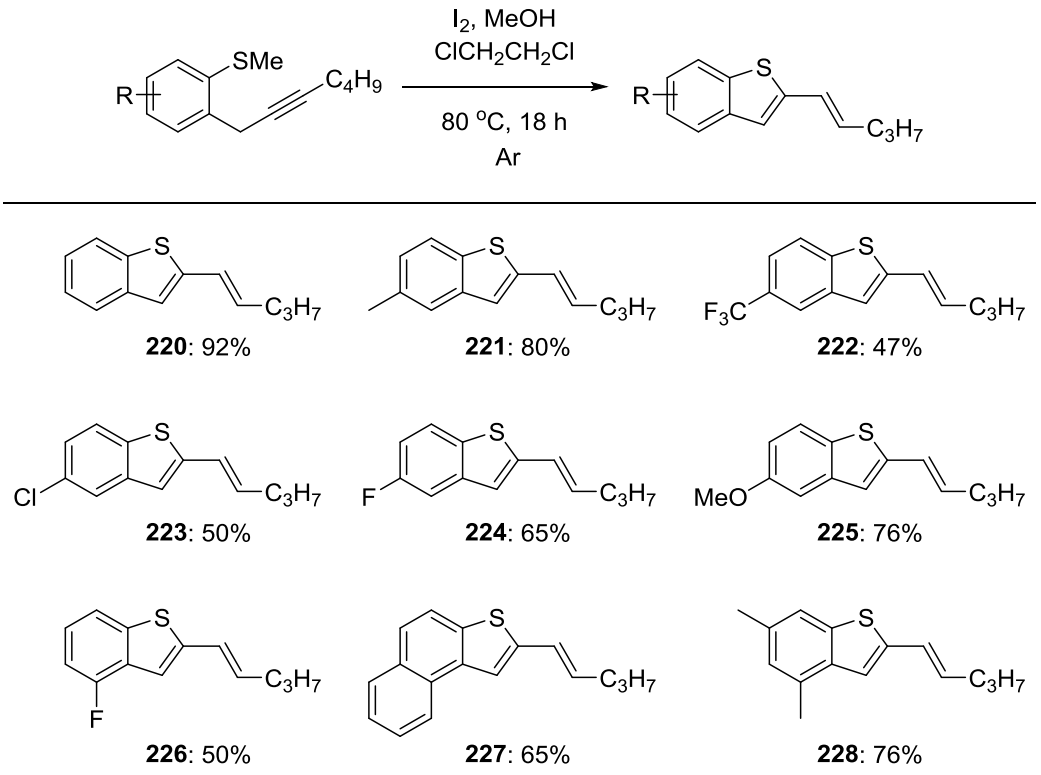
[a]yields determined by ^1H NMR spectroscopy using $MeNO_2$ as internal standard. 2,6-DTBP = 2,6- di-*tert*-butylpyridine. All reactions run for 18 h. (see general experimental, section 3.1).

Work carried out with Yuntong Zhang.

Initial tests had shown that the addition of base (caesium carbonate in this case) to our iodine-mediated cyclisation conditions allowed the synthesis of alkene **220** in 53% isolated yield, with alkane **215** also produced in 32% isolated yield (entry **1**). It was quickly realised that the production of alkane **215** as a side product was a significant problem in this reaction. Changing the base from $CsCO_3$ to 2,6-DTBP had a detrimental effect on the yield of both **220** and side product **215** (entry 2), whereas addition of Et_3N had little effect on either (entry 3), and increasing the equivalents of iodine used had a slight negative effect on the yield also (entry 5). Yields using 1,2-dichloroethane as the reaction solvent were found to be comparable to those in toluene. In 1,2-

dichloroethane, switching of the base to 2,6-DTBP had little impact on the yields (entry 7) and heating was found to be essential as the reaction produced neither **220** or **215** when carried out at room temperature (entry 8). Only **215** was produced when the reaction was carried out in 1,2-dichloroethane without any base present.

Interestingly the addition of 50 equivalents of MeOH to the reaction significantly increased the yield of alkene **220** whilst completely supressing the production of alkane side product **215** (entry 10). Pleasingly, lowering the equivalents of iodine used from 2 to 1.1 (entry 11) and increasing the amount of MeOH to 100 equivalents gave alkene **220** in 92% isolated yield, again with no production of **215** (entry 12). A quick screen of different alcohols showed MeOH to be the most efficient with the use of isopropylalcohol giving a 77% yield of **220**. With these optimised conditions in hand we began to investigate the scope of this variant of iodine-mediated cyclisation.

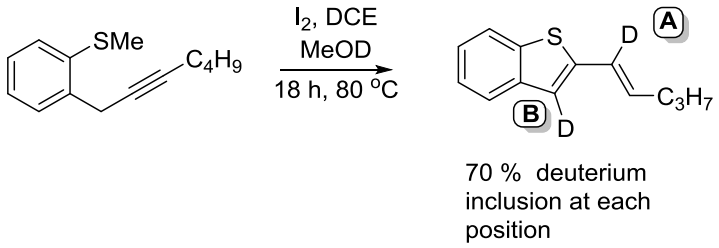


Scheme 63

As can be seen in Scheme 63 a range of different propargylated sulfide products were compatible with these reaction conditions. Electron rich substrates provide the corresponding alkenyl-substituted benzothiophenes in high yields (**225**, **227** and **228**), with the high yield of alkene **227** (from propargylated naphthyl sulfide) being of particular interest. In this investigation, the formation of **227** represented the first

synthesis of a more highly conjugated benzothiophene skeleton using an iodine-mediated cyclisation method. As mentioned, highly conjugated benzothiophene containing compounds are of great interest as organic electronic material components or precursors. Electron poor substrates delivered conjugated alkene products in lower yields (**222, 223** and **226**). This can be rationalised by considering the reduced nucleophilicity of the sulfide moiety in the starting material, caused by electron withdrawing groups around the ring, making initial attack onto the activated alkyne less favourable.

Furthermore, when cyclisation was performed with deuterated methanol, 70% deuterium inclusion was observed in both benzylic/vinylic position **A** and C3 position **B** (Scheme 64). This observation suggests that at some point during the reaction mechanism protons at these positions are readily exchangeable.

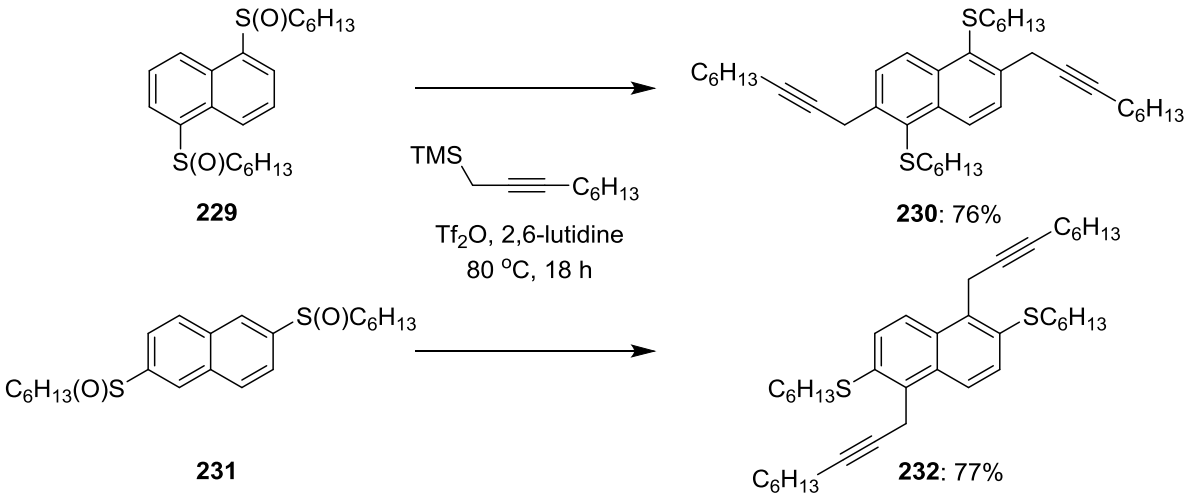


Scheme 64

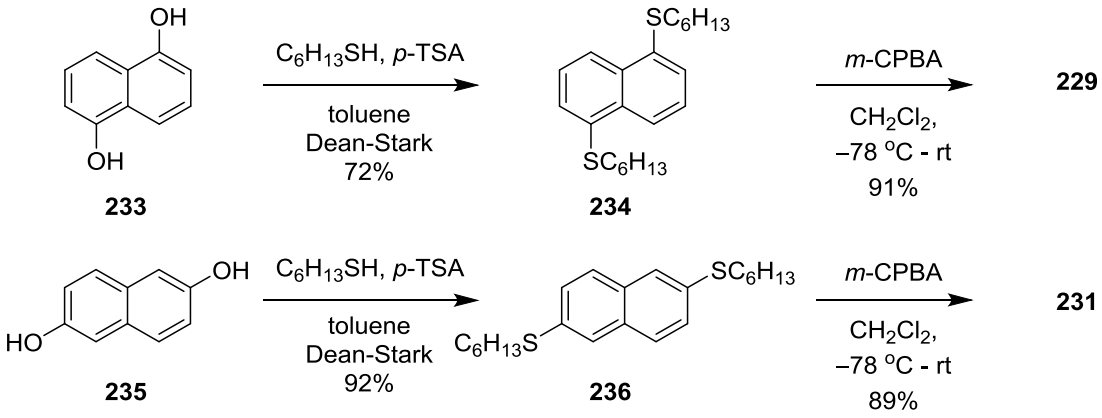
2.2.5 Cyclisations to Give Highly Conjugated Benzothiophene-Containing Scaffolds

The feasibility of a synthetic approach to naphthodithiophene (NDT) motifs combining sulfoxide-directed, metal-free cross-couplings with iodine-mediated heterocyclisations was then investigated. The preparation of these types of molecule typically involve Pd-catalysed Sonogashira couplings,[56] therefore a metal-free approach would be desirable to avoid any metal contamination of NDT products. To begin this investigation *bis*-propargylated napthyl sulfides **230** and **232** were first synthesised from *bis*-sulfoxide coupling substrates (Scheme 65). The sulfoxide starting materials **229** and **231** were easily prepared by *m*CPBA oxidation of sulfides **234** and **236**, which were in turn prepared by nucleophilic aromatic substitution of corresponding diols **233** and **235** by hexanethiol (Scheme 66). Note that both isomers were prepared in order to gain

access to two separate NDT structural isomers. The observed regioselectivity in the propargylation of **231** may be rationalised by considering the increased loss of aromaticity when propargylation occurs at the alternative site.

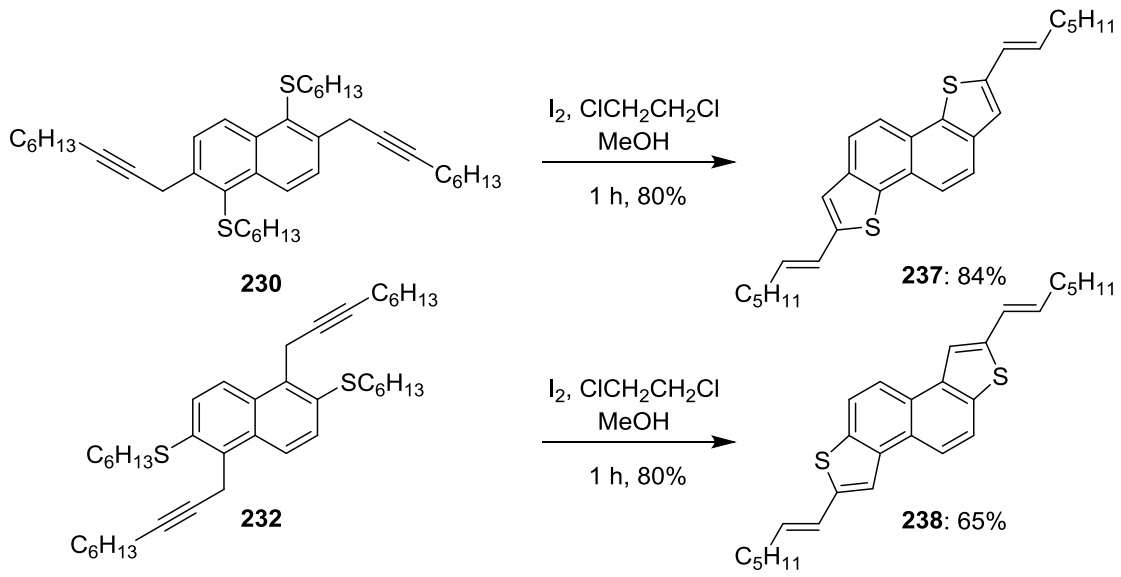


Scheme 65



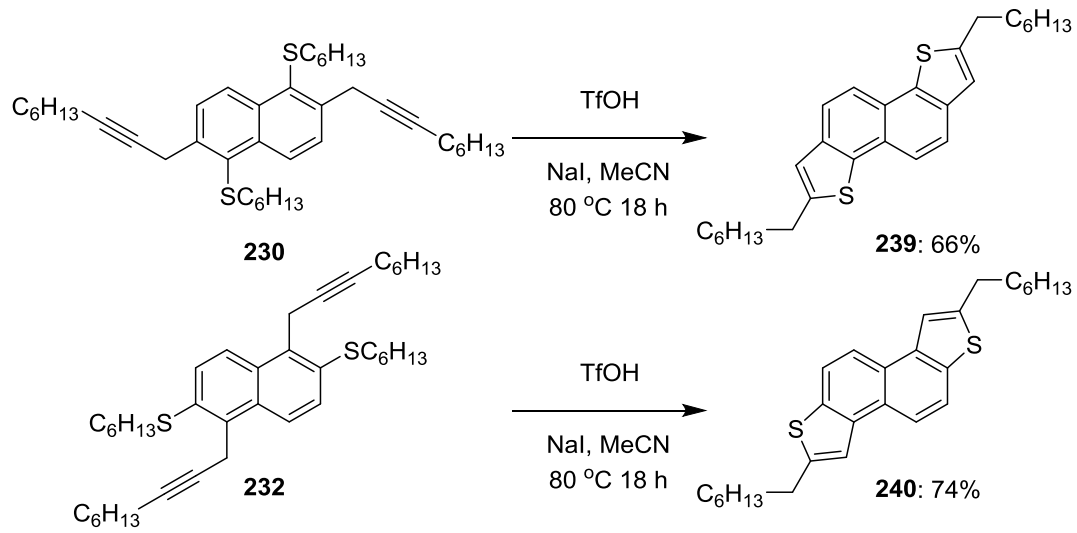
Scheme 66

Iodine-mediated cyclisation of both **230** and **232** under eliminative conditions gave highly conjugated functionalised NDT products **237** and **238** in high yield (Scheme 67). Under these conditions, optimal yields for NDT products from the two-directional iodine-mediated cyclisations were observed after only one hour, compared to eighteen hours when using less conjugated starting materials. The drop in yield observed after this time was possibly due to the instability of the electron rich products in the presence of an excess of iodine.

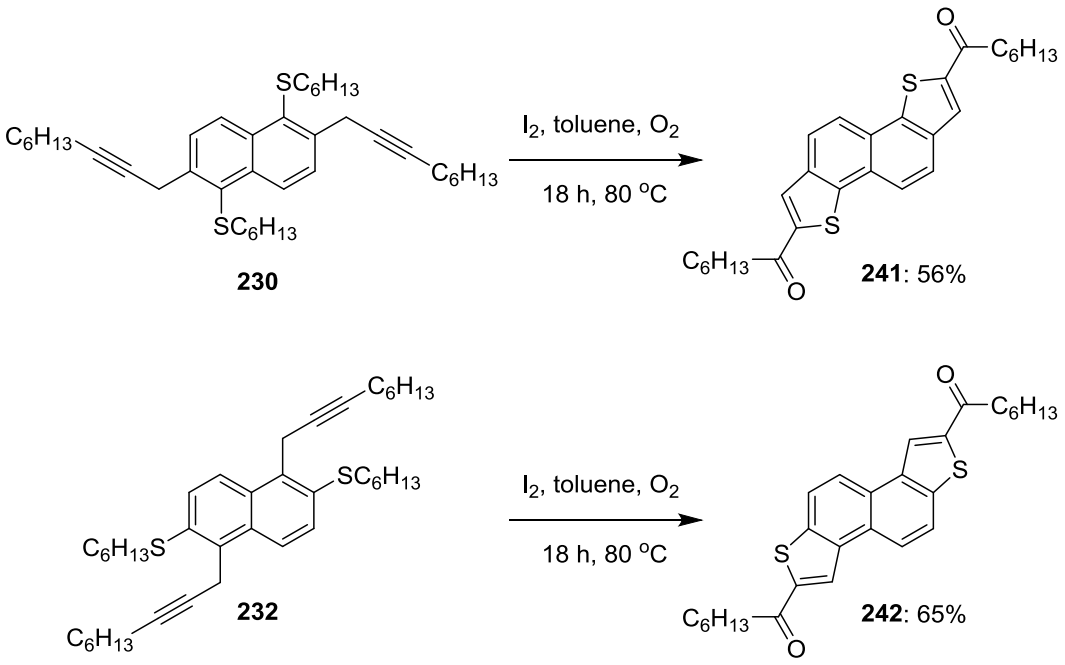


Scheme 67

Parallel work by Dr Andrew J. Eberhart put acid-mediated reductive cyclisation (Scheme 68) and iodine-mediated oxidative cyclisation methodologies (Scheme 69) to use in the synthesis of substituted NDTs. Using the same naphthyl propargyl sulfide starting materials (**230** and **232**), NDT di-ketones **239** and **240**, along with alkyl-NDTs **241** and **242**, were synthesised in high yield. The acid-mediated cyclisation conditions employed here differ from the conditions reported in discussion, however, theses conditions where already well known from the groups previous work: TsOH encourages cyclisation of parent sulfides **230** and **232** and NaI facilitates dealkylation of the sulfonium intermediate formed.[50]



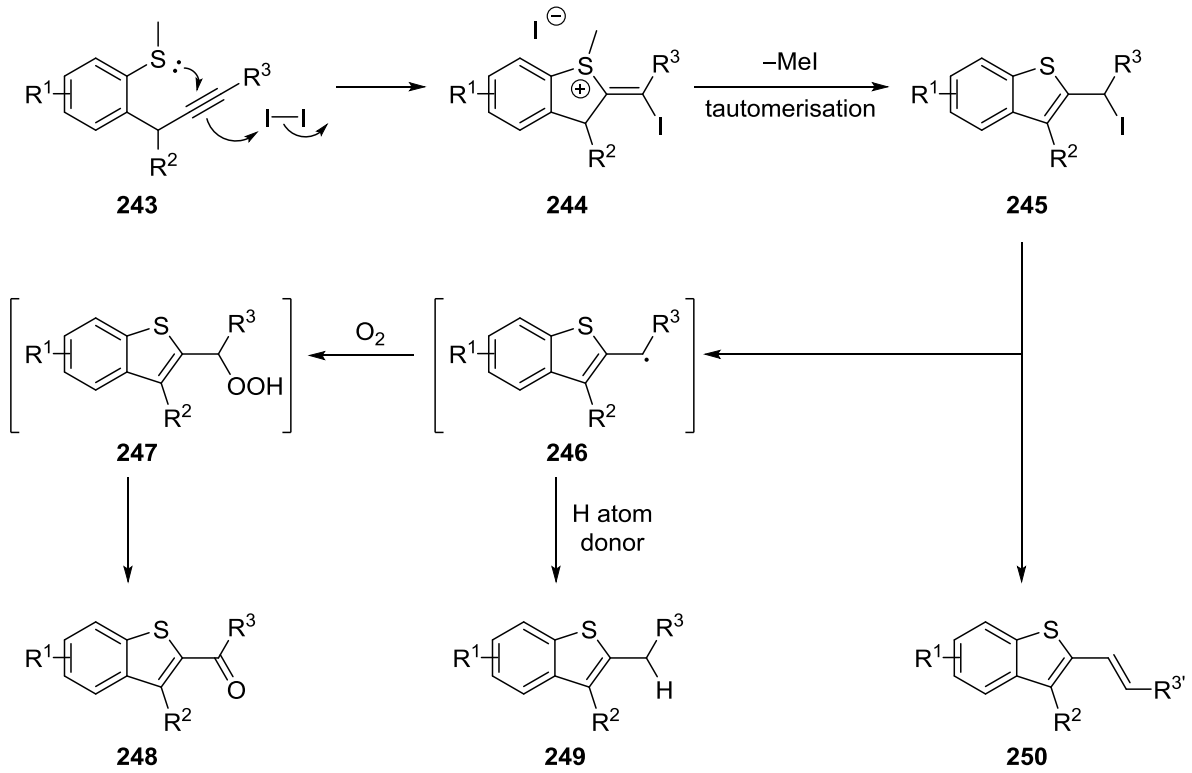
Scheme 68



Scheme 69

2.2.6 Iodine-Mediated Cyclisations: Mechanisms

Proposed mechanisms for all three iodine-mediated cyclisations are outlined in Scheme 70.

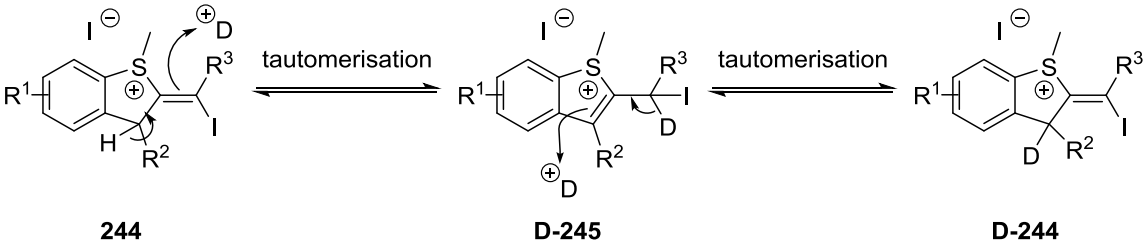


Scheme 70

As can be seen, the mechanism is thought to involve iodide intermediate **245**, which is formed by intramolecular attack of sulfide **243** onto the iodine-activated alkyne, subsequent demethylation of **244** by iodide, and tautomerisation. When carried out in an NMR tube a distinct peak at approx. 2.2 ppm shows the production of methyliodide in the reaction, therefore suggesting that iodide acts as a demethylating agent in the mechanism. At this point, the judicial choice of reaction conditions effects the product formed. Under oxidative conditions it is believed that iodide intermediate **245** decomposes under heating to form stabilised radical **246**, which can be intercepted by molecular oxygen to form hydroperoxide **247** which, after decomposition produces ketones **248**. Similarly, in the absence of oxygen and with the addition of 1,4-cyclohexadiene, radical intermediate **246** can accept a hydrogen atom to give alkyl

cyclisation products **249**. When iodide **245** is formed in a more polar solvent system, as used in the eliminative conditions, simple elimination of hydrogen iodide furnishes conjugated alkene products **250**. Here the addition of methanol as a polar protic co-solvent could play a crucial function in encouraging HI elimination.

The inclusion of deuterium at the vinylic and C3 postion when the reaction is run using MeOD can be explained when considering the ease at which these protons can exchange by tautomerisation in intermediate **244** (Scheme 71).

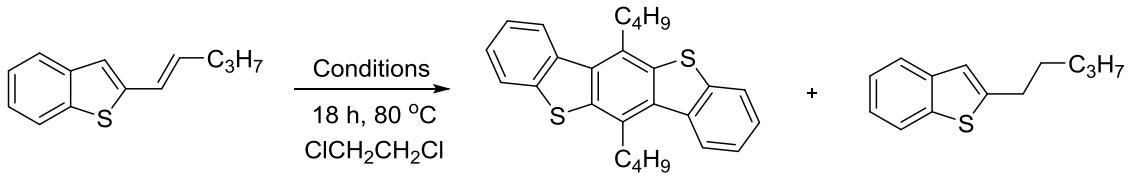


Scheme 71

2.2.7 Access to Benzodithiophene Scaffolds: A Novel Dimerisation

With NDT structures now easily accessible through the combination of our sulfoxide-directed metal-free propargylations and iodine-mediated cyclisations, our attention focused on optimising the formation of highly conjugated benzodithiophene (BDT) scaffolds. Such molecules have proved to be useful small molecule materials in the development of organic field effect transistors and photovoltaics.[75-78] During the optimisation of eliminative iodine-mediated cyclisations to give 2-alkenylbenzothiophenes, as described above, the production of small amounts of BDT scaffold **112** was observed under certain conditions. The optimisation of a protocol to give exclusively these scaffolds is shown below (Table 2).

Table 2



220 **251** **215**

Entry	I_2 (eq.)	Conc. (M)	Additive	Yield(%) **251**	Yield(%) **215**	Comments
1	1	0.02	-	28[a]	26[a]	-
2	0.7	0.02	-	29[a]	24[a]	-
3	0.5	0.02	-	31[a]	32[a]	-
4	0.5	0.02	-	29[a]	29[a]	1 eq of **9** added to (1 eq **9** + 1eq I_2)
5	0.5	0.02	-	26[a]	25[a]	I_2 added over 6 h
6	0.5	0.02	H_2O (50 eq.)	26[a]	23[a]	-
7	0.5	0.02	AcOH (1 eq.)	31[a]	30[a]	-
8	0.5	0.02	AcOH (50 eq.)	27[a]	27[a]	-
9	0.5	0.02	MeOH	24[a]	-	-
10	0.5	0.02	-	26[a]	19[a]	No light
11	0.5	0.02	Styrene	-	-	-
12	0.5	0.02	2-methyl-2-butene	-	-	-
13	0.5	0.02	2-ethyl-1-butene	-	-	-
14	0.5	0.02	O_2	-	-	Solvent bubbled with O_2
15	0.5	0.01	-	30[a]	30[a]	-
16	1	0.01	-	26[a]	20[a]	-
17	2	0.01	-	26[a]	18[a]	-
18	3	0.01	-	27[a]	15[a]	-
19	5	0.01	-	33[a]	12[a]	-
20	**10**	**0.01**	**-**	**43**	**-**	**-**

[a]yields determined by ^{1}H NMR spectroscopy using $MeNO_2$ as internal standard. (see General Experimental, section 3.1)

Initially, the production of BDT **251** proceeded in moderate yield with one equivalent of I_2 (entry **1**). As shown in entries **2** and **3**, reducing the amount of I_2 present in the reaction mixture resulted in a small increase in yield. Different protocols for the addition of I_2 to the reaction were investigated (entries **4** and **5**) however, none provided any significant improvement in yield. As the mechanism at the time was believed to require the protonation of an intermediate alkene, the inclusion of different proton sources (entries **6**-**9**) was investigated. Unfortunately these experiments showed no significant improvement when compared to control experiments, leading to a re-evaluation of the proposed mechanism. When carried out in the dark the reaction showed little difference in the yield of **251** and **215** along with no significant change in their ratio (entry **10**), ruling out the decomposition of any reactive benzylic iodide intermediates by light. On analysis of the results to date, BDT product **251** was typically formed in a 2:1 ratio with the alkane side product **215** in many of the conditions tested. It was hypothesised side product **215** was formed by the reduction of the alkene starting material by a reactive intermediate on the route to BDT formation. Addition of a sacrificial alkene into the reaction was conceived as a method to by-pass this unfavourable reaction, however when a selection of alkene additives were tested (entries **11**-**13**), complete degradation of starting material and no production of either BDT or alkane product was observed. This is most likely caused by the myriad of different reactions that could result from iodine-activation of both the starting alkenyl starting material and the sacrificial alkenes.

Therefore, we decided to investigate the effects of oxidants on the yield of the reaction in an effort to verify our new hypothesis, as the addition of a suitable oxidant would decrease the amount of alkane produced, therefore increasing BDT production. Molecular oxygen proved an ineffective oxidant as when the reaction was run with oxygenated solvent under an oxygen atmosphere, only starting material was recovered (entry **14**). The possibility of excess I_2 being a suitable oxidant was then investigated. Pleasingly, increasing the equivalents of iodine not only decreased the production of alkane side product but also increased the yield of the desired dimerisation product (entries **16**-**20**, Figure 5).

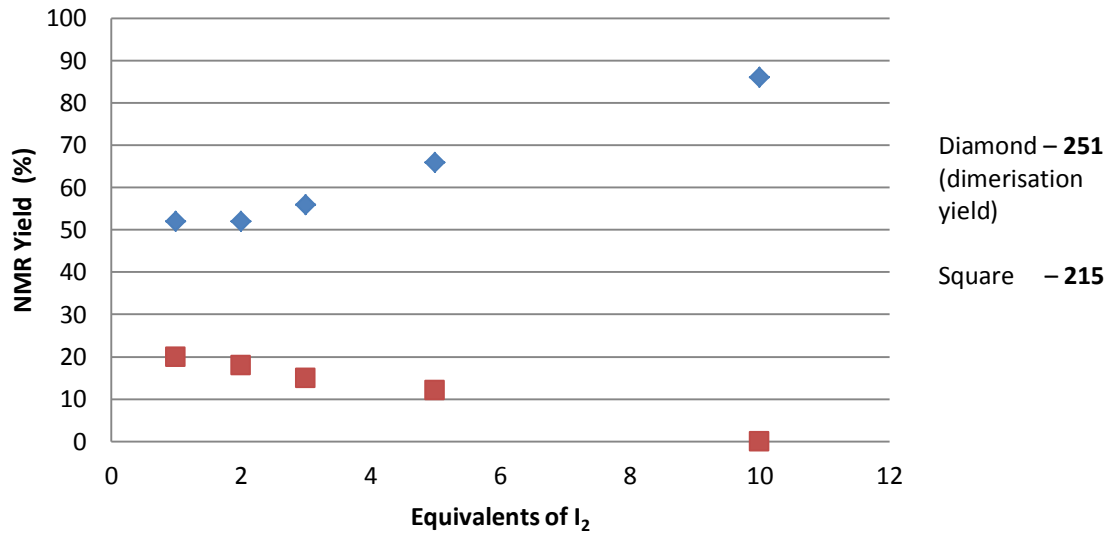
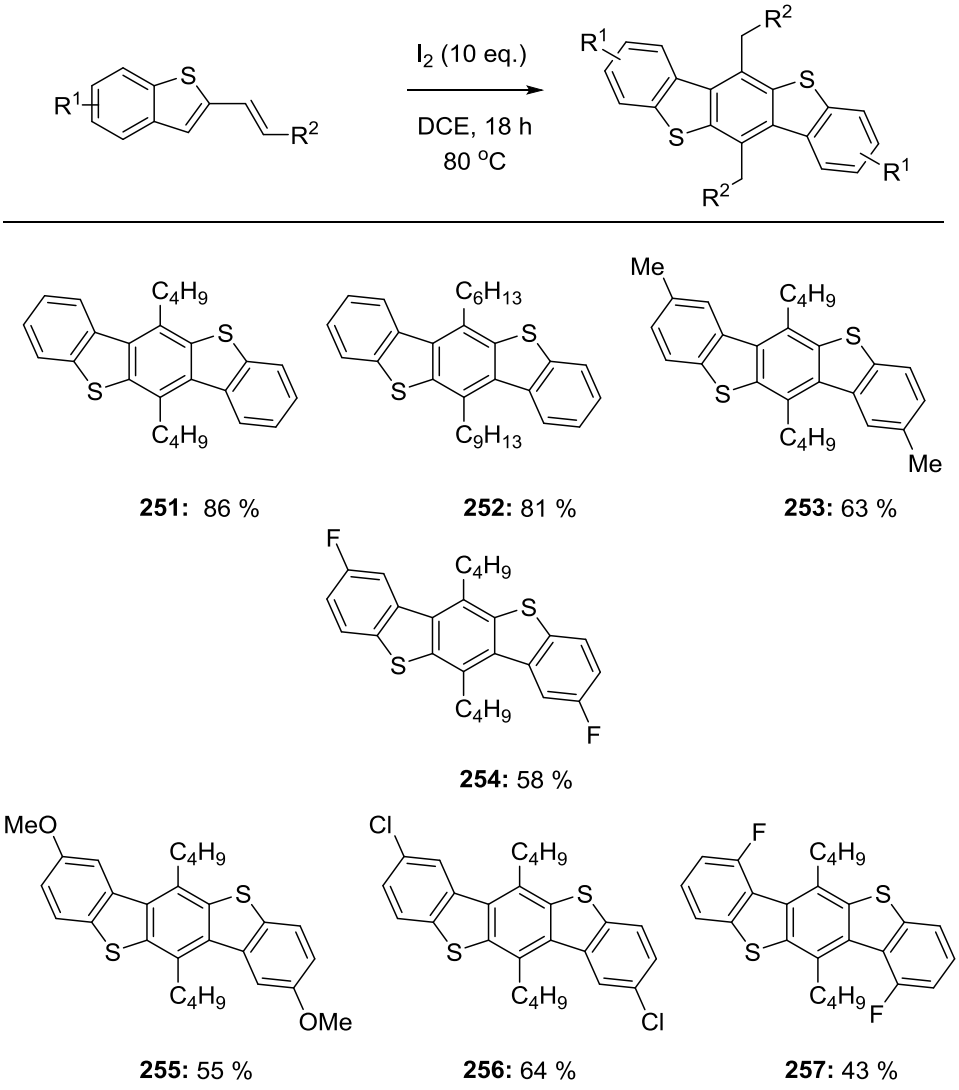


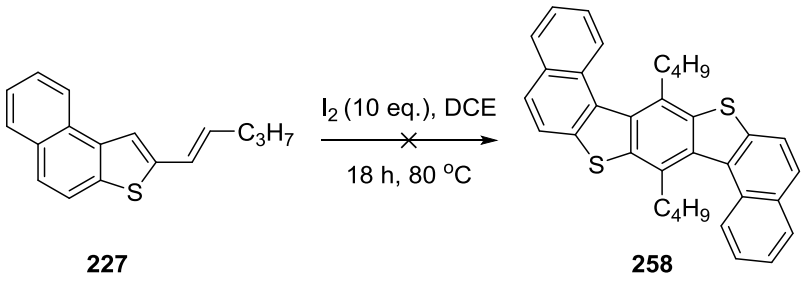
Figure 5

Furthermore, 10 equivalents of iodine (entry **20**) provided an excellent yield of **251** with no observed alkane side product. It is possible that molecular iodine was a suitable oxidant for this reaction due to its mild oxidative nature, meaning that when the product was formed it was not degraded by stronger oxidants. Our optimised conditions allowed us to investigate the scope of BDT synthesis using alkenes from our previous cyclisation studies (Scheme 72).



Scheme 72

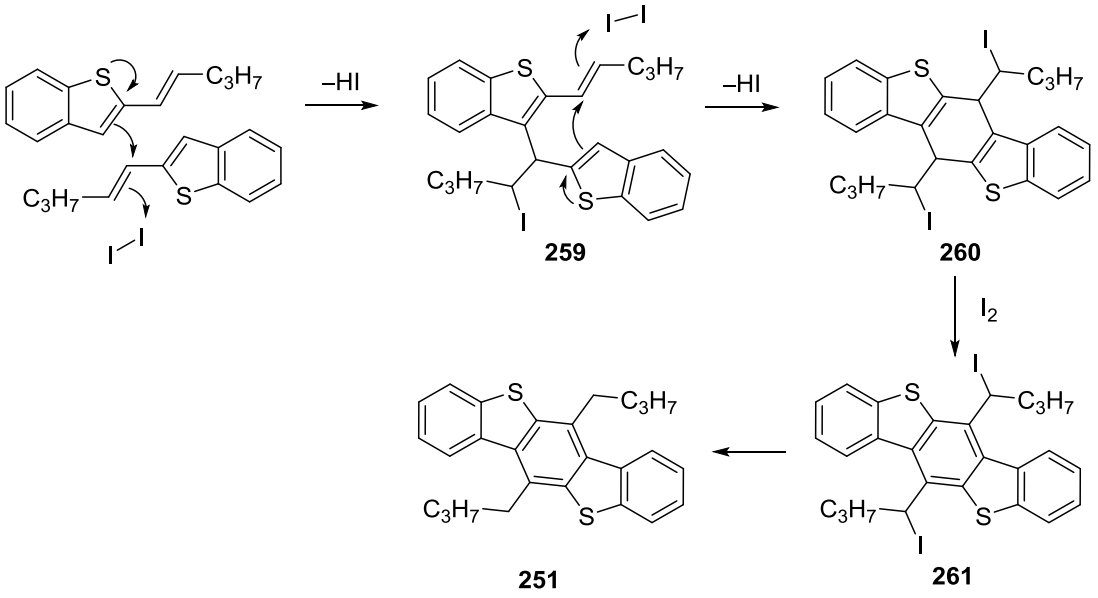
Pleasingly, the reaction proceeded for a range of different alkenylbenzothiophene starting materials. Longer alkyl chains were tolerated on the alkene (compound **252**) and substitution *para* to sulfur was widely accepted (compounds **253**-**256**). A slightly lower yield was observed for compound **257** possessing a *meta*-fluoro substituent. This can be rationalised on electronic grounds when considering the electron-withdrawing effects of the fluorine atom on the nucleophilicity of the benzothiophene.



227 **258**

Scheme 73

Increasing the electron density present in the BDT products resulted in a drop in yield (**255**). This may be due to the oxidative environment they are formed in causing decomposition. Unfortunately, dimerisation to give highly conjugated heptacene structure **258** failed: the reaction showed complete consumption of starting material but no formation of product, and only a complex mixture of inseparable compounds was observed (Scheme 73).

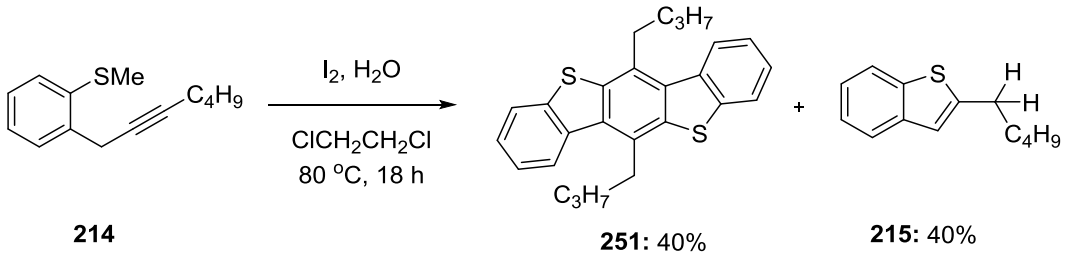


259 **260** **261** **251**

Scheme 74

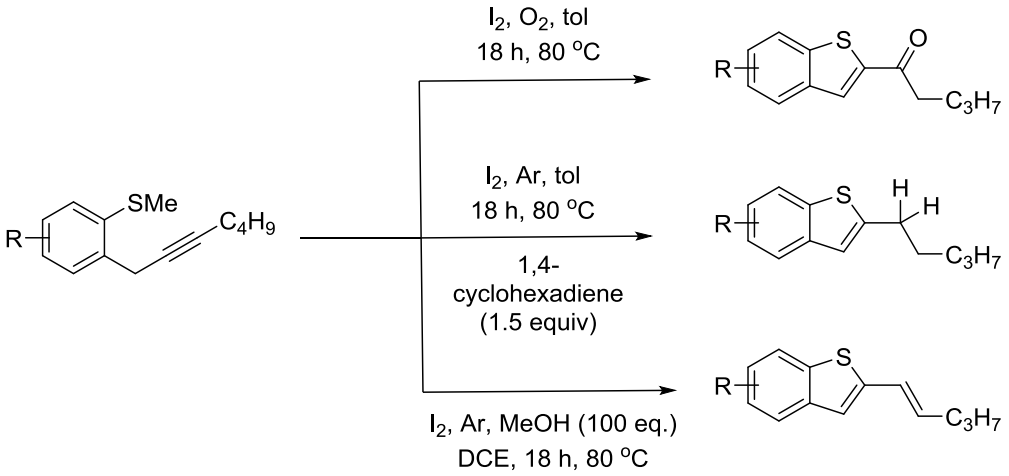
Scheme 74 presents a proposed mechanism for the dimerisation of 2-alkenylbenzothiophenes. Taking into consideration the conditions screened during optimisation, the mechanism is believed to proceed by a pair of nucleophilic attacks of benzothiophene onto an iodo-activated alkene, with the first addition being intermolecular and the second being intramolecular. Following rearomatisation, intermediate **260** is formed with the production of two equivalents of HI. Oxidation of **260** by excess I_2 leads to dibenzyliodide compound **261** and based on the known instability of these compounds, **261** could plausibly decompose via a radical or ionic process to give the final product **251**. It is not yet clear whether this final step is driven by heat, light or the presence of excess iodine. As mentioned above, it is possible that the reduction of the starting alkene to the alkane side product observed during optimisation studies was due to the alkene acting as an oxidant of intermediate **260**. Using this hypothesis it is easy to rationalise the observed 2:1 ratio of product to starting material as each pair of alkene molecules which react to form intermediate **260** would require one further alkene molecule to facilitate oxidation to the fully conjugated system. The addition of a large excess of iodine could easily override reduction of the starting material and act as a mild oxidant to produce final product **251**.

A “one-pot” combination of both cyclisation and dimerisation was also investigated (Scheme 75). This proved a challenging synthetic problem, as optimised conditions for cyclisation and dimerisation were incompatible, meaning a compromise between the two was needed. For example, whilst methanol was essential for the efficient production of alkenyl benzothiophene products any attempted dimerisations with methanol present in the mixture failed. After extensive optimisation, the highest yield for this ‘”one-pot” protocol (40%) was achieved when the reaction was carried out in 1,2-dichloroethane with 3 eq. of I_2 and 100 eq. of water, however this reaction produced an equal amount of the reduced alkane as well.



Scheme 75

As demonstrated in this section, iodine-mediated cyclisations of our propargylation products offer a valuable, metal-free course to a range of substituted benzothiophenes (Scheme 76). Through judicial choice of conditions, ketone/aldehyde, methyl/methylene or alkenyl products can be prepared, allowing the synthesis of substituted NDTs and highly conjugated BDT scaffolds. Also, by varying substitution on the aryl ring of the starting arylpropargylsulfides the electronics of these products can be 'tuned', an essential factor when optimising materials for use in organic electronics.



Scheme 76

To demonstrate the viability of our NDT and BDT structures, in collaboration with the group of Professor Mike Turner at the Organic Materials Innovation Centre at the University of Manchester compounds NDTs (**237**, **238**, **239**, **240**, **241**, **242**) and BDTs (**251**-**257**) were tested for their material properties. Cyclic voltammetry and UV/Vis spectroscopy was carried out to determine the HOMO/LUMO levels and energy gaps for these compounds. In particular NDT structures **239**-**242** showed a low lying HOMO of < −5.5 eV and a band gap greater than 3 eV. Following this finding, thin films of compounds **239**-**242** were formed and characterised, using atomic force microscopy and X-ray diffraction, and organic field effect transistors were prepared and analysed using the conventional thin film transistor techniques. Compounds **240** and **242** demonstrated hole transporting (p-type) behaviour in a field effect transistor and in particular, compound **242** showed a moltility of 0.2 $cm^2\ V^{-1}\ s^{-1}$, a high on/off ratio of 10^7 and a threshold voltage of −22 V, performance consistent with reported literature.[79]

2.3 Selective Functionalisation of Benzothiophenes

Functionalisation at C3 of benzothiophene motifs is underdeveloped when compared with functionalisation at C2, with reported techniques requiring directing groups, pre-functionalisation and metal catalysts. Due to the presence of these structures in many pharmaceutically important compounds[80-84] (for examples, see Figure 6) and the known risk of metal contamination in compounds intended for human consumption, a mild, metal-free process for the selective C3 functionalisation of benzothiophene motifs would be a valuable synthetic achievement.[85]

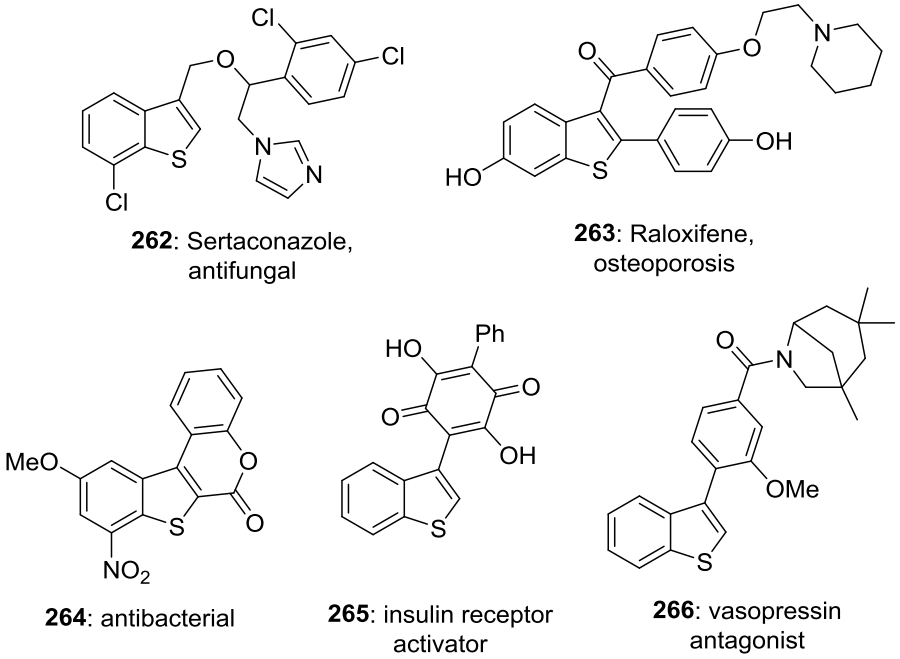
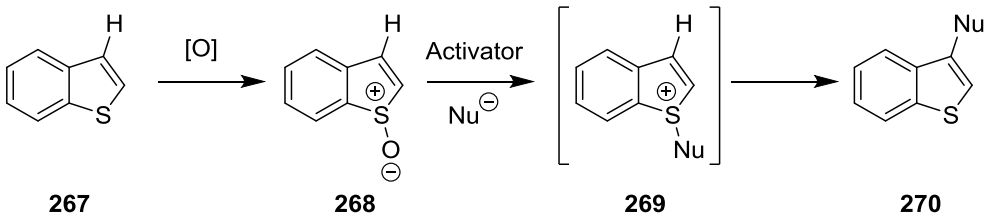


Figure 6

Having developed the previously described procedures for the synthesis of substituted benzothiophenes, the possibility of using the sulfur atom intrinsic to benzothiophenes to selectively functionalise these scaffolds using interrupted Pummerer chemistry was deemed an interesting avenue of investigation. In this case, we hypothesised that with the oxidation of benzothiophene **267** and subsequent activation of the resultant benzothiophene *S*-oxide (**268**), nucleophiles could be trapped to form sulfonium intermediates (**269**), avoiding a direct additive Pummerer-type reaction, and delivered to the C3 position regiospecifically (Scheme 77).

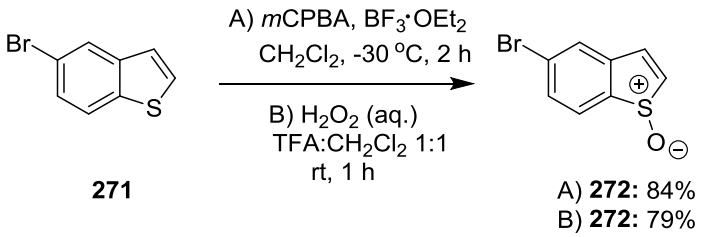


267 **268** **269** **270**

Scheme 77

2.3.1 Benzothiophene *S*-Oxides: Synthesis and Reactivity

Benzothiophene *S*-oxides are a reactive species and a largely unexplored class of organic compounds. This is largely due to their reactive nature which makes thier isolation a delicate and often unsuccessful process. A variety of conditions have been reported for the oxidation of thiophenes and benzothiophenes to give the corresponding *S*-oxides. These include the use of metal complexes, hypervalent iodine reagents and even molecular chlorine. To make our procedure as operationally simple as possible we decided to employ two different sets of oxidation conditions that were reported in the literature[86-88] (Scheme 78). Either oxidation with *m*-CPBA in the presence of boron trifluoride dietherate at low temperatures, or alternatively, oxidation with hydrogen peroxide in trifluoroacetic acid and dichloromethane. For example, both methods gave the product *S*-oxide (**272**) from 5-bromobenzothiophene **271** in high yields.



271

A) **272:** 84%
B) **272:** 79%

Scheme 78

Before further discussion, a brief consideration of the reactivity and stability of thiophene/benzothiophene *S*-oxides is warranted. Thiophene *S*-oxides are unstable in concentrated solutions if not kinetically or thermodynamically stabilised, meaning that the synthesis and isolation of these molecules for our investigation was not feasible.[89]

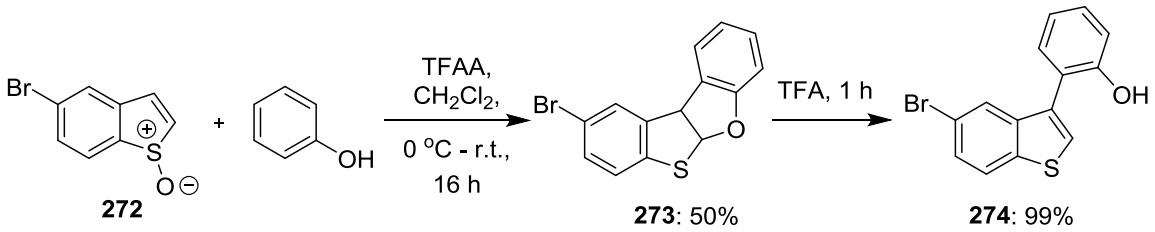
Benzothiophene *S*-oxides on the other hand have been reported with a variety of different substitution patterns. The inherent instability of this family of compounds originates from three main processes. Firstly, over oxidation of the labile *S*-oxide can produce the *S,S*-dioxide. The conditions we selected for the oxidation however, this was easily controlled as once the *S*-oxide was formed it was prevented from further reaction by protonation or coordination to $BF_3 \bullet OEt_2$.[90] Secondly, at high concentrations benzothiophene *S*-oxides are prone to dimerisation reactions, through a [4+2] or [2+2] mechanism.[88, 90, 91] Lastly, thiophene and benzothiophene *S*-oxides are known to undergo photolysis to liberate the parent thiophene/benzothiophene.

Luckily for our investigation, 5-bromobenzothiophene *S*-oxide **272** was found to be easily synthesised and isolated in high yields and was surprisingly stable, even when stored without refrigeration or an inert atmosphere for months. It was for these reasons that **272** was chosen as a model substrate for our investigation.

2.3.2 Selective Arylation of Benzothiophenes Using Phenols

Reported methods for the selective C3 arylation of benzothiophenes traditionally use palladium catalysts[92-95] and pre-functionalised coupling partners[96-99]; whilst recent advances have solved many problems with regioselectivity and harsh conditions, the risk of metal contamination remains. It was for this reason that, inspired by the work of Yorimitsu et al.,[34] we investigated the possibility of selective C3 metal-free arylation of benzothiophene *S*-oxides using phenols.

Initially, we explored the coupling of easily isolable 5-bromobenzothiophene *S*-oxide **272** and phenol and were pleased to find that in dichloromethane with the addition of TFAA, thioacetal **273** was formed in 50% yield (Scheme 79). To our delight, it was quickly noticed that this thioacetal product was an intermediate of selective arylation and, upon acidic hydrolysis with trifluoroacetic acid, produced arylated benzothiophene **274** in quantitative yield with respect to thioacetal **273**.



Scheme 79

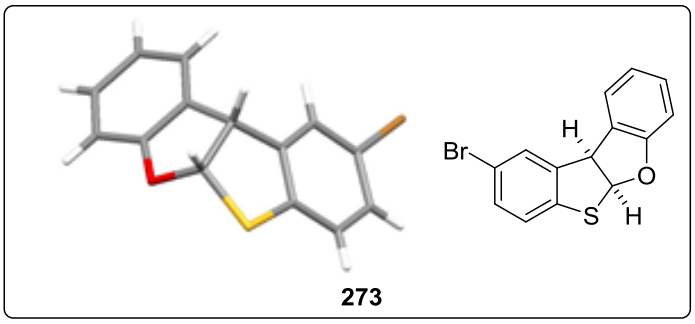
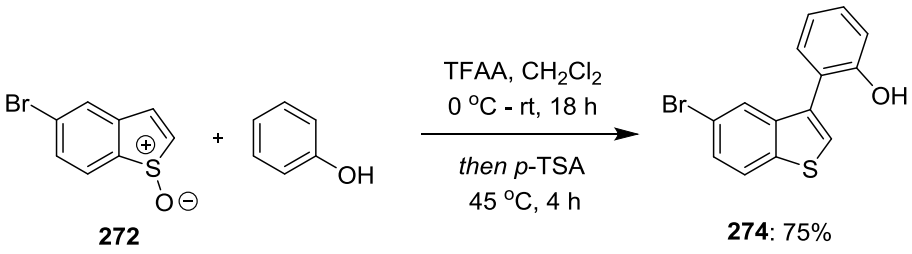


Figure 7

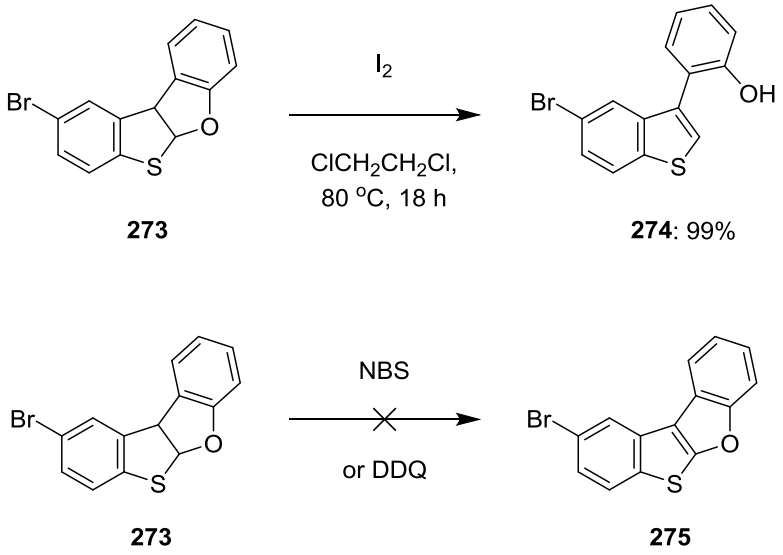
X-ray crystallography elucidated the structure of intermediate **273** and proved that C-C bond formation occurred at the C3 position (Figure 7). This result provided a solid starting point for the optimisation of metal-free arylation reactions. Very little adjustment was needed to the originally employed conditions: activation and addition of the phenol was carried out at the lower temperature of −40 °C and trifluoroacetic acid was replaced with *para*-toluenesulfonic acid for thioacetal opening. These changes resulted in a 75% yield of **274** over two steps. (Scheme 80).



Scheme 80

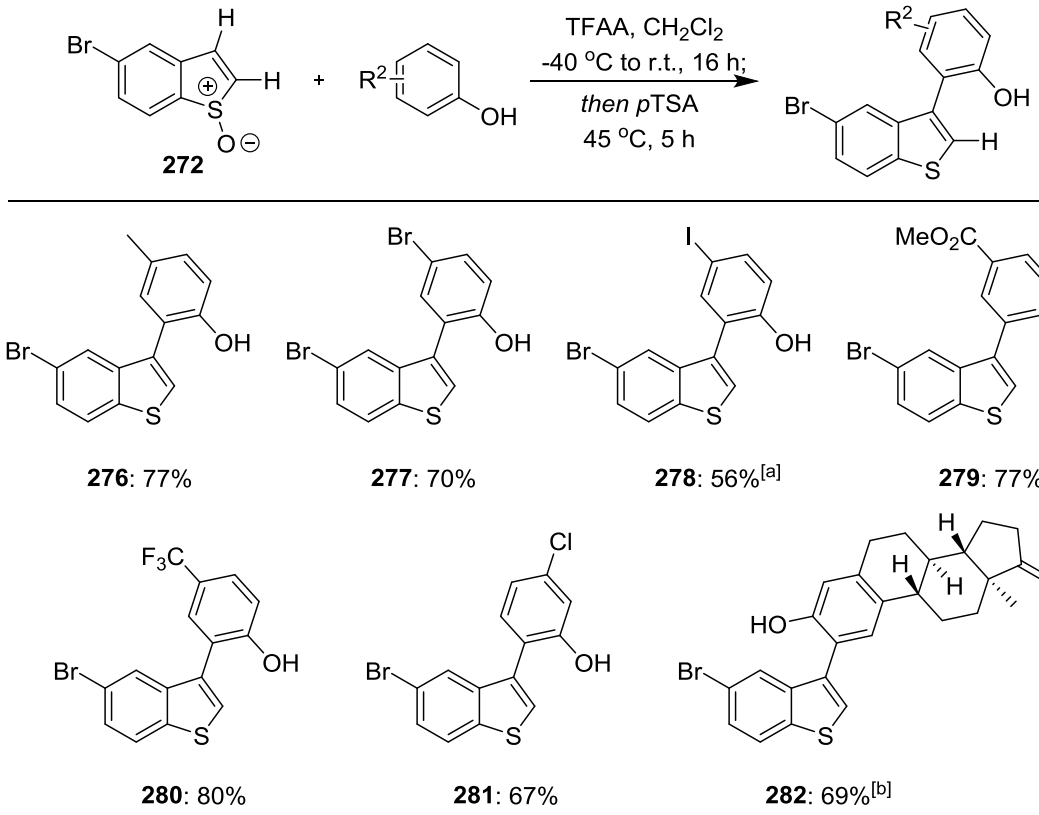
Thioacetal intermediate **273** showed a somewhat surprising reluctance to oxidise and give highly conjugated benzo[4,5]thieno[2,3-*b*]benzofuran system **275**

(Scheme 81). Inspired by our earlier use of molecular iodine as a mild oxidant in the formation of highly conjugated systems, similar conditions were employed in an attempt to oxidise thioacetal **273**. Unexpectedly, these conditions gave quantitative conversion of thioacetal **273** into arylated benzothiophene product **274**. The use of *N*-bromosuccinimide also failed to produce the benzo[4,5]thieno[2,3-*b*]benzofuran (**275**) scaffold and even strong oxidants such as DDQ failed in this undertaking.



Scheme 81

Possessing now the optimised conditions for selective C3 arylation of benzothiophene *S*-oxides, we moved to investigate the scope of this reaction. Using 5-bromobenzothiophene *S*-oxide **272** a wide variety of readily available phenols gave high yields in the coupling reaction (Scheme 82). As shown, a range of para-substituted phenols were well tolerated in the reaction, with electron withdrawing groups (**279** and **280**), halides (**277** and **278**) and moderately electron rich phenols (**276**) giving high yields. Highly electron rich phenols, such as *para*-methoxyphenol, performed poorly in the reaction, liberating mostly the parent benzothiophene. On coupling with *meta*-chlorophenol, complete selectivity was observed not only at the C3 position of the benzothiophene motif but also at the 2-position of the phenol, giving **281** exclusively. More complicated phenols, such as estrone, also proved effective coupling partners (**282**), however, in this case (as in some other examples), it was important to use iodine when opening the thioacetal intermediate (30% vs. 69%).

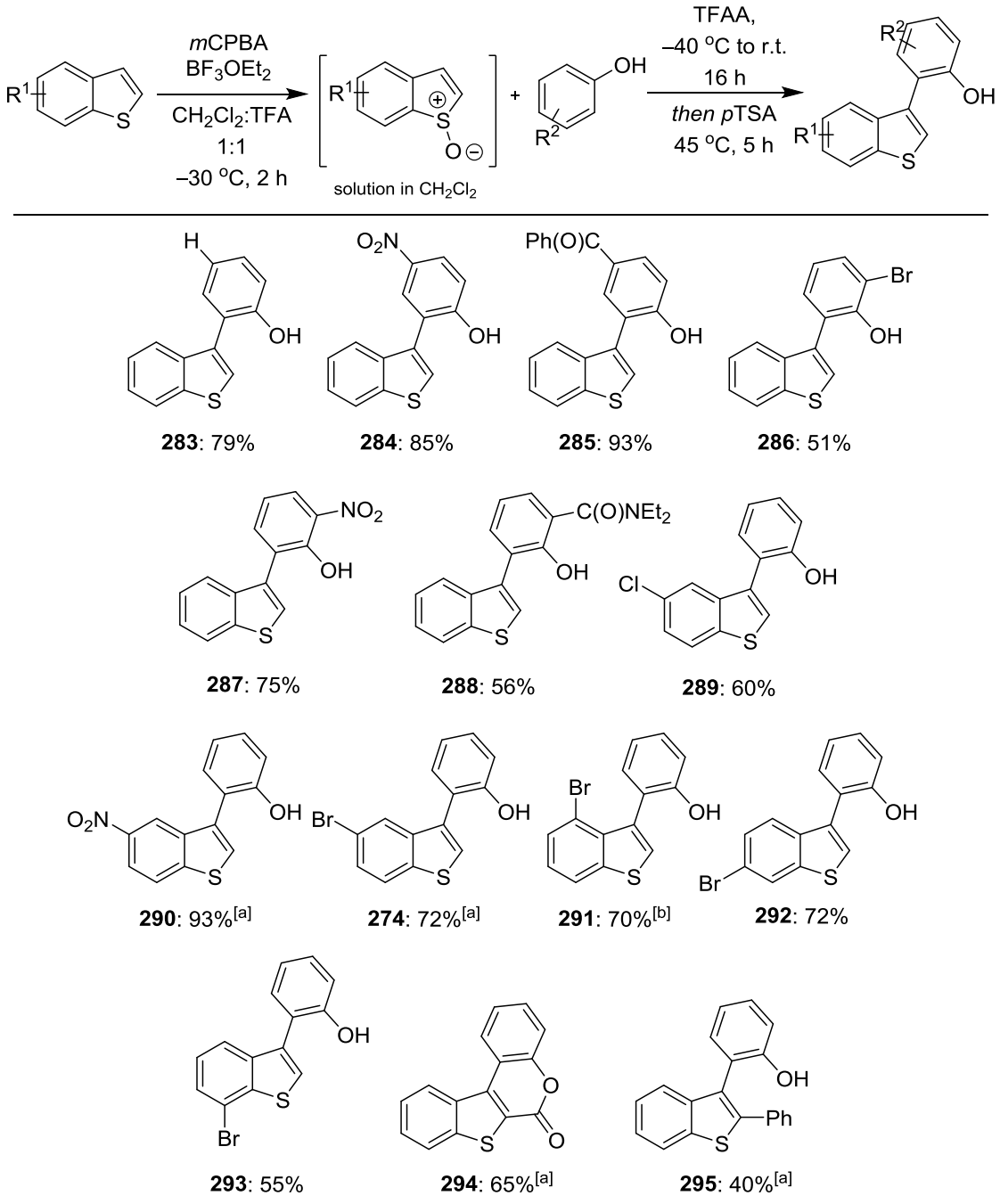


[a] *TFA used instead of pTSA.* [b] *I_2 used instead of pTSA.*

Work carried out with Dr. Jose Fernandez-Salas

Scheme 82

Well aware of the reactivity of benzothiophene *S*-oxides, we were unsurprised to observe that the isolation of *S*-oxides bearing no functionality at the C2 and C3 position was difficult. To this end, we designed a simple protocol for the oxidation and arylation of benzothiophenes. After oxidation of the chosen benzothiophene with *m*CPBA, using the previously described conditions, a simple work up and filtration gave a solution of the desired benzothiophene *S*-oxide that could be directly used in the arylation reaction. As can be seen in Scheme 83, different phenols with both *para*- (**283**-**285**) and *ortho*- (**286**-**288**) substitution were well tolerated in this reaction, with especially high yields being observed using *para*-nitrophenol (**284**) and *para*-(phenylketo)phenol (**285**).



[a] *from isolated benzothiophene S-oxide.* [b] *using I_2 instead of pTSA.*

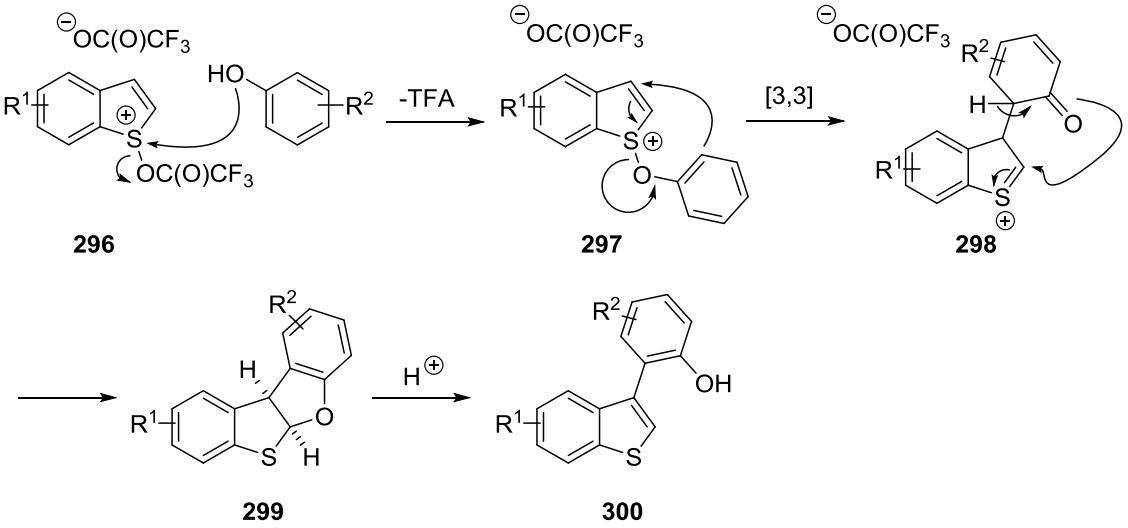
Work carried out with Dr. Jose Fernandez-Salas, and Kristen Hedke

Scheme 83

The development of this oxidation/arylation protocol allowed investigation of the scope of the benzothiophene coupling partner. It was found that the inclusion of chloro (**289**) and nitro (**190**) substituents at C5 were well tolerated, as was the easily functionalisible aryl bromide moitey at all positions around the benzene ring (**274, 291-**

293). Unfortunately, electron rich benzothiophenes, such as 5-methoxybenzothiophene, performed poorly, giving no product along with complete destruction of starting material, most likely due to the high instability of the intermediate benzothiophene *S*-oxide. Substitution at C2 provided interesting examples: a methyl ester substituent at this position gave isothiacoumestan **294**, the product of spontaneous lactonisation between phenol and ester moieties. Product **294** constitutes the core structure of known antibacterial **264** (figure 6). 2-Phenylbenzothiophene *S*-oxide also underwent smooth arylation to give **295**, a somewhat surprising result considering the steric properties of the phenyl group. The inclusion of bromo or cyano groups at the C2 position only resulted in a complex mixture with no product observable, possibly due to decomposition of the thioacetal intermediate.

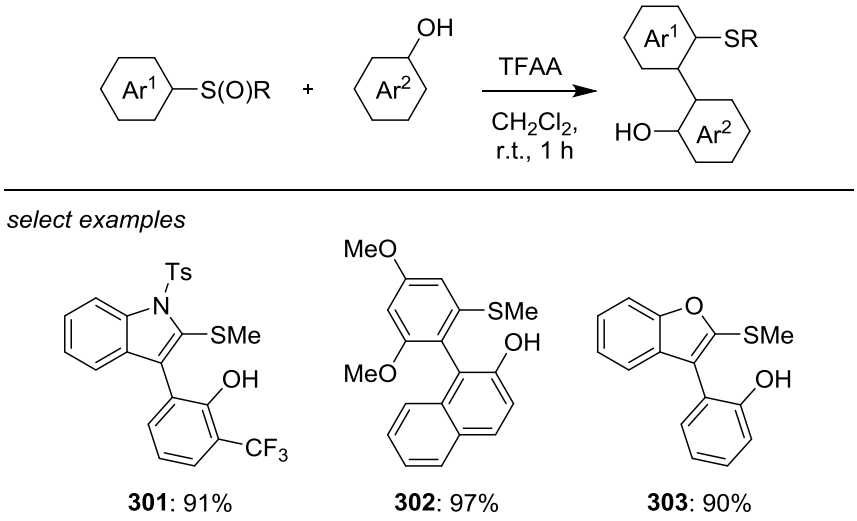
A mechanism for the selective C3 arylation of benzothiophene *S*-oxides is proposed in Scheme 84. With literature precedent showing the viability of nucleophilic attack by phenols onto activated sulfoxides, the proposed mechanism begins with attack of phenol onto activated benzothiophene *S*-oxide **296**, forming sulfoxonium species **297**. Additional energy (provided by warming from -40 ^{o}C to room temperature) allows sulfoxonium **297** to undergo a charge accelerated [3,3]-sigmatropic rearrangement thus giving thionium ion **298**. Rearomatisation of the benzene ring and subsequent attack onto the electrophilic thionium furnishes thioacetal intermediate **299** which can be opened using acid to give the final arylated benzothiophene product **300**.



Scheme 84

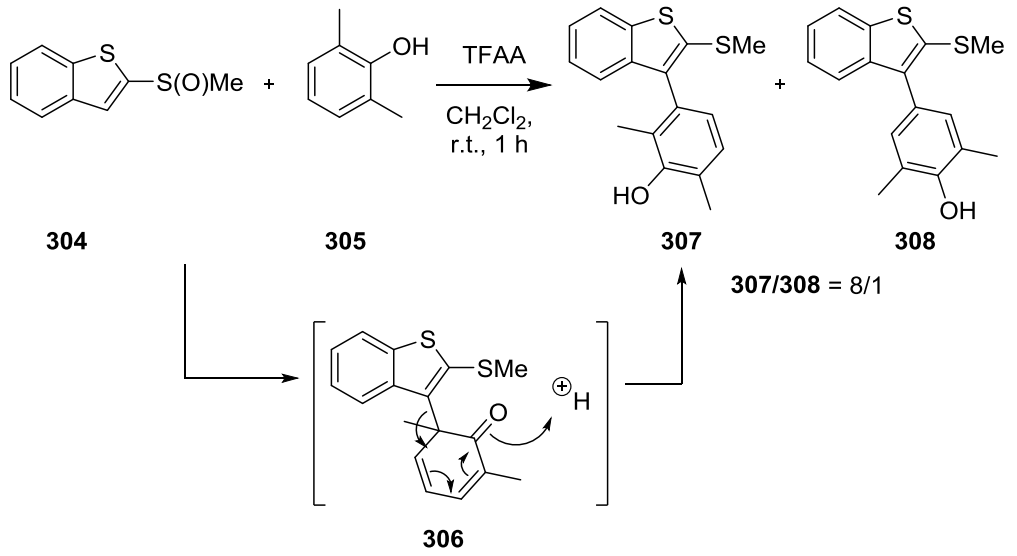
Strong experimental evidence for this proposed mechanism comes from the isolation and full characterisation of thioacetal intermediate **273**, including X-ray structure determination (figure 7). During the course of optimisation and exploration of the scope, no product from para attack of any phenol was observed in any reaction, suggesting that not only is an interrupted Pummerer pathway in operation but that activated benzothiophene *S*-oxides are highly electrophilic at sulfur.

During investigation into C3 selective arylations of benzothiophenes, Yorimitsu reported that combining phenolic nucleophiles with activated aryl sulfoxides is an efficient route to the synthesis of biaryl systems (Scheme 85). In a reaction reminiscent of their previous work, aryl sulfoxides activated by TFAA were able to intercept a range of phenols and then, at room temperature, rearrange via a [3,3]-sigmatropic rearrangement, to give biaryl motifs after rearomatisation.[100]



Scheme 85

Their studies provided evidence for an interrupted Pummerer mechanism: the use of 2,6-dimethylphenol showed a large preference for product **307** over Friedel-Crafts product **308** (Scheme 86). Product **307** was largely favoured over the production of direct addition (**308**) and was proposed to be formed by an interrupted Pummerer/rearrangement sequence to give intermediate **306**, followed by a 1,2-shift and rearomatisation to give **307**.



Scheme 86

Overall, our selective C3 arylation of benzothiophenes represents the coupling of two inherently nucleophilic sites (benzothiophene C3 and C2 in phenol) and, in contrast to previous studies, this approach avoids the installation and use of a formal directing group, instead using the intrinsic sulfur of benzothiophenes to capture and selectively deliver nucleophiles.

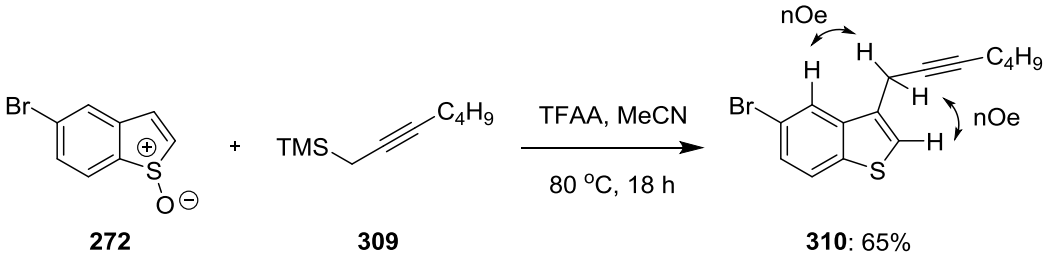
2.3.3 Selective Alkylation of Benzothiophenes

2.3.3.1 Propargylations of Benzothiophenes

Whilst selective C3 C-H arylations of benzothiophene have been reported, the selective C3 C-H alkylation of these systems is a significant challenge and methodologies for these transformations are in short supply. The handful of procedures that have been reported for the selective C3 alkylation of benzothiophenes are limited in scope,[101] require metal catalysts,[102] harsh conditions and/or ancillary directing groups at C2.[103, 104] Seeing this, we proposed that a marriage of our previously described *ortho*-propargylation/allylation chemistry and our newer benzothiophene *S*-oxide chemistry would offer a valuable entry to C3 alkylated benzothiophenes.

The investigation into this proposed alkylation protocol began with the exposure of 5-bromobenzothiophene *S*-oxide to our standard propargylation conditions for heterocyclic systems (Scheme 87). We were pleased to find that this reaction proceeded nicely, giving already a good yield of C3 propargylated benzothiophene **310**. Based on

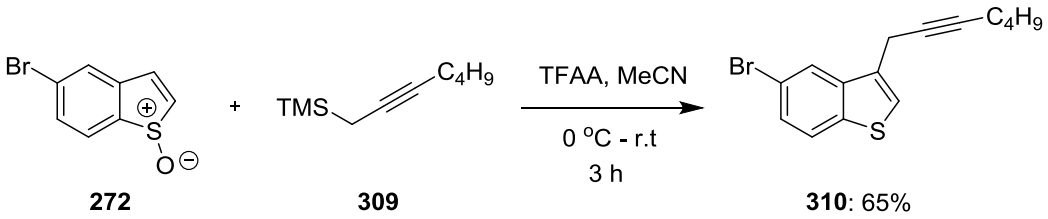
previous work, we were confident that alkylation would occur selectively at C3 and confirmation of this came through the use of nuclear Overhauser effect NMR spectroscopy. The benzylic/propargylic protons of the product showed a marked through-space interaction with the proton at C4 of the benzothiophene, an interaction that would be impossible if propargylation had occurred at C2.



272 **309** **310**: 65%

Scheme 87

Encouraged by the selectivity and yield of this initial reaction, fully optimised conditions were developed. It was quickly found that the reaction did not require heating and was complete in three hours (Scheme 88).

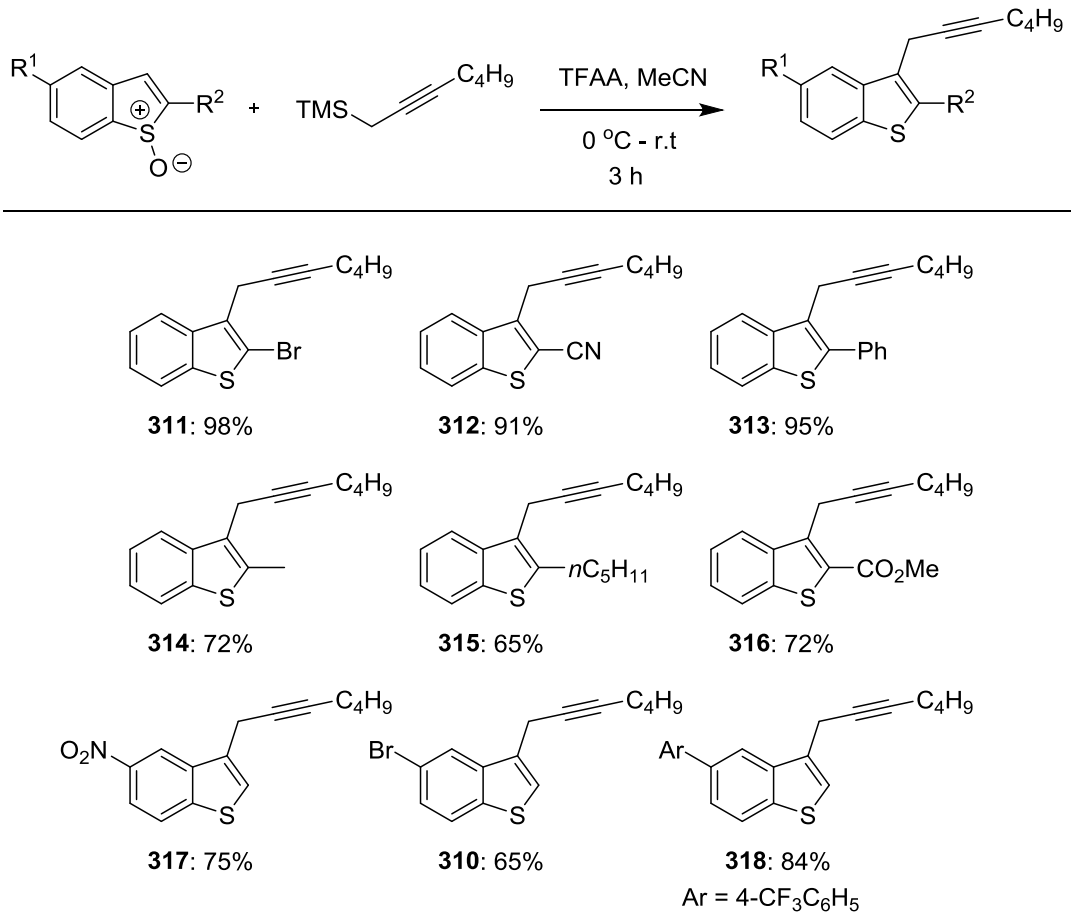


272 **309** **310**: 65%

Scheme 88

With optimised conditions in hand, along with proof of the C3 selectivity of alkylation, we moved to investigate the scope of the selective alkylation with respect to the benzothiophene *S*-oxide. Easily isolable C2-substituted benzothiophene *S*-oxides were synthesised along with a handful of C5-substituted substrates known to be stable from previous studies. Scheme 89 shows that under optimised conditions, propargylation of C2 substituted benzothiophene *S*-oxides occurs in high yields and pleasingly, with a range of functionality at C2. Sulfoxide substrates bearing bromo (**311**), nitrile (**312**) and phenyl (**313**) substituents gave products that were isolated in

exceedingly high yields. Alkyl (**314** and **315**) and ester (**316**) containing compounds also gave products in good yields.



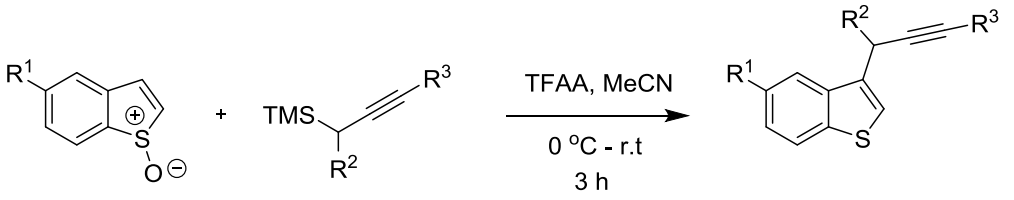
Scheme 89

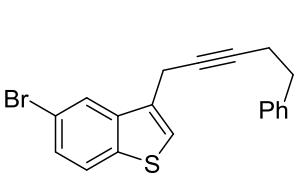
Sulfoxides bearing no substituents at C2 but functionality at C5, also gave selective C3 alkylation: 5-Nitro (**317**), 5-bromo (**310**), and 5-aryl (**318**) propargylated benzothiophenes were all isolated in good yield. More electron rich systems performed poorly in these conditions, as was the case for the selective arylation described previously. Note that isolable benzothiophene *S*-oxides with no C2 or C3 substitution, are all electron deficient, possibly explaining the incompatibility of more electron rich systems with these conditions due to the instability of the electron rich benzothiophene *S*-oxides.

A variety of propargyl silane coupling partners showed compatibility with the alkylation conditions, allowing the use of primary alkyl (**319**), alkyl halide (**320**), secondary alkyl (**321**) and silyl (**322**) substituents at the terminal position (Scheme 90). Interestingly, the use of terminal and phenyl propargyl silanes proceeded with good

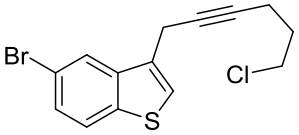
yields (**323** and **324**). The attempted use if these propargyl silanes in our previous studies had proved unsuccessful. Terminal propargyl alkylation product **323** is a key intermediate in the synthesis of an inducer of bacterial biofilms.[105] Secondary propargyl silanes provided branched products **325** and **326** that would be inaccessible through traditional metallation/trapping techniques.[106]

Also demonstrated in Scheme 90 is the use of a combined oxidation/ alkylation procedure for non-isolable benzothiophene *S*-oxides. Compounds **327**-**331** were synthesised by oxidation of the chosen benzothiophene with *m*-CPBA followed by a simple work-up and filtration. It was necessary, before propargylation, to conduct a solvent swap from dichloromethane to acetonitrile, a task easily achieved by addition of MeCN to the solution of benzothiophene *S*-oxide in dichloromethane followed by evaporation of the latter solvent *in vacuo*. Repetition of this procedure gave a solution of *S*-oxide starting material in acetonitrile that could be used directly in the alkylation step.

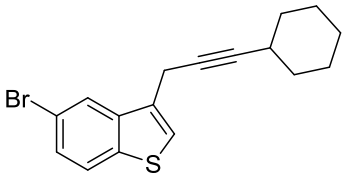




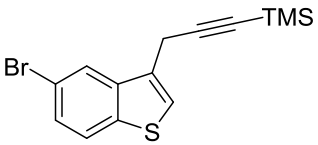
319: 81%



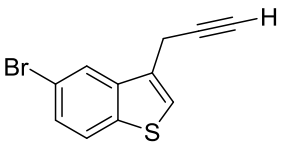
320: 84%



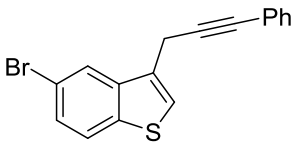
321: 82%



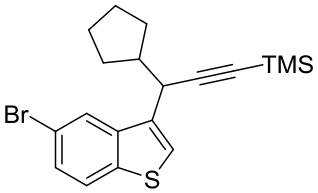
322: 91%



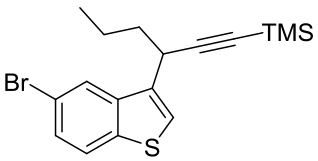
323: 58%



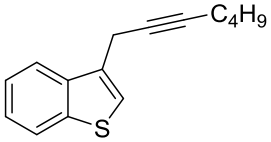
324: 59%



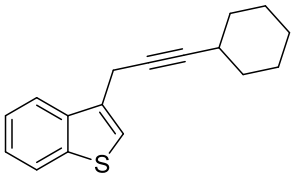
325: 85%



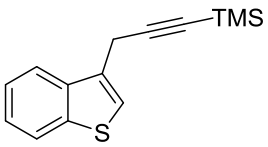
326: 83%



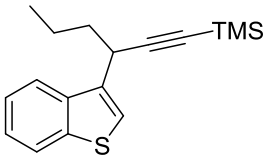
327: 60%[a]



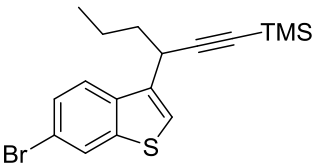
328: 60%[a]



329: 80%[a]



330: 76%[a]



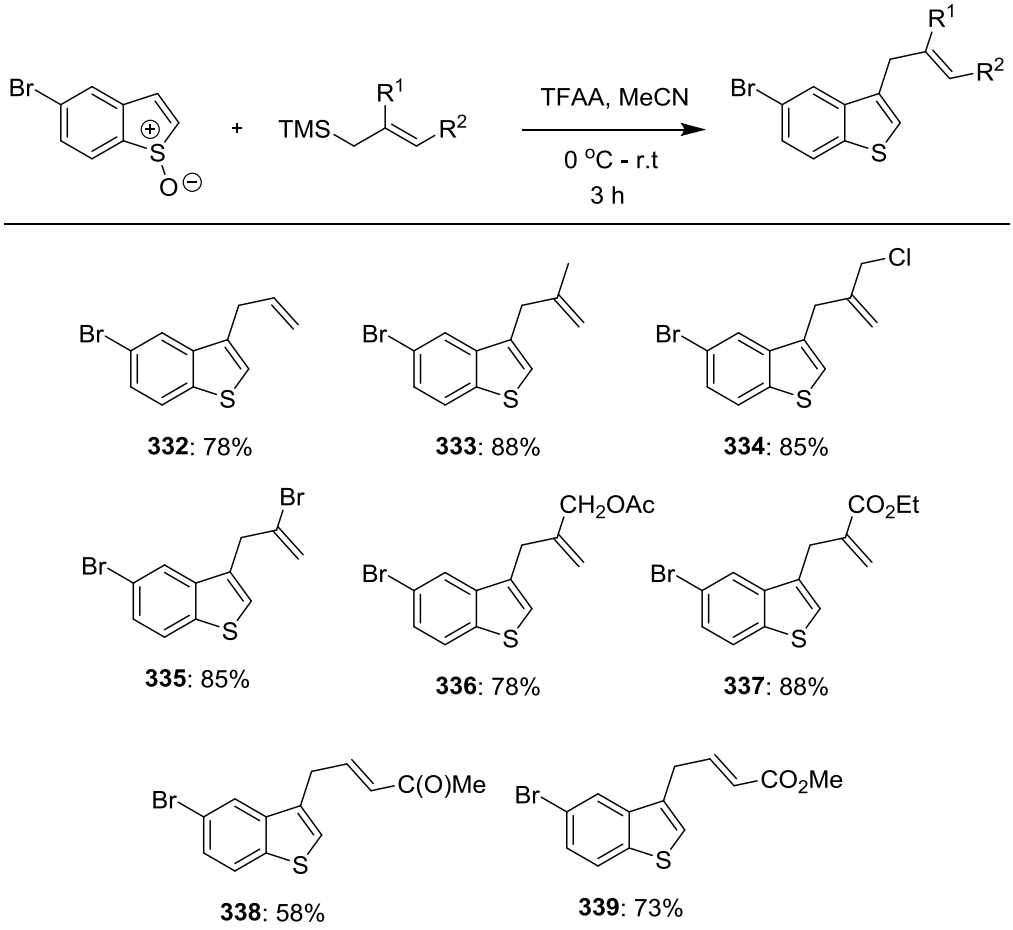
331: 86%[a]

[a] *in situ* oxidation and propargylation from benzothiophene

Scheme 90

2.3.3.2 Allylations of Benzothiophenes

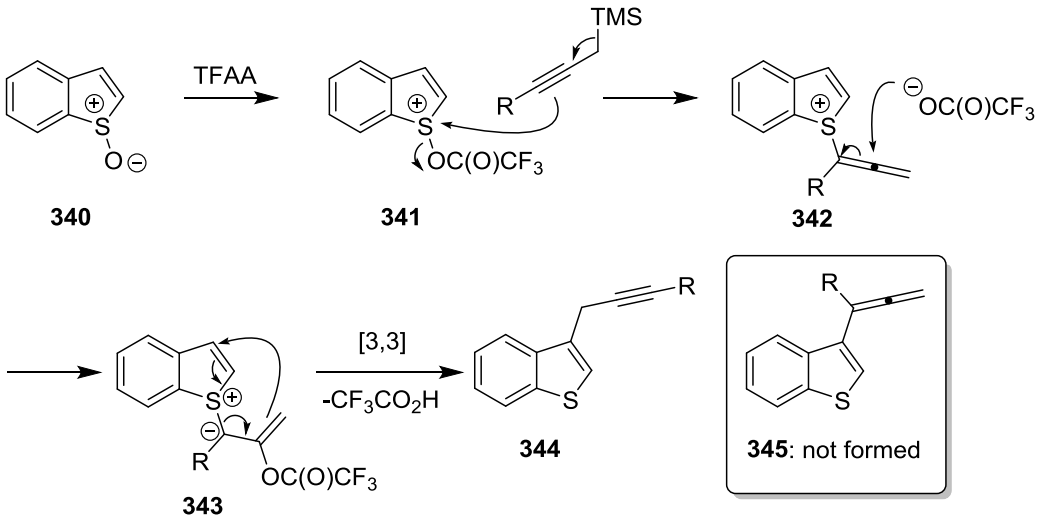
Allyl silanes also proved highly effective coupling partners in the selective C3 alkylation of benzothiophene *S*-oxides (Scheme 91). Allylation proceeded smoothly with unsubstituted allyl silane (**332**) and β-methyl (**333**), β-chloromethyl (**334**), β-bromo (**335**), β-methylacetate (**336**), and β-ester (**337**) allyl silanes all gave high yields. Allyl silanes, such as γ-keto (**338**) and γ-ester (**339**), both possessing internal carbon-carbon double bonds, also gave the expected products good yield and provided evidence for an interrupted Pummerer pathway (*vide infra*).



Scheme 91

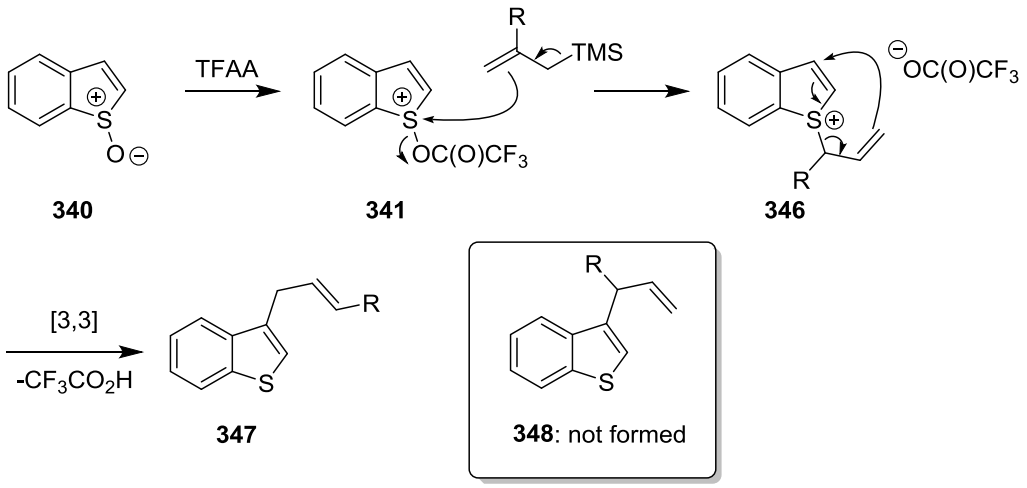
In previous work exploring the sulfoxide-directed, metal-free allylations of aromatic and heteroaromatic sulfoxides, forcing conditions were required in order to facilitate the proposed charge-accelerated [3,3]-sigmatropic rearrangement and afford products of allylation.[107, 108] In this case, however, allylation occurred quickly and cleanly under much milder conditions, presumably due to the lesser aromaticity in the 5-

membered ring of benzothiophene *S*-oxides when compared to aromatic sulfoxides. Both propargylation and allylation mechanisms are proposed to proceed through the previously reported mechanism. In the case of propargylation (Scheme 92), it is believed that the propargyl silane coupling partner attacks activated *S*-oxide **341** through an S_E2' mechanism forming allenylsulfonium salt **342**. Attack of trifluoroacetate provides sulfur ylide **343**, which undergoes rearrangement. Elimination of TFA then furnishes propargylated benzothiophene **344**.



Scheme 92

This mechanism is supported by the observation of propargylated products exclusively. Allenyl species **345** that would result from an additive-type Pummerer reaction were not observed. In contrast to our previous investigations into the propargylation of aromatic sulfoxides, allenylsulfonium intermediates **342** could not be identified even when the addition was conducted at low temperatures. This again demonstrates the highly reactive nature of the benzothiophenyl allenyl sulfonium intermediates. Allylation is believed to proceed by similar attack of the allyl silane coupling partner on activated sulfoxide **341** to form allylsulfonium salt **346** followed by a charge accelerated [3,3]-sigmatropic rearrangement to give allylated benzothiophene **347** (Scheme 93).



Scheme 93

As for the selective propargylations, allylsulfonium intermediates rearranged at low temperaturesand the proposed intermediates could not be observed. Evidence for the interrupted Pummerer mechanism, rather than a direct addition pathway, came by way of the exclusive formation of allylated benzothiophenes **338** and **339** when γ-substituted allylsilanes were employed: such products as **348** cannot form through direct addition of the allyl silane to the heterocyclic ring.

2.3.4 Conclusion and Future Work

2.3.4.1 Conclusion

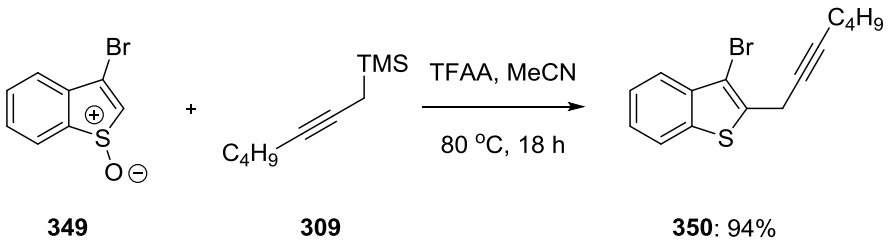
In conclusion, our work has shown the utility of sulfoxide-directed, metal-free C-H functionalisation reactions in the synthesis and derivatisation of sulfur-containing heterocycles. Using previously reported propargylated aromatic sulfides, along with new, branched variants of these compounds, in novel diversity-introducing heterocyclisations, a wide range of privileged benzothiophene cores have been constructed, including highly conjugated naphthodithiophene scaffolds. A new iodine-mediated dimerisation protocol has utilised the alkenyl products of these heterocyclisations to synthesise a handful of substituted benzodithiophene cores, Testing of our NDT and BDT cores showed results in agreement with those reported in the literature.

Furthermore, underexplored benzothiophene *S*-oxides have been presented as valuable intermediates in the selective, metal-free functionalisation of

benzothiophenes. Using either isolated benzothiophene *S*-oxides or those produced *in situ*, a range of phenols and propargyl and allyl silanes can be coupled exclusively at the C3 position of benzothiophenes. This reaction is believed to proceed through an interrupted Pummerer reaction followed by a facile charge accelerated [3,3]-sigmatropic rearrangement, facilitated by the lack of aromaticity in the 5-membered ring of the benzothiophene *S*-oxide moiety.

2.3.4.2 Current and Future Work

As shown above, selective C3 propargylation is possible on benzothiophene *S*-oxides containing substitution at different positions. We have recently become interested in the reactivity of this class of molecules when the C3 position is blocked. It was found that when C3 substituted 3-bromobenzothiophene *S*-oxide **349** was activated by trifluoroacetic acid in the presence of propropargyl silane **309**, C-C bond formation occurred exclusively at the C2 position in high yield (Scheme 94).

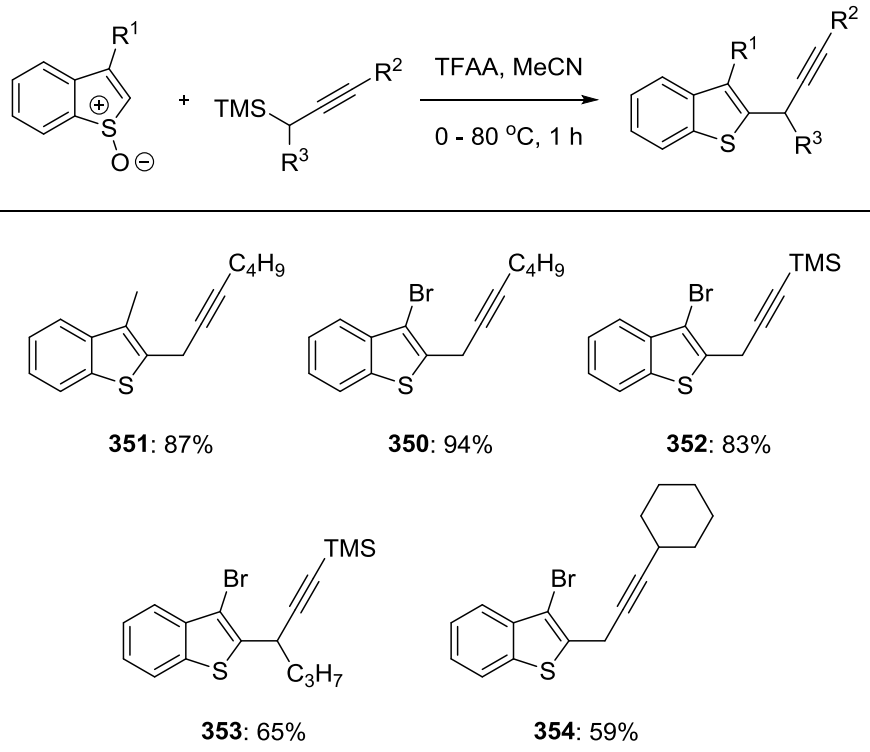


349 **309** **350**: 94%

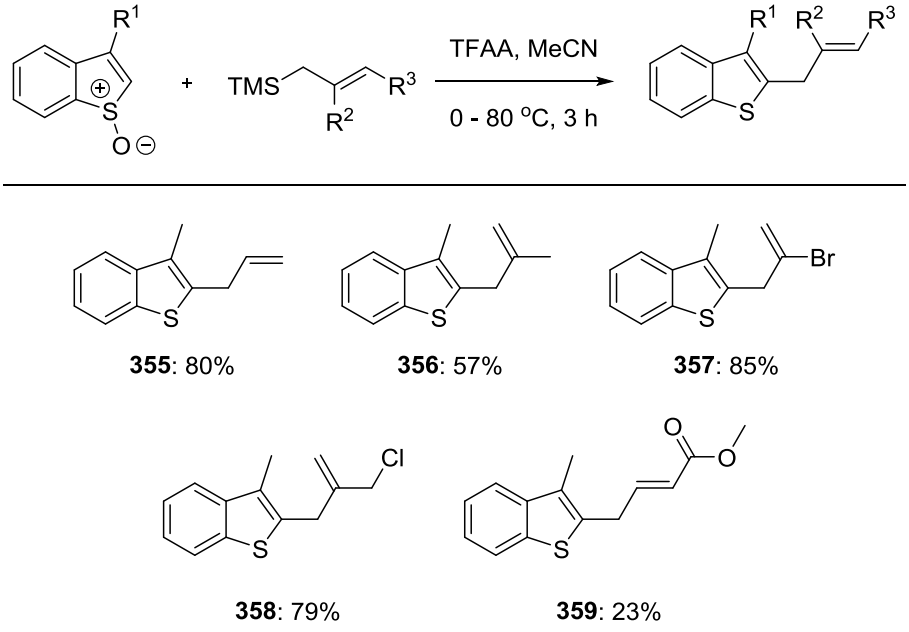
Scheme 94

This surprising result opens a new avenue for the use of benzothiophene *S*-oxides in the selective functionalisation of benzothiophenes. Alkylations at the C2 positions often require metal-halogen exchange or deprotonation followed by trapping with a nucleophile. Our strategy allows the use of metals and/or strong bases to be avoided. Initial studies into the scope of this reaction have shown promising results (Scheme 95). Benzothiophene *S*-oxides bearing methyl (**351**) and bromo (**350, 352**-**354**) substitution at the C2 position performed well with a variety of silanes, including a branched propargyl silane (**353**). A range of allyl silanes also proved to be successful nucleophiles (Scheme 96) and allylated benzothiophenes bearing bromide (**357**), methylchloride (**358**) substituents were all isolated in good yield and again (as with C3

allylation) the use of a γ-substituted allylsilane to give ester **359** gave evidence for an interrupted Pummerer pathway, although this reaction still requires some optimisation.

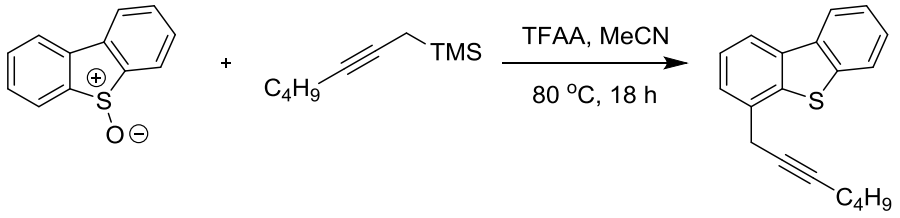


Scheme 95



Scheme 96

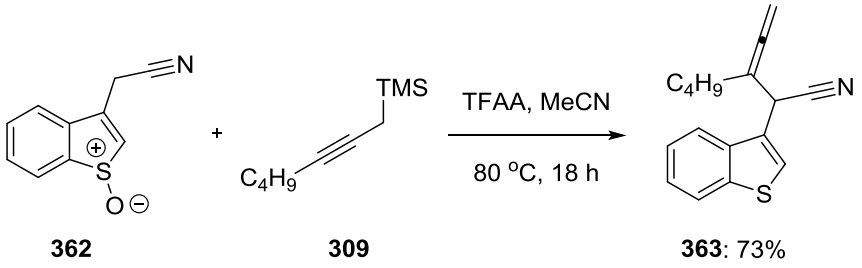
Additionally, the use of dibenzothiophene *S*-oxide **360** under these propargylation conditions interestingly gave C4 propargylated dibenzothiophene **361** in good yield (Scheme 97). Dibenzothiophene *S*-oxides are stable and easy to isolate and can be synthesised in more conventional fashion (*m*CPBA, Dichloromethane, r.t.). The lack of a reactive C3 or C2 position in dibenzothiophene *S*-oxides allows propargylation to occur only at the C4 position although heating is required to afford this transformation.



360 **309** **361**: 78%

Scheme 97

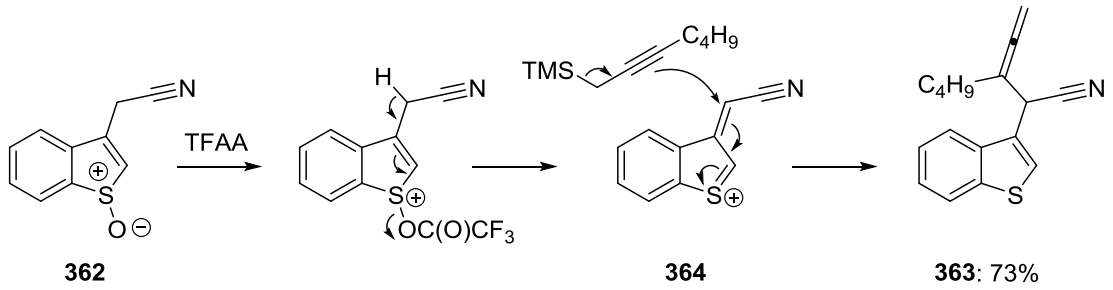
Interestingly, when attempting to propargylate 3-carbonitrilebenzothiophene *S*-oxide **362**, allenylated compound **363** was the sole product formed in 73% yield (Scheme 98).



362 **309** **363**: 73%

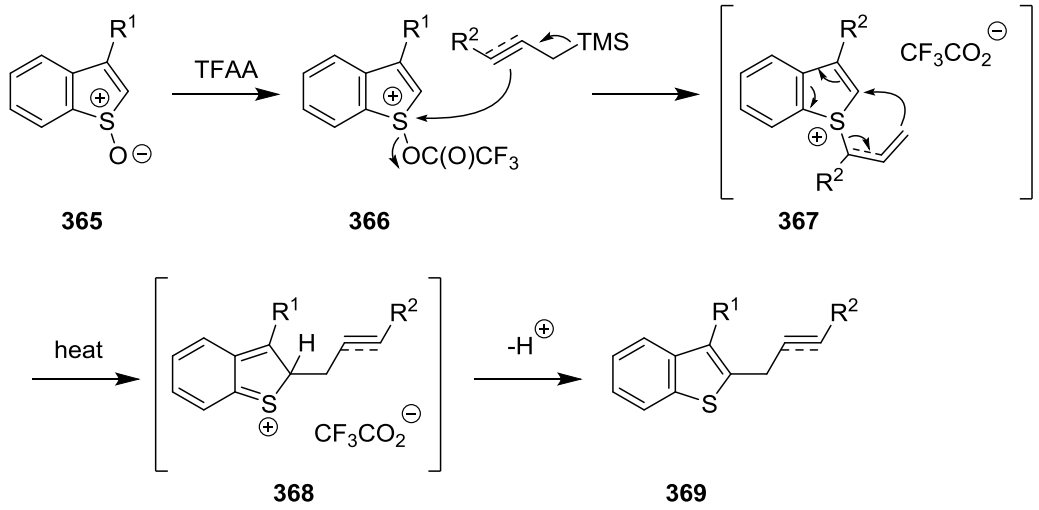
Scheme 98

Presumably, allenylation occurrs through the formation of extended thionium ion **364**, facilitated by the increase in acidity of the benzylic protons by the neighbouring nitrile group (Scheme 99). Direct nucleophilic attack of the propargyl silane onto the extended thionium intermediate yields allenylated product **363**. Further study into this process could provide an interesting approach to functionalising C3 alkykl substituents of benzothiophenes with a range of nucleophiles.



Scheme 99

Carbon-carbon bond formation at the C2 position of benzothiophene *S*-oxides is proposed to occur through a similar mechanism to that for the analogous reaction at C3 (Scheme 100). Activated benzothiophene *S*-oxides (**366**) intercept the allyl or propargyl silane, forming sulfonium salts **367** that can undergo a charge-accelerated [3,3]-pseudosigmatropic rearrangement to give coupling products **369**.



Scheme 100

In comparison to the selective C3 functionalisation reported earlier, the charge-accelerated [3,3]-sigmatropic rearrangement proposed to take place during C2 functionalisation requires the dearomatisation of two rings and this is likely the reason why heating is essential to promote this reaction. As both propargylation and allylation in this case require heating, further investigation using NMR techniques may allow us to

identify sulfonium intermediates present in the reaction mechanism and give more direct evidence for an interrupted Pummerer pathway.

Chapter 3: Experimental

3.1 General Eperimental

All experiments were performed under an atmosphere of nitrogen, using anhydrous solvents, unless stated otherwise. THF was distilled from sodium/benzophenone and dichloromethane was distilled from CaH_2. All other solvents and reagents were purchased from commercial sources and used as supplied. All sulfides and sulfoxides were prepared following known procedures.

^{1}H NMR spectra were recorded at 300, 400 or 500 MHz. ^{13}C NMR spectra were recorded at 75, 100 or 125 MHz. All chemical shift values are reported in ppm, with coupling constants in Hz. NMR yields were determined using 1 ml of a stock solution of a known amount of the selected internal standard in $CDCl_3$.

Mass spectra were obtained using positive or negative electrospray (ES), electron ionization (EI) or chemical ionization (CI) methodology. Infra-red spectra were recorded neat using FT/IR spectrometers. Melting points were measured on solids as obtained after chromatography.

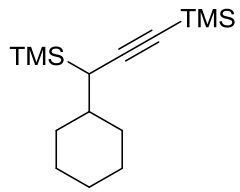
Column chromatography was carried out using 35 – 70 μ, 60Å silica gel. Routine TLC analysis was carried out on silica gel 60 F254 coated aluminium sheets of 0.2 mm thickness. Plates were viewed using a 254 nm ultraviolet lamp and developed by dipping in aqueous potassium permanganate solution.

The preparation and characterisation data of all silanes and propargylated compounds not reported in this section can be found in *Angew. Chem. Int. Ed.* **2013**, 14, 4008-4011.

3.2 Experimental Data

3.2.1 General Procedure A: Preparation of 1,3-*Bis*propargyl Silanes

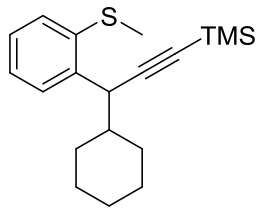
(1,3-*bis*(Trimethylsilyl))-3-cyclohexyl-prop-1-yne 137[61]



To a solution of 3-cyclohexyl-1-propyne (5.0 mmol, 0.89 ml) in THF (5 ml) under nitrogen at -78 ^{o}C was added *n*-butyllithium (1.6 M in hexanes, 5.25 mmol, 3.28 ml). The mixture was stirred at -78 ^{o}C for 30 min before chlorotrimethylsilane (5.5 mmol, 0.69 ml) was added. The resultant white slurry was warmed to room temperature where it was maintained for 1 hour, after which it was cooled to -40 ^{o}C and treated with *t*-butyllithium (1.7 M in pentane, 5.5 mmol, 3.23 ml). The yellow solution formed was then stirred at -40 ^{o}C for 2 hours before addition of chlorotrimethylsilane (6 mmol, 0.76 ml). The reaction mixture was then allowed to warm to room temperature and was stirred for a further 1 hour before quenching the reaction with water (15 ml). The layers where separated and the organic layer extracted with diethyl ether (3 x 10 ml). The solution was then dried with $MgSO_4$ and the solvent removed *in vacuo.* The crude product was purified by column chromatography on silica gel using 100% hexane as the eluent to give **137** as a clear oil (0.153 g, 3.20 mmol, 64%); $\boldsymbol{\delta_H}$ (400 MHz, $CDCl_3$) 0.11 (9 H, s, Si(C*H*$_3$)$_3$), 0.14 (9 H, s, Si(C*H*$_3$)$_3$), 1.09-1.49 (7 H, m, cyclohexyl 7 x C*H*), 1.55-1.64 (2 H, m, cyclohexyl 2 x C*H*), 1.67 (1 H, d, *J* = 4.5, Si-C*H*), 1.71-1.74 (2 H, m, cyclohexyl 2 x C*H*); $\boldsymbol{\delta_C}$ (125 MHz) -1.8 (Si(*C*H$_3$)$_3$), 0.4 (Si(*C*H$_3$)$_3$), 26.0 (cyclohexyl-*C*H$_2$), 26.5 (cyclohexyl-*C*H$_2$), 26.6 (cyclohexyl-*C*H$_2$), 29.2 (cyclohexyl-*C*H$_2$), 31.0 (cyclohexyl-*C*H$_2$), 34.1 (cyclohexyl-*C*H), 37.7 (Si-*C*H), 86.2 (C*C*Si), 108.5 (*C*CSi); $\boldsymbol{\nu_{max}}$ (neat)/cm^{-1} 643, 693, 731, 757, 838, 1053, 1247, 1449, 1656, 1889, 2147, 2852, 2926; **HRMS** (APCI): Calcd. for $C_{15}H_{30}Si_2$ $(M)^+$,266.1886; found 266.1883.

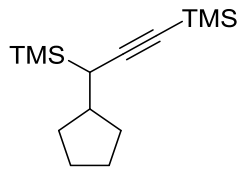
3.2.2 General Procedure B: Propargylation of Aryl Sulfoxides

(3-Cyclohexyl-3-(2-methylsulfanyl)phenyl)prop-1-yn-1-yl)trimethylsilane 139



To an oven dried tube flushed with N_2, was added methyl phenyl sulfoxide (70.0 mg, 0.5 mmol) and 1,3-*bis*(trimethylsilyl)-3-cyclohexyl-1-propyne (199 mg, 0.75 mmol) in MeCN (3 ml). Triflic anhydride (12 µL, 0.75 mmol) and 2,6-lutidine (14 µL, 1.25 mmol) were then added sequentially at room temperature and the reaction mixture was heated for 18 hours at 60 °C. After cooling to room temperature, the solution was quenched with aqueous saturated $NaHCO_3$ (6 ml) and the aqueous layer was extracted with EtOAc (3 x 5 ml). The combined organic layer was washed successively with aqueous HCl 1.0 M (5ml) and brine (5 ml), dried ($MgSO_4$) and concentrated *in vacuo*. The crude product was purified by column chromatography on silica gel eluting with 1% EtOAc in *n*-hexane to yield **139** (0.120g, 0.31 mmol, 63%) as a yellow oil; $\boldsymbol{\delta_H}$ (500 MHz, $CDCl_3$) 0.20 (9 H, s, Si(C*H*$_3$)$_3$), 1.10-1.37 (5 H, m, cyclohexyl), 1.58- 1.75 (6 H, m, cyclohexyl), 2.47 (3 H, s, SC*H*$_3$), 4.13 (1 H, d, *J* = 5.2, C*H*), 7.16-7.27 (3 H, m, ArC*H*), 7.53 (1 H, d, *J* = 7.5, ArC*H*); $\boldsymbol{\delta_C}$ (125 MHz) 0.05 ((*C*H$_3$)$_3$Si), 16.5 (cyclohexyl CH_2), 25.9 (cyclohexyl CH_2), 26.1 (cyclohexyl CH_2), 26.2 (cyclohexyl CH_2), 28.0 (cyclohexyl CH_2), 31.4 (cyclohexyl CH), 41.6 (*C*H), 42.3 (S-*C*H$_3$), 87.4 (Si*C*C), 107.1 (SiC*C*), 124.8 (Ar*C*H), 126.6 (Ar*C*H), 126.8 (Ar*C*H), 128.6 (Ar*C*H), 136.25 (Ar*C*), 139.2 (Ar*C*); *m/z* (GCMS) 316.2; $\boldsymbol{\nu_{max}}$ (neat)/cm^{-1} 543, 584, 627, 639, 661, 699, 734, 752, 838, 878, 948, 996, 1042, 1061, 1247, 1317, 1442, 1464, 1587, 2168, 2851, 2923; **HRMS** (APCI): Calcd. for $C_{19}H_{28}SSi$ $(M)^+$, 316.1675; found 316.1680

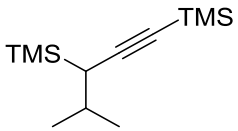
(1,3-*bis*(Trimethylsilyl))-3-cyclopropyl-prop-1-yne 140



As described in general procedure **A**, to 3-cyclopentyl-1-propyne (0.65 ml, 5.0 mmol) was added *n*-BuLi (3.28 ml**,** 5.25 mmol), chlorotrimethylsilane (0.69 ml, 5.5

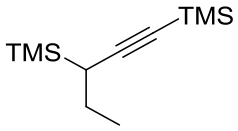
mmol), *t*-BuLi (3.23 ml, 5.5 mmol) and chlorotrimethylsilane (0.76 ml, 6.0 mmol). Purification by flash column chromatography using *n*-hexane as eluent gave **140** (0.88 g, 4.92 mmol, 98%) as a colourless oil that gradually turned to clear pink on exposure to air. δ_H (400 MHz, $CDCl_3$) 0.10 (9 H, s, Si(CH_3)$_3$), 0.14 (9 H, s, Si(CH_3)$_3$), 1.38-1.54 (4 H, m, cyclopentyl 2 x CH_2), 1.61-1.75 (4 H, m, cyclopentyl 2 x CH_2), 1.82 (1 H, d, *J* = 5.5, C*H*-Si), 1.89-1.97 (1 H, m, cyclopentyl C*H*); δ_C (125 MHz) -1.9 (Si(*C*H_3)$_3$), 0.7 (Si(*C*H_3)$_3$), 25.7 (cyclopentyl *C*H_2), 25.8 (cyclopentyl *C*H_2), 30.9 (cyclopentyl *C*H_2), 33.7 (cyclopentyl *C*H_2), 39.6 (cyclopentyl *C*H), 85.5 (*C*CSi), 109.1 (C*C*Si); ν_{max} (neat)/cm^{-1} 627, 644, 694, 757, 833, 1247, 2151, 2954; **HRMS** (APCI): Calcd. for $C_{14}H_{28}Si_2$ $(M)^+$, 252.1729; found 252.1725.

(1,3-*bis*(Trimethylsilyl))-4-methyl-pent-1-yne 141



As described in general procedure **A**, to 4-methyl-1-pentyne (0.59 ml, 5 mmol) was added *n*-BuLi (3.28 ml**,** 5.25 mmol), chlorotrimethylsilane (0.69 ml, 5.5 mmol), *t*-BuLi (3.23 ml, 5.5 mmol) and chlorotrimethylsilane (0.76 ml, 6.0 mmol). Purification by flash column chromatography using *n*-hexane as eluent gave **141** (0.63 g, 2.84 mmol, 57%) as a clear oil. δ_H (400 MHz, $CDCl_3$) 0.11 (9 H, s, Si(CH_3)$_3$), 0.14 (9 H, s, Si(CH_3)$_3$), 0.98 (3 H, d, *J* = 6.7, CH_3), 1.04 (3 H, d, *J* = 6.6, CH_3), 1.69 (1 H, d, *J* = 4.3, C*H*-Si(CH_3)$_3$), 1.86-1.91 (1 H, m, C*H*(CH_3)$_2$); δ_C (125 MHz) 0.0 (Si(*C*H_3)$_3$), 2.4 (Si(*C*H_3)$_3$), 22.4 (*C*H-(Si(CH_3)$_3$), 26.0 (*C*H_3), 29.9 (*C*H_3), 31.9 (*C*H(CH_3)$_2$), 88.5 (C*C*-Si), 110.0 (*C*C-Si); ν_{max} (neat)/cm^{-1} 538, 555, 595, 627, 950, 1104, 1159, 2342, 2359, 2972; **HRMS** (APCI): Calcd. for $C_{12}H_{26}Si_2$ $(M)^+$, 226.1573; found 226.1569.

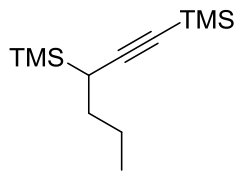
(1,3-*bis*(Trimethylsilyl))-pent-1-yne 142[109]



As described in general procedure **A**, to pent-1-yne (0.98 ml, 10 mmol) was added *n*-BuLi (6.56 ml, 10.5 mmol), chlorotrimethylsilane (1.38 ml, 11 mmol), *t*-BuLi (6.46 ml, 11 mmol) and chlorotrimethylsilane (1.52 ml, 12 mmol). Purification by flash column chromatography using *n*-hexane as eluent gave **142** (0.53 g, 3.5 mmol, 35%) as a clear oil that gradually turned to clear pink on exposure to air. δ_H (400 MHz, $CDCl_3$) 0.08

(9 H, s, Si(CH_3)$_3$), 0.14 (9 H, s, Si(CH_3)$_3$), 1.07 (3 H, t, *J* = 7.2, CH_3), 1.35-1.55 (2 H, m, CH_2), 1.58-1.61 (1 H, m, C*H*); **δ_C** (125 MHz) -3.5 (Si(*C*H$_3$)$_3$), 0.0 (Si(*C*H$_3$)$_3$), 13.9 (*C*H$_3$), 22.0 (*C*H), 23.1 (*C*H$_2$), 84.3 (C*C*-Si), 109.6 (*C*C-Si); **ν_{max}** (neat)/cm^{-1} 636, 658, 696, 757, 833, 896, 984, 1027, 1067, 1146, 1248, 1406, 2151, 2958; **HRMS** (APCI): Calcd. for $C_{11}H_{24}Si_2$ (M)$^+$, 212.1417; found 212.1415.

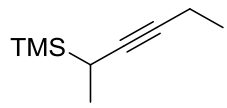
(1,3-*bis*(Trimethylsilyl))-pent-1-yne 143[109]



As described in general procedure **A**, to 1-hexyne (0.814 g, 10 mmol) was added *n*-BuLi (3.28 ml**,** 5.25 mmol), chlorotrimethylsilane (0.69 ml, 5.5 mmol), *t*-BuLi (3.23 ml, 5.5 mmol) and chlorotrimethylsilane (0.76 ml, 6.0 mmol). Purification by flash column chromatography using *n*-hexane as eluent gave **143** (2.10 g, 9.29 mmol, 93%) as a clear oil. **δ_H** (500 MHz, $CDCl_3$) 0.08 (9 H, s, Si(CH_3)$_3$), 0.13 (9 H, s, Si(CH_3)$_3$), 0.92 (3 H, t, *J* = 7.0 Hz, CH_3), 1.32 – 1.45 (3 H, m, CH_2 + C*H),* 1.62 – 1.71 (2 H, m, CH_2); **δ_C** (125 MHz) -3.6 (Si(*C*H$_3$)$_3$), 0.0 (Si(*C*H$_3$)$_3$), 13.4 (*C*H$_3$), 20.8 (*C*H$_2$), 22.3 (*C*H$_2$), 30.8 (*C*H), 84.0 (C*C*-Si), 109.7 (*C*C-Si); **ν_{max}** (neat)/cm^{-1} 617, 636, 695, 757, 832, 962, 1053, 1138, 1247, 1465, 2152, 2957; **HRMS** (APCI): Calcd. for $C_{12}H_{26}Si_2$ (M)$^+$, 226.1573; found 226.1572.

3.2.3 General Procedure C: Preparation of Propargyl Silanes

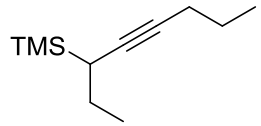
2-Trimethylsilyl-hex-3-yne 144



To a solution of 4-octyne (0.56 ml, 5 mmol) in THF (1 M) under nitrogen at -40 ^{o}C was added *t*-BuLi (1.7 M in pentane, 3.23 ml, 5 mmol). The mixture was stirred at -40 ^{o}C for 2 hours before the addition of chlorotrimethylsilane (0.75 ml, 10 mmol). The reaction was then allowed to warm to room temperature and stirred for an additional hour before the addition of water 15 ml. The resultant layers were separated and the aqueous phase extracted with diethyl ether (3 x 15 ml) and the organic phases combined, dried with $MgSO_4$, and the solvent removed *in vacuo*. The crude mixture was

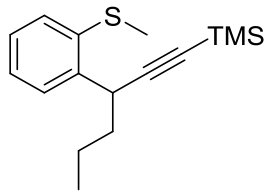
purified by flash column chromatography on silica gel using 100% hexane as the eluent to give **144** as a clear oil (0.18 g, 1.2 mmol, 24%); δ_H (400 MHz, $CDCl_3$) 0.06 (9 H, s, Si(C*H*$_3$)$_3$), 1.10-1.14 (6 H, m, 2 x C*H*$_3$), 1.58-1.64 (1 H, m, C*H*), 2.17 (2 H, qd, *J* = 7.5, 2.6, C*H*$_2$); δ_C (125 MHz) -3.9 (Si(*C*H$_3$)$_3$), 12.3 (*C*H$_3$), 12.5 (*C*H$_3$), 14.4 (*C*H$_2$), 14.7 (*C*H-Si), 80.7 (*C*C), 82.4 (C*C*); ν_{max} (neat)/cm^{-1} 582, 642, 692, 753, 835, 970, 1000, 1057, 1247, 1319, 1461, 1680, 1715, 2958; **HRMS** (APCI): Calcd. for $C_9H_{18}Si$ $(M)^+$, 154.1177; found 154.1172.

3-Trimethylsilyl-oct-4-yne 145



As described in general procedure **C**, to 4-octyne (1.46 ml, 10 mmol) was added *t*-BuLi (6.46 ml, 5 mmol) and chlorotrimethylsilane (1.5 ml, 10 mmol). Purification by flash column chromatography using *n*-hexane as eluent gave **145** (1.16 g, 6.4 mmol, 64% yield) as a clear oil; δ_H (400 MHz, $CDCl_3$) 0.07 (9 H, s, Si(C*H*$_3$)$_3$), 0.98 (3 H, t, *J* = 7.4, C*H*$_3$), 1.07 (3 H, t, *J* = 7.2, C*H*$_3$), 1.29-1.40 (1 H, m, C*H*), 1.47-1.54 (4 H, m, 2 x C*H*$_2$), 2.16 (2 H, td, *J* = 6.9, 2.5, C*H*$_2$); δ_C (100 MHz) -3.1 (Si(*C*H$_3$)$_3$), 13.5 (*C*H$_3$), 14.4 (*C*H$_3$), 21.0 (*C*H$_2$), 21.9 (*C*H$_2$), 22.8 (*C*H$_2$), 22.9 (*C*H-Si), 80.7 (*C*C), 81.7 (C*C*); ν_{max} (neat)/cm^{-1} 572, 613, 692, 757, 836, 1046, 1159, 1247, 1338, 1377, 1461, 1714, 2871, 2932, 2959; **HRMS** (APCI): Calcd. for $C_{11}H_{22}Si$ $(M)^+$, 182.1487; found 182.1490.

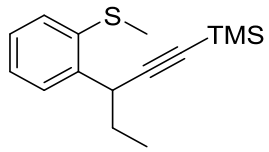
Trimethyl(3(2-(methylsulfanyl)phenyl)hex-1-yn-1yl)silane 149



As described in general procedure **B**, methyl phenyl sulfoxide (70 mg, 0.5 mmol), 1,3-*bis*(trimethylsilyl)-1-hexyne (169 mg, 0.75 mol), triflic anhydride (12 µl, 0.75 mmol), 2,6-lutidine (14 µl, 1.25 mmol) and MeCN (3 ml) were heated at 60 °C for 18 hours. Purification by column chromatography on silica gel eluting with 1% EtOAc in *n*-hexane gave **149** (0.072 g, 0.26 mmol, 52%) as a yellow oil; δ_H (400 MHz, $CDCl_3$) 0.21 (9 H, s, Si(C*H*$_3$)$_3$), 0.97 (3 H, t, *J* = 7.3, C*H*$_3$), 1.49-1.75 (4 H, m, 2 x C*H*$_2$), 2.48 (3 H, s, SC*H*$_3$), 4.24 (1

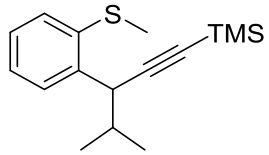
H, dd, *J* = 8.9, 5, C*H*-C), 7.18-7.25 (3 H, m, ArC*H*), 7.59-7.62 (1 H, m, ArC*H*); **δ_C** (125 MHz) 0.1 (Si(*C*H_3)$_3$), 13.7 (CH_2CH_2*C*H_3), 16.7 (CH_2*C*H_2CH_3), 20.6 (*C*$H_2CH_2CH_3$), 35.3 (*C*HCH_2), 39.3 (S*C*H_3), 86.7 (C*C*-Si), 108.5 (*C*C-Si), 125.6 (Ar*C*H), 126.9 (Ar*C*H), 127.2 (Ar*C*H), 127.8 (Ar*C*H), 135.9 (Ar*C*), 140.9 (Ar*C*); **ν_{max}** (neat)/cm^{-1} 567, 651, 697, 733, 756, 838, 868, 908, 957, 1040, 1111, 1248, 1438, 1465, 1588, 2168, 2872, 2957; **HRMS** (APCI): Calcd. for $C_{16}H_{24}SSi$ $(M)^+$, 276.1368; found 276.1356.

Trimethyl(3-(2-methylsulfanyl)pent-1-yn-yl)silane 150



As described in general procedure **B**, methyl phenyl sulfoxide (323 mg, 2.3 mmol), 1,3-*bis*(trimethylsilyl)-1-pentyne (0.53 g, 3.4 mmol), triflic anhydride (0.58 ml, 3.4 mmol), 2,6-lutidine (0.67 ml, 5.7 mmol) and MeCN (14 ml) were heated at 60 °C for 18 hours. Purification by column chromatography on silica gel eluting with 1% EtOAc in *n*-hexane gave **150** (0.317 g, 1.19 mmol, 52%) as a yellow oil; **δ_H** (400 MHz, $CDCl_3$) 0.20 (9 H, s, Si(C*H*$_3$)$_3$), 1.05 (3 H, t, *J* = 7.3, C*H*$_3$), 1.6 -1.84 (2 H, m, C*H*$_2$), 2.47 (3 H, s, S-C*H*$_3$), 4.16 (1 H, dd, *J* = 8.7, 4.9, C*H*), 7.17-7.25 (3 H, m, ArC*H*), 7.59 (1 H, m, ArC*H*); **δ_C** (125 MHz) 0.4 (Si(*C*H_3)$_3$), 12.0 (*C*H_3), 17.0 (*C*H_2), 30.5 (*C*H), 37.4 (S*C*H_3), 87.3 (Si-*C*C), 108.6 (Si-C*C*), 125.8 (Ar*C*H), 127.2 (Ar*C*H), 127.5 (Ar*C*H), 128.2 (Ar*C*H), 136.3 (Ar*C*), 140.8 (Ar*C*); **ν_{max}** (neat)/cm^{-1} 650, 697, 746, 838, 984, 1038, 1248, 1438, 1464, 2168, 2961; **HRMS** (APCI): Calcd. for $C_{15}H_{22}SSi$ $(M)^+$, 262.1211; found 262.1200.

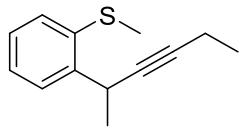
Trimethyl(4-methyl-3-(2-(methylsulfanyl)phenyl)pent-1-yn-1-yl)silane 151



As described in general procedure **B**, methyl phenyl sulfoxide (70 mg, 0.5 mmol), 1,3-*bis*(trimethylsilyl)-4-methyl-1-pentyne (170 mg, 0.75 mmol), triflic anhydride (12 µl, 0.75 mmol), 2,6-lutidine (14 µl, 1.25 mmol) and MeCN (3 ml) were heated at 60 °C for 18 hours. Purification by column chromatography on silica gel eluting with 1% EtOAc in *n*-hexane gave **151** (84.2 mg, 0.30 mmol, 61%) as a yellow oil; **δ_H** (400 MHz, $CDCl_3$) 0.21 (9 H, s, Si(C*H*$_3$)$_3$), 0.90 (3 H, d, *J* = 6.7, C*H*$_3$), 1.08 (3 H, d, *J* = 6.7, C*H*$_3$), 1.96-2.04 (1 H, m,

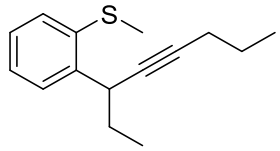
C*H*(CH_3)$_2$), 2.47 (3 H, s, SC*H*$_3$), 4.16 (1 H, d, *J* = 4.8, C*H*), 7.17-7.27 (3 H, m, ArC*H*), 7.56 (1 H, dd, *J* = 7.4, 1.5, ArC*H*); **δ_C** (125 MHz) -0.1 (Si(*C*H_3)$_3$), 16.4 (*C*H_3), 17.1 (*C*H_3), 21.1 (*C*H(CH_3)$_2$), 32.5 (*C*H), 42.2 (S*C*H_3), 87.8 (*C*C-Si), 106.2 (C*C*-Si), 124.8 (Ar*C*H), 126.5 (Ar*C*H), 126.8 (Ar*C*H), 128.4 (Ar*C*H), 136.1 (Ar*C*), 139.4 (Ar*C*); **ν_{max}** (neat)/cm^{-1} 561, 615, 630, 678, 698, 744, 838, 908, 1009, 1040, 1135, 1248, 1318, 1366, 1383, 1438, 1465, 1587, 2169, 2870, 2959; **HRMS** (APCI): Calcd. for $C_{16}H_{24}SSi$ $(M)^+$, 276.1368; found 276.1356.

(2-(Hex-3-yn-2-yl)phenyl)(methyl)sulfide 152



As described in general procedure **B**, methyl phenyl sulfoxide (70 mg, 0.5 mmol), 2-trimethylsilyl-3-hexyne (115 mg, 0.75 mmol), triflic anhydride (12 µl, 0.75 mmol), 2,6-lutidine (14 µl, 1.25 mmol) and MeCN (3 ml) were heated at 60 °C for 18 hours. Purification by column chromatography on silica gel eluting with 1% EtOAc in *n*-hexane gave **152** (0.054 g, 0.27 mmol, 53%) as a yellow oil; **δ_H** (400 MHz, $CDCl_3$) 1.16 (3 H, t, *J* = 7.6, C*H*$_3$CH$_2$), 1.43 (3 H, d, *J* = 7.1, C*H*$_3$CH), 2.24 (2 H, qd, *J* = 7.5, 2.3, CH$_3$C*H*$_2$), 2.48 (3 H, s, SC*H*$_3$), 4.23 (1 H, qt, *J* = 7.0, 2.2, CH$_3$C*H*), 7.17-7.26 (3 H, m, ArC*H*), 7.62 (1 H, m, ArC*H*); **δ_C** (125 MHz) 12.5 (CH$_2$*C*H$_3$), 14.2 (CH*C*H$_3$), 16.6 (*C*H$_2$CH$_3$), 23.5 (*C*HCH$_3$), 28.9 (S*C*H$_3$), 82.2 (*C*C-CH$_2$CH$_3$), 83.2 (C*C*-CH$_2$CH$_3$), 125.7 (Ar*C*H), 126.7 (Ar*C*H), 127.14 (Ar*C*H), 127.1 (Ar*C*H), 135.6 (Ar*C*), 142.6 (Ar*C*); **ν_{max}** (neat)/cm^{-1} 560, 608, 686, 967, 1042, 1154, 1189, 1257, 1318, 1368, 1437, 1467, 1568, 1587, 1715, 2920, 2973, 3058; **HRMS** (APCI): Calcd. for $C_{13}H_{15}S$ $(M - H)^-$, 203.0889; found 203.0891.

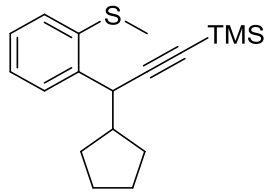
Methyl(2-(oct-4-yn-3-yl)phenyl)sulfide 153



As described in general procedure **B**, methyl phenyl sulfoxide (70 mg, 0.5 mmol), 3-trimethylsilyl-4-octyne (136 mg, 0.75 mmol), triflic anhydride (12 µl, 0.75 mmol), 2,6-lutidine (14 µl, 1.25 mmol) and MeCN (3 ml) were heated at 60 °C for 18 hours. Purification by column chromatography on silica gel eluting with 1% EtOAc in *n*-hexane gave **153** (0.046 g, 0.22 mmol, 45%) as a yellow oil; **δ_H** (400 MHz, $CDCl_3$) 1.01-1.07 (6 H,

m, 2 x CH_3), 1.53- 1.84 (4 H, m, 2 x CH_2), 2.23 (2 H, td, *J* = 7.0, 2.2, CH_2), 2.47 (3 H, s, SCH_3), 4.10 (1 H, m, ArC*H*), 7.17-7.26 (3 H, m, ArC*H*), 7.60 (1 H, dd, *J* = 7.5, 5.9, ArC*H*); **δ_C** (125 MHz) 11.5 (*C*H_3(CH_2)$_2$), 13.2 (*C*H_3CH_2CH), 16.3 (CH_3*C*H_2CH_2), 20.5 (CH_3*C*H_2CH), 22.2 (CH_3CH_2*C*H_2), 30.1 (CH_3CH_2*C*H), 35.8 (S-*C*H_3), 81.3 (CH_2*C*C), 82.4 (C*C*-CH), 125.1 (Ar*C*H), 126.3 (Ar*C*H), 126.7 (Ar*C*H), 127.5 (Ar*C*H), 135.62 (Ar*C*), 141.1 (Ar*C*); **ν_{max}** (neat)/cm^{-1} 625, 692, 816, 906, 967, 1042, 1061, 1276, 1338, 1377, 1438, 1587, 2870, 2929, 2961; **HRMS** (APCI): Calcd. for $C_{15}H_{20}S$ $(M + H)^+$, 232.1280; found 232.1276.

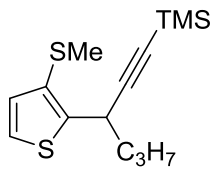
(3-Cyclopentyl-3-(2-(methylsulfanyl)phenyl)prop-1-yn-1yl)trimethylsilane 154



As described in general procedure **B**, methyl phenyl sulfoxide (70 mg, 0.5 mmol), 1,3-*bis*(trimethylsilyl)-3-cyclopentyl-1-propyne (189 mg, 0.75 mmol), triflic anhydride (12 µl, 0.75 mmol), 2,6-lutidine (14 µl, 1.25 mmol) and MeCN (3 ml) were heated at 60 °C for 18 hours. Purification by column chromatography on silica gel eluting with 1% EtOAc in *n*-hexane gave **154** (87.4 mg, 0.29 mmol, 57%) as a yellow oil; **δ_H** (400 MHz, $CDCl_3$) 0.20 (9 H, s, Si(CH_3)$_3$), 1.46-1.70 (9 H, m, cyclopentyl H), 2.47 (3 H, s, SCH_3), 4.30 (1 H, d, *J* = 6.1, C*H*), 7.17-7.25 (3 H, m, ArC*H*), 7.58 (1 H, dd, *J* = 7.4, 1.6, ArC*H*); **δ_C** (125 MHz) 0.5 (Si(*C*H_3)$_3$), 17.1 (cyclopentyl-*C*H_2), 25.5 (cyclopentyl-*C*H_2), 25.7 (cyclopentyl-*C*H_2), 29.1 (cyclopentyl-*C*H_2), 31.1 (cyclopentyl-*C*H), 39.9 (*C*H), 45.5 (S*C*H_3), 87.3 (C*C*-Si), 108.0 (*C*C-Si), 125.7 (Ar*C*H), 127.1 (Ar*C*H), 127.4 (Ar*C*H). 128.6 (Ar*C*H), 136.3 (Ar*C*), 140.8 (Ar*C*); **ν_{max}** (neat)/cm^{-1} 635, 697, 757, 838, 941, 1042, 1247, 1438, 1465, 1587, 2168, 2865, 2954; **HRMS** (APCI): Calcd. for $C_{17}H_{23}SSi$ $(M - CH_3)^+$, 287.1284; found 287.1277.

3.2.4 General Procedure D: Propargylation of Heterocycles

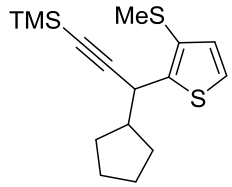
(3-(3-(Methylthio)thiophen-2-yl)hex-1-yn-1-yl)trimethylsilane 174



To an oven-dried tube flushed with N_2, was added 3-(methylsulfinyl)thiophene (0.06 g, 0.41 mmol) and 1,3-*bis*(trimethylsilane)hex-1-yne (0.13 g, 0.61 mmol) in MeCN

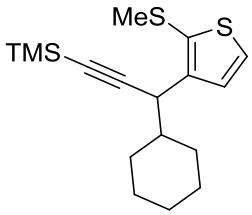
(3 ml). Trifluoroacetic anhydride (0.14 ml, 0.61 mmol) was then added at -40 °C and the reaction was allowed to warm to room temperature over 18 hours. The solution was quenched with aqueous saturated $NaHCO_3$ (6 ml) and the aqueous layer was extracted with EtOAc (3 x 5 ml). The combined organic layer was dried ($MgSO_4$) and concentrated *in vacuo*. The crude product was purified by column chromatography on silica gel eluting with 100% *n*-hexane to yield **174** as a colourless oil (0.070 g, 0.26 mmol, 64%). δ_H (500 MHz, $CDCl_3$) 0.18 (9 H, s, Si(C*H*$_3$)$_3$), 0.95 (3 H, t, *J* = 7.4 Hz, C*H*$_3$), 1.40 – 1.62 (2 H, m, CH$_3$C*H*$_2$), 1.68 – 1.85 (2 H, m, CHC*H*$_2$), 2.39 (3 H, s, S-C*H*$_3$), 4.27 (1 H, dd, *J* = 8.4, 6.2 Hz, ArC*H*), 6.98 (1 H, d, *J* = 5.3 Hz, ArC*H*), 7.19 (1 H, d, *J* = 5.3 Hz, ArC*H*); δ_C (125 MHz, $CDCl_3$) 0.0 (Si(*C*H$_3$)$_3$), 13.7 (*C*H$_3$), 19.2 (*C*H$_3$), 20.4 (*C*H$_2$), 32.3 (*C*H), 40.4 (*C*H$_2$), 86.6 (C), 107.8 (C), 123.1 (Ar*C*H), 128.5 (Ar*C*), 129.7 (Ar*C*H), 144.5 (Ar*C*); ν_{max} (neat)/cm^{-1} 637, 666, 700, 759, 838, 953, 1029, 1248, 2169, 2957; **HRMS** (APCI): Calcd. for $C_{14}H_{22}S_2Si$ $(M)^+$, 282.0927; found 282.0913.

(3-cyclopentyl-3-(3-(methylthio)thiophen-2-yl)prop-1-yn-1-yl)trimethylsilane 175



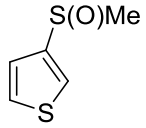
As described in general procedure **D**, to a mixture of methyl thienyl sulfoxide (0.073 g, 0.5 mmol) and 1,3-bis(trimethylsilyl)-3-cyclopentyl-1-propyne (0.195 g, 0.75 mol) in MeCN at -40 °C was added TFAA (0. 21 ml, 1.5 mmol) and the mixture left to warm to room temperature over 18 h. The crude product was purified by column chromatography on silica gel eluting with 100% *n*-hexane to yield **175** (0.041g, 0.15 mmol, 30%); δ_H (400 MHz, $CDCl_3$) 0.17 (9 H, s, Si(C*H*$_3$)$_3$), 1.32 - 1.43 (1 H, m, cyclopentyl H), 1.49 - 1.80 (7 H, m, cyclopentyl H), 2.24 (1 H, sxt, *J* = 7.8 Hz, cyclopentyl H), 2.38 (3 H, s, SC*H*$_3$), 4.24 (1 H, d, *J* = 7.3 Hz, C*H*), 6.97 (1 H, d, *J* = 5.3 Hz, ArC*H*), 7.19 (1 H, d, *J* = 5.1 Hz, ArC*H*); δ_C (100 MHz, $CDCl_3$) 0.0 (Si(*C*H$_3$)$_3$), 19.3 (cyclopentyl-*C*), 25.3 (cyclopentyl-*C*), 25.4 (cyclopentyl-*C*), 29.9 (cyclopentyl-*C*), 30.7 (cyclopentyl-*C*), 37.1 (*C*H), 47.0 (S*C*H$_3$), 86.8 (*C*CSi), 107.3 (C*C*Si), 123.3 (Ar*C*H), 128.7 (Ar*C*H), 129.4 (Ar*C*), 144.2 (Ar*C*); ν_{max} (neat)/cm^{-1} 547, 573, 672, 748, 878, 899, 984, 1023, 1159, 1247, 1447, 1449, 2179, 2751, 2925; **HRMS** (APCI): Calcd. for $C_{16}H_{24}S_2Si$ $(M)^+$, 308.1089; found 308.1082.

(3-Cyclohexyl-3-(2-(methylthio)thiophen-3-yl)prop-1-yn-1-yl)trimethylsilane 176



As described in general procedure **D**, to a mixture of methyl thienyl sulfoxide (0.073 g, 0.5 mmol) and 1,3-bis(trimethylsilyl)-3-cyclohexyl-1-propyne (0.199 g, 0.75 mmol) in MeCN at -40 ^{o}C was added TFAA (0. 211 ml, 1.5 mmol) and the mixture left to warm to room temperature over 18 h. The crude product was purified by column chromatography on silica gel eluting with 100% *n*-hexane to yield **176** (0.032 g, 0.09 mmol, 20%); $\boldsymbol{\delta_H}$ (400 MHz, $CDCl_3$) 0.18 (9 H, s, Si(C*H*$_3$)$_3$), 1.13 - 1.23 (4 H, m, cyclohexyl-*H*), 1.54 - 1.82 (6 H, m, cyclohexyl-*H*), 1.91 - 1.99 (1 H, m, cyclohexyl-*H*), 2.38 (3 H, s, SC*H*$_3$), 4.11 (1 H, d, *J* = 6.8 Hz, C*H*), 6.98 (1 H, d, *J* = 5.3 Hz, ArC*H*), 7.20 (1 H, d, *J* = 5.3 Hz, ArC*H*); $\boldsymbol{\delta_C}$ (100 MHz, $CHCl_3$) 0.0 (Si(C*H*$_3$)$_3$), 19.3 (S*C*H$_3$), 26.1 (cyclohexyl-*C*), 26.3 (cyclohexyl-*C*), 26.3 (cyclohexyl-*C*), 29.6 (cyclohexyl-*C*), 31.1 (cyclohexyl-*C*), 38.9 (cyclohexyl-*C*), 44.5 (cyclohexyl-*C*), 87.6 (*C*CSi(CH$_3$)$_3$), 106.9 (C*C*Si(CH$_3$)$_3$), 123.4 (Ar*C*H), 129.2 (Ar*C*), 129.4 (Ar*C*H), 143.2 (Ar*C*); $\boldsymbol{\nu_{max}}$ (neat)/cm^{-1} 535, 573, 678, 758, 838, 891, 994, 1023, 1070, 1149, 1247, 1347, 1449, 2169, 2851, 2923; **HRMS** (APCI): Calcd. for $C_{17}H_{26}S_2Si$ $(M)^+$, 322.1245; found 322.1239.

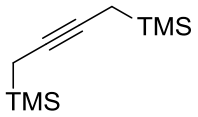
3-(Methylsulfinyl)thiophene 177[110]



To a solution of 3-(methylthio)thiophene (1.07 g, 8.25 mmol) in dichloromethane (8.25 ml, 1 M) at 0 ^{o}C, was added dropwise a solution of *m*-CPBA (1.99 g, 8.25 mmol) in dichloromethane. The resulting mixture was stirred at 0 ^{o}C for 1 hour before warming to room temperature after which it was stirred for a further 1 hour. The reaction was quenched with sat. $NaHCO_3$ solution (10 ml) and the layers separated. The aqueous layer was washed with dichloromethane (3 x 5 ml) and the combined organic layers dried with $MgSO_4$ and the solvent removed *in vacuo*. The resulting crude mixture was purified by column chromatography eluting with chloroform: ethyl acetate (95:5) to give

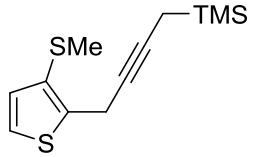
177 as a clear oil (1.17 g, 7.65 mmol, 92%); δ_H (300 MHz, $CDCl_3$) 7.74 (1 H, dd, *J* = 2.9, 1.2 Hz, ArC*H*), 7.48 (1 H, dd, *J* = 5.1, 3.0 Hz, ArC*H*), 7.25 (1 H, dd, *J* = 5.3, 1.3 Hz, ArC*H*), 2.78 (3 H, s, SCH_3); δ_C (75 MHz, $CDCl_3$) 144.6 (Ar*C*), 128.5 (Ar*C*H), 125.4 (Ar*C*H), 122.6 (Ar*C*H), 42.8 (S*C*H_3); **HRMS** (APCI): Calcd. for $C_5H_6S_2O$ $(M)^+$, 145.9855; found 145.9856.

1,4-*bis*(Trimethylsilyl)-2-butyne 178



To a suspension of Li granules (1 g, 140 mmol) and DTBB (0.26 g, 1 mmol) in dry THF (30 ml) at –40 °C was added a solution of 1,4-dichloro-2-butyne (0.98 ml, 10 mmol) and TMSCl (3 ml, 20 mmol) in THF (30 ml) over 1.5 h using a syringe pump. The reaction mixture was then carefully hydrolysed with water and extracted with diethyl ether. The combined organic layer was washed with water, brine, dried ($MgSO_4$) and concentrated *in vacuo*. The crude product was purified using column chromatography on silica gel using 100% hexane as the eluent to give **178** as a clear oil (0.837 g, 4.2 mmol, 42%); δ_H (400 MHz, $CDCl_3$) 0.09 (18 H, s, 2 x Si(CH_3)$_3$), 1.45 (4 H, s, 2 x CH_2); δ_C (100 MHz, $CDCl_3$); -2.0 ($(CH_3)_3Si$), 7.2 (CH_2), 75.6 (2 x C*C*); ν_{max} (neat)/cm^{-1} 597, 672, 695, 758, 836, 1054, 1142, 1181, 1247, 2955; ***m/z*** (GCMS) 198.1.

Trimethyl(4(3-(methylthio)thiophen-2-yl)but-2-yn-1-yl)silane 179

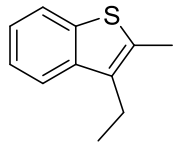


As described in general procedure **D**, to a mixture of methyl thienyl sulfoxide (0.073 g, 0.5 mmol) and 1,4-bis(trimethylsilyl)but-2-yne (0.199 g, 0.75 mmol) in MeCN at -40 ^oC was added TFAA (0. 211 ml, 1.5 mmol) and the mixture left to warm to room temperature over 18 h. The crude product was purified by column chromatography on silica gel eluting with 100% *n*-hexane to yield **179** (0.032 g, 0.09 mmol, 20%); δ_H (400 MHz) 0.12 (9 H, s, Si(CH_3)$_3$), 1.49 (2 H, t, *J* = 2.7 Hz, CH_2-Si), 2.37 (3 H, s, SCH_3), 3.77 (2 H, t, *J* = 2.7 Hz, CH_2), 6.98 (1 H, d, *J* = 5.1 Hz, ArC*H*), 7.16 (1 H, d, *J* = 5.3 Hz, ArC*H*); δ_C (100 MHz) -2.0 (Si(*C*H_3)$_3$), 7.0 (*C*H_2), 18.9 (*C*H_2), 19.1 (S*C*H_3), 75.5 (CC), 80.0 (CC), 122.7 (Ar*C*H), 128.4 (Ar*C*), 129.9 (Ar*C*H), 140.4 (Ar*C*); ν_{max} (neat)/cm^{-1} 558, 608, 648, 698, 731, 759,

790, 841, 908, 970, 1146, 1247, 1295, 1418, 2920, 2954; **HRMS** (APCI): Calcd. for $C_{11}H_{15}S_2Si$ $(M - CH_3)^-$, 239.0370; found 239.0361.

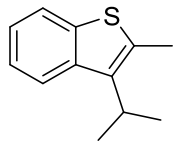
3.2.5 Gerenal Procedure E: Acid-Mediated Cyclisations

2-methyl-3-ethylbenzothiophene 196



A microwave vial equipped with a magnetic stirrer, was charged with trimethyl(3-(2-methylsulfanyl)pent-1-yn-yl)silane (0.131 g, 0.5 mmol) and *p*-TSA (0.095 g, 0.5 mmol) and the mixture dissolved in EtOH (0.2 M). The solution was then heated at 150 ^oC for 1 h 45 min in a microwave. The solution was quenched with aqueous saturated $NaHCO_3$ (6 ml) and the aqueous layer was extracted with Et_2O (3 x 5 ml). The combined organic layer was dried ($MgSO_4$) and concentrated *in vacuo*.. The crude product was purified by column chromatography on silica gel eluting with 100% *n*-hexane to yield 2-methyl-3-ethylbenzothiophene **196** (0.049 g, 0.28 mmol, 56%) as a yellow oil; $\boldsymbol{\delta_H}$ (400 MHz, $CDCl_3$) 1.23 (3 H, t, *J* = 7.6 Hz, CH_2CH_3), 2.51 (3 H, s, CH_3), 2.82 (2 H, q, *J* = 7.6 Hz, CH_2CH_3), 7.28 (1 H, t, *J* = 8.2 Hz, ArC*H*), 7.35 (1 H, t, *J* = 7.9 Hz, ArC*H*), 7.64 (1 H, d, *J* = 7.9 Hz, ArC*H*), 7.77 (1 H, d, *J* = 7.8 Hz, ArC*H*); $\boldsymbol{\delta_C}$ (100 MHz, $CDCl_3$) 13.5 (CH_3), 14.1 (CH_2 CH_3), 19.5 (CH_2CH_3), 121.0 (Ar*C*H), 122.1 (Ar*C*H), 123.3 (Ar*C*H), 123.7 (Ar*C*H), 133.5 (Ar*C*), 138.4 (Ar*C*), 140.1 (Ar*C*); $\boldsymbol{\nu_{max}}$ (neat)/cm^{-1} 573, 638, 709, 729, 757, 808, 907, 925, 1021, 1104, 1152, 1174, 1319, 1374, 1432, 1456, 2869, 2964; **HRMS** (APCI): Calcd. for $C_{11}H_{12}S$ $(M)^+$, 176.0654; found 176.0655.

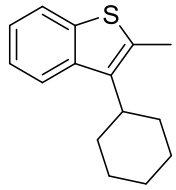
2-methyl-3-isopropylbenzothiophene 197



As in general procedure **E**, Trimethyl(4-methyl-3-(2-(methylsulfanyl)phenyl)pent-1-yn-1-yl)silane (0.064 g, 0.36 mmol) and *p*-TSA (0.068 g, 0.36 mmol) in EtOH (2 ml) were heated at 150 ^oC in a microwave. The crude product was purified by column chromatography on silica gel eluting with 100% *n*-hexane to yield 2-methyl-3-

isopropylbenzothiophene **197** (0.028 g, 0.15 mmol, 42%); δ_H (400 MHz, $CDCl_3$) 1.46 (6 H, dd, *J* = 7.3, CH_3), 2.54 (3 H, s, CH_3), 3.42 (1 H, spt, *J* = 7.2 Hz, C*H*(CH_3)$_2$), 7.25 (1 H, t, *J* = 7.6 Hz, ArC*H*), 7.32 (1 H, t, *J* = 8.1 Hz, ArC*H*), 7.76 (1 H, d, *J* = 7.8 Hz, ArC*H*), 7.83 (1 H, d, *J* = 8.1 Hz, ArC*H*); δ_C (100 MHz, $CDCl_3$) 14.5 (*C*H_3), 21.5 (CH(*C*H_3)$_2$), 27.7 (*C*H(CH_3)$_2$), 122.1 (Ar*C*H), 122.2 (Ar*C*H), 122.9 (Ar*C*H), 123.3 (Ar*C*H), 132.9 (Ar*C*), 136.7 (Ar*C*), 138.5 (Ar*C*), 139.6 (Ar*C*); ν_{max} (neat)/cm^{-1} 648, 674, 729, 760, 947, 1066, 1106, 1173, 1189, 1363, 1384, 1432, 1456, 2870, 2952, 2961; **HRMS** (APCI): Calcd. for $C_{12}H_{14}S$ $(M)^+$, 190.0811; found 190.0808.

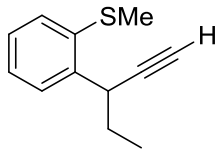
2-methyl-3-cyclohexylbenzothiophene 195



As in general procedure **E**, (3-cyclohexyl-3-(2-methylsulfanyl)phenyl)prop-1-yn-1-yl)trimethylsilane (0.060 g, 0.2 mmol) and *p*-TSA (0.038 g, 0.2 mmol) in EtOH (2 ml) were heated at 150 ^oC in a microwave. The crude product was purified by column chromatography on silica gel eluting with 100% *n*-hexane to yield **195** (0.037 g, 0.16 mmol, 81%); δ_H (400 MHz, $CDCl_3$) 1.33 - 1.53 (4 H, m, 4 x cyclohexyl C*H*), 1.76 - 2.07 (7 H, m, 7 x cyclohexyl C*H*), 2.56 (3 H, s, CH_3), 3.01 (5 H, tt, *J* = 12.4, 3.6 Hz, cyclohexyl C*H*), 7.25 (1H, td, *J* = 7.0 Hz x 2, 1.26 Hz x 2, ArC*H*), 7.32 (1H, td, J = 7.8, 1.26 Hz, ArC*H*), 7.76 (1 H, d, *J* = 6.6 Hz, ArC*H*), 7.88 (1 H, d, *J* = 8.1 Hz, ArC*H*); δ_C (100 MHz, $CDCl_3$) 14.8 (*C*H_3), 26.3 (2 x *C*H_2), 27.3 (*C*H_2), 31.3 (2 x *C*H_2), 38.8 (*C*H), 122.1 (Ar*C*H), 122.3 (Ar*C*H), 122.8 (Ar*C*H), 123.3 (Ar*C*H), 133.2 (Ar*C*), 136.0 (Ar*C*), 138.4 (Ar*C*), 139.9 (Ar*C*); ν_{max} (neat)/cm^{-1} 641, 728, 889, 1136, 1150, 1173, 1431, 1447, 2849, 2923; **HRMS** (APCI): Calcd. for $C_{15}H_{18}S$ $(M)^+$, 230.1124; found 230.1127.

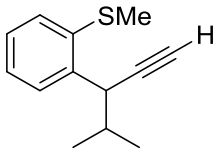
3.2.6 General Procedure F: Deprotections

Methyl(2-(pent-1-yn-3-yl)phenyl)sulfide 210



In a vial fitted with a magnetic stirrer bar was placed trimethyl(3-(2-methylsulfanyl)pent-1-yn-yl)silane (0.116 g, 0.45 mmol) and K_2CO_3 (0.124 g, 0.90 mmol) dissolved in MeOH (3 ml). The mixture was left to stir for 4 hours at room temperature before the solvent was removed *in vacuo*. The resulting crude product was purified by column chromatography on silica gel eluting with 100% *n*-hexane to yield **210** as a colourless oil (0.042 g, 0.27 mmol, 60%); δ_H (400 MHz, $CDCl_3$) 1.08 (3 H, t, *J* = 7.3 Hz, C*H*$_3$), 1.65 - 1.91 (2 H, m, C*H*$_2$), 2.26 (1 H, d, *J* = 2.4 Hz, CC*H*), 2.49 (3 H, s, SC*H*$_3$), 4.11 - 4.19 (1 H, m, C*H*), 7.17 - 7.32 (3 H, m, ArC*H*), 7.60 (1 H, d, *J* = 7.1 Hz, ArC*H*); δ_C (100 MHz, $CDCl_3$) 11.8 (*C*H$_3$), 16.7 (*C*H), 29.9 (*C*H$_2$), 35.8 (S*C*H$_3$), 70.5 (C*C*H), 85.9 (*C*CH), 125.6 (Ar*C*H), 126.9 (Ar*C*H), 127.4 (Ar*C*H), 127.7 (Ar*C*), 136.0 (Ar*CH*), 140.1 (Ar*C*); ν_{max} (neat)/cm^{-1} 577, 695, 746, 889, 967, 1097, 1255, 1378, 1466, 1588, 2113, 2872, 2923, 2965, 3294; **HRMS** (APCI): Calcd. for $C_{12}H_{14}S$ $(M)^+$, 190.0816; found 190.0810.

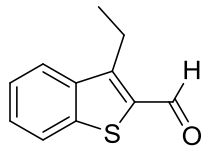
Methyl(2-(4-methylpent-1-yn-3-yl)phenyl)sulfide 211



As described in general procedure **F** compound trimethyl(4-methyl-3-(2-(methylsulfanyl)phenyl)pent-1-yn-1-yl)silane (0.278 g, 1 mmol) and K_2CO_3 (0.276 g, 2 mmol) were dissolved in methanol (5 ml) and stirred at room temperature for 4 hours. The crude product was purified by column chromatography on silica gel eluting with 100% *n*-hexane to yield **211** (0.142 g, 0.91 mmol, 91%); δ_H (400 MHz, $CDCl_3$) 0.95 (3 H, d, *J* = 6.7 Hz, C*H*$_3$), 1.08 (3 H, d, *J* = 6.7 Hz, C*H*$_3$), 2.04 (1 H, sxt, *J* = 6.4 Hz, C*H*$(CH_3)_2$), 2.26 (1 H, d, *J* = 2.4 Hz, CC*H*), 2.49 (3 H, s, SC*H*$_3$), 4.11 - 4.18 (1 H, m, C*H*), 7.16 - 7.31 (3 H, m, ArC*H*), 7.58 (1 H, d, *J* = 8.4 Hz, ArC*H*); δ_C (100 MHz, $CDCl_3$) 16.7 (*C*H$_3$), 17.7 (*C*H$_3$), 21.3 (*C*H), 32.7 (*C*H), 41.4 (S*C*H$_3$), 71.6 (C*C*H), 84.1 (*C*CH), 125.2 (Ar*C*H), 126.7 (Ar*C*H), 127.3

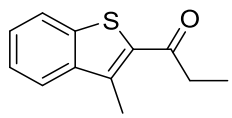
(Ar*C*), 128.5 (Ar*C*H), 136.4 (Ar*C*), 139.3 (Ar*C*H); ν_{max} (neat)/cm^{-1} 546, 696, 744, 841, 968, 1009, 1041, 1061, 1086, 1171, 1248, 1384, 1465, 1587, 2168, 2869, 2922, 2959, 3058, 3296; **HRMS** (ESI): Calcd. for $C_{12}H_{13}S$ (M -CH_3), 189.0732; found 189.0733.

3-ethylbenzo[*b*]thiophene-2-carbaldehyde 212



To an oven dried tube fitted with a magnetic stirrer bar and under a nitrogen atmosphere was added **210** (0.02 g, 0.1 mmol), toluene which had been bubbled with oxygen for 10 min (2 ml) and I_2 (0.017 g, 0.07 mmol). The resulting mixture was then further bubbled with oxygen for 10 min before heating to 80 ^{o}C for 18 hours. Saturated sodium thiosulfate solution (4 ml) was then added, the organic layer was separated and the aqueous layer extracted with Et_2O (3 x 2 ml). The combined organic layers were then washed with brine (2 ml), dried with $MgSO_4$, filtered and the solvent removed *in vacuo.* The resulting mixture was purified by flash column chromatography using hexanes to give aldehyde **212** as a white solid (0.009 g, 0.052 mmol, 52%); **mp**: 103 -102 ^{o}C; δ_H (400 MHz, $CDCl_3$) 1.42 (3 H, t, *J* = 7.6 Hz, C*H*$_3$), 3.30 (2 H, q, *J* = 7.6 Hz, C*H*$_2$), 7.45 (1 H, t, *J* = 7.7 Hz, ArC*H*), 7.52 (1 H, t, *J* = 7.2 Hz, ArC*H*), 7.89 (1 H, d, *J* = 8.1 Hz, ArC*H*), 7.93 (1 H, d, *J* = 8.1 Hz, ArC*H*) 10.34 (1 H, s, C*H*O); δ_C (100 MHz, $CHCl_3$) 16.2 (*C*H$_3$), 20.0 (*C*H$_2$), 123.5 (Ar*C*H), 123.9 (Ar*C*H), 124.8 (Ar*C*H), 128.3 (Ar*C*H), 137.0 (Ar*C*), 139.1 (Ar*C*), 142.6 (Ar*C*), 149.7 (Ar*C*), 183.8 (*C*HO); ν_{max} (neat)/cm^{-1} 544, 614, 709, 762, 850, 972, 1088, 1163, 1247, 1350, 1448, 1524, 1560, 1651, 2832, 2918, 2967; **HRMS** (ESI): Calcd. for $C_{11}H_{10}SO$ $(M)^+$, 190.0447; found 190.0446.

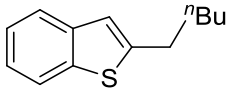
1-(3-methylbenzo[b]thiophen-2-yl)propan-1-one 213



To an oven-dried tube was added (2-Hex-3-yn-2-yl)phenyl)(methyl)sulfide **152** (20.0 mg, 0.1 mmol), Iodine (17.7 mg, 0.07 mmol) and toluene (2 ml, 0.05 M). Oxygen was bubbled through the reaction for 10 minutes before the mixture was heated to 80

°C for 18 hours. After this period the reaction was allowed to stir for 48 hours at room temperature before it was quenched with sat. sodium thiosulphate solution (5 ml). The aqueous phase was separated and extracted with Et_2O (3 X 5 ml). The combined organic layers were then washed with brine (5 ml), dried using Na_2SO_4 and filtered before the solvent was removed *in vacuo*. Purification by preparative thin layer chromatography eluting with hexane gave **213** as a white solid (19.5 mg, 0.095 mmol, 95%); **mp:** 83-85 °C; δ_H (400 MHz, $CDCl_3$) 1.26 (3 H, t, *J* = 7.19 Hz, C*H*$_3$), 2.78 (3 H, s, C*H*$_3$), 2.99 (2 H, q, *J* = 7.31 Hz, C*H*$_2$), 7.37 - 7.59 (2 H, m, ArC*H*), 7.76 - 7.97 (2 H, m, ArC*H*); δ_C (100 MHz, $CDCl_3$) 8.28 (*C*H$_3$), 13.84 (*C*H$_3$), 36.00 (*C*H$_2$), (122.73 (Ar*C*H), 124.08 (Ar*C*H), 124.64 (Ar*C*H), 127.38 (Ar*C*H), 135.08 (Ar*C*), 139.15 (Ar*C*), 139.76 (Ar*C*), 140.49 (Ar*C*), 196.37 (*C*O); ν_{max} (neat/cm^{-1}) 729, 814, 874, 977, 1040, 1090, 1157, 1262, 1315, 1380, 1408, 1449, 1517, 1558, 1644, 2846, 2918, 2971, 3064; **HRMS** (ESI): Calcd. for $C_{12}H_{12}SO$ $(M)^+$, 204.0603; found 204.0597.

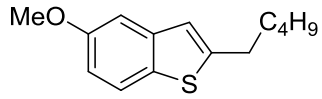
3.2.7 General Procedure G: Iodine-Mediated Cyclisations to Give Alkyl Subsitution 2-Pentylbenzo[*b*]thiophene 215



Under an N_2 atmosphere a solution of iodine (17.8 mg, 0.07 mmol) in toluene (2.0 ml) was added to a solution of (2-(hept-2-yn-1-yl)phenyl)(methyl)sulfide (21.8 mg, 0.100 mmol) and 1,4-cycloheaxadiene (20.0 mg, 0.25 mmol) in toluene (2.0 ml) at room temperature. The reaction mixture was stirred for 18h at 80 °C before diluting with Et_2O (5 ml) and quenching with saturated aqueous $Na_2S_2O_3$ (5 ml). The aqueous layer was then extracted with Et_2O (2 × 5 ml) and the combined organic layers washed with brine (5 ml), dried (Na_2SO_4) and concentrated *in vacuo*. The crude product was purified by preparative thin-layer chromatography on silica gel eluting with *n*-hexane to yield **215** (17.9 mg, 0.088 mmol, 88% yield) as a yellow oil; δ_H (500 MHz, $CDCl_3$) 0.89 - 0.95 (3 H, m, C*H*$_3$), 1.34 - 1.43 (4 H, m, 2 × *C*H$_2$), 1.73 - 1.81 (2 H, m, C*H*$_2$), 2.88 - 2.94 (2 H, m, C*H*$_2$), 7.00 - 7.02 (1 H, m, ArC*H*), 7.23 - 7.28 (1 H, m, ArC*H*), 7.31 (1 H, td, *J* = 7.6, 1.1, ArC*H*), 7.67 (1 H, d, *J* = 7.6, ArC*H*), 7.78 (1 H, d, *J* = 7.6, ArC*H*); δ_C (125 MHz, $CDCl_3$) 14.0 (*C*H$_3$), 22.4 (*C*H$_2$), 30.7 (C*C*H$_2$CH$_2$), 30.8 (CCH$_2$*C*H$_2$), 31.3 (*C*H$_2$), 120.4 (Ar*C*H), 122.1 (Ar*C*H), 122.6 (Ar*C*H), 123.3 (Ar*C*H), 124.0 (Ar*C*H), 139.3 (Ar*C*), 140.2 (Ar*C*), 146.9 (Ar*C*); ν_{max} (neat)/cm^{-}

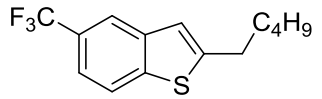
[1] 726, 746, 764, 818, 855, 1015, 1067, 1261, 1275, 1436, 1457, 2856, 2928, 2955; **HRMS** (EI): Calcd. for $C_{13}H_{16}S$ $(M)^+$, 204.0967; found 204.0970.

5-Methoxy-2-pentylbenzo[*b*]thiophene 216



As described in general procedure **G** (2-(hept-2-yn-1-yl)-4-methoxyphenyl)(methyl)sulfide (0.024 g, 0.1 mmol), toluene (4 ml), I_2 (0.017 g, 0.07 mmol) and 1,4-cyclohexadiene (0.014 ml, 0.15 mmol) were added to an oven dried tube and the resulting mixture was heated at 80 ^oC for 18 hours. The resulting mixture was purified by flash column chromatography using 10% EtOAc in hexanes to give benzothiophene **216** as a yellow solid (0.012 g, 0.061 mmol, 61%); $\boldsymbol{\delta_H}$ (400 MHz, $CDCl_3$) 0.92 (3 H, t, *J* = 6.8 Hz, C*H*$_3$), 1.35 - 1.42 (4 H, m, 2 x C*H*$_2$), 1.75 (2 H, quin, *J* = 7.3 Hz, C*H*$_2$), 2.88 (2 H, t, *J* = 7.5 Hz, C*H*$_2$), 3.86 (3 H, s, OC*H*$_3$), 6.88 - 6.95 (2 H, m, 2 x ArC*H*), 7.15 (1 H, d, *J* = 2.2 Hz, ArC*H*), 7.62 (1 H, d, *J* = 8.8 Hz, ArC*H*); $\boldsymbol{\delta_C}$ ($CDCl_3$) 14.0 (*C*H_3), 22.4 (*C*H_2), 30.8 (*C*H_2), 30.8 (*C*H_2), 31.2 (*C*H_2), 55.5 (O*C*H_3), 105.2 (Ar*C*H), 113.2 (Ar*C*H), 120.3 (Ar*C*H), 122.7 (Ar*C*H), 131.5 (Ar*C*), 141.2 (Ar*C*), 148.3 (Ar*C*), 157.3 (Ar*C*); $\boldsymbol{\nu_{max}}$ (neat)/cm^{-1} 579, 675, 694, 773, 854, 938, 1069, 1154, 1198, 1269, 1377, 1457, 1568, 1596, 2849, 2918, 2955; **HRMS** (GCMS): Calcd. for $C_{14}H_{18}SO$ $(M)^+$, 234.1073; found 234.1074.

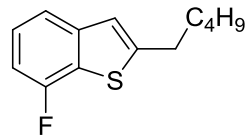
2-Pentyl-5-(trifluoromethyl)benzo[*b*]thiophene 217



As described in general procedure **G** (2-(hept-2-yn-1-yl)-4-(trifluoromethyl)phenyl)(methyl)sulfide (0.024 g, 0.1 mmol), toluene (4 ml), I_2 (0.017 g, 0.07 mmol) and 1,4-cyclohexadiene (0.014 ml, 0.15 mmol) were added to an oven dried tube and the resulting mixture was heated at 80 ^oC for 18 hours. The resulting mixture was purified by flash column chromatography using 10% EtOAc in hexanes to give benzothiophene **217** as a yellow oil (0.018 g, 0.067 mmol, 67%); $\boldsymbol{\delta_H}$ (400 MHz, $CDCl_3$) 0.9 (1 H, t, *J* = 8.1 Hz, C*H*$_3$), 1.3 - 1.4 (4 H, m, 2 x C*H*$_2$), 1.8 (2 H, quin, *J* = 7.3 Hz, C*H*$_2$), 2.9 (2 H, t, *J* = 7.6 Hz, C*H*$_2$), 7.1 (1 H, s, ArC*H*), 7.5 (1 H, d, *J* = 8.3 Hz, ArC*H*), 7.9 (1 H, d, *J* = 8.4 Hz, ArC*H*), 7.9 (1 H, s, ArC*H*); $\boldsymbol{\delta_C}$ (100 MHz, $CDCl_3$) 14.0 (*C*H_3), 22.4 (*C*H_2), 30.7 (*C*H_2), 30.8

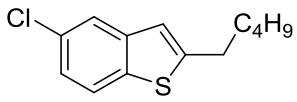
(CH$_2$), 31.2 (CH$_2$), 119.6 (ArCCF$_3$), 120.5 (ArCH), 122.5 (ArCH), 139.8 (ArCH), 142.3 (ArC), 149.3 (ArC); ν_{max} (neat)/cm^{-1} 609, 677, 761, 810, 911, 1073, 1147, 1263, 1332, 1436, 2930; **HRMS** (GCMS): Calcd. for $C_{14}H_{15}SF_3$ (M)$^+$, 272.0841; found 272.0844.

7-Fluoro-2-pentylbenzo[*b*]thiophene 218



As described in general procedure **G** (2-(hept-2-yn-1-yl)-6-fluorophenyl)(methyl)sulfide (24.0 mg, 0.2 mmol), toluene (4 ml), I_2 (17.0 mg, 0.07 mmol) and 1,4-cyclohexadiene (0.014 ml, 0.15 mmol) were added to an oven-dried tube and the resulting mixture was heated at 80 ^{o}C for 18 h. The resulting mixture was purified by column chromatography using 10% EtOAc in hexanes to give **218** as a yellow oil (14.0 mg, 0.069 mmol, 69%); δ_H (500 MHz, $CDCl_3$) 0.93 (3 H, t, J = 6.0 Hz, CH_3), 1.39 (4 H, d, J = 2.4 Hz, 2 x CH_2), 1.75 (2 H, quin, J = 6.8 Hz, CH_2), 2.88 (2 H, t, J = 7.6 Hz, CCH_2), 6.96 (1 H, s, ArCH), 7.07 (1 H, t, J = 8.9 Hz, ArCH), 7.46 (1 H, d, J = 8.9 Hz, ArCH), 7.59 (1 H, dd, J = 8.4, 5.3 Hz, ArCH); δ_C (100 MHz, $CDCl_3$) 13.7 (CH$_3$), 22.1 (CH$_2$), 30.4 (CH$_2$), 30.5 (CH$_2$), 31.0 (CCH$_2$), 108.0 (dd, J = 25.4, 1.0 Hz, ArCH), 112.5 (d, J = 24.5 Hz, ArCH), 119.5 (ArCH), 123.2 (d, J = 9.1 Hz, ArCH), 136.4 (d, J = 1.8 Hz, ArC), 139.8 (d, J = 10.0 Hz, ArC), 146.2 (d, J = 3.6 Hz, ArC), 159.6 (d, J = 245.2 Hz, ArCF); ν_{max} (neat)/cm^{-1} 585, 731, 828, 847, 913, 1193, 1214, 1249, 1467, 1542, 1573, 1603, 2857, 2929; **HRMS** (GCMS): Calcd. for $C_{13}H_{15}SF$ (M)$^+$, 222.0873; found 222.0872.

5-Chloro-2-pentylbenzo[*b*]thiophene 219

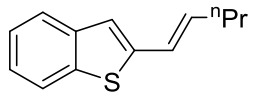


To an oven dried tube fitted with a magnetic stirrer bar and under a nitrogen atmosphere was added (4-chloro-2-(hept-2-yn-1-yl)phenyl)(methyl)sulfide (0.025 g, 0.1 mmol), toluene (4 ml), I_2 (0.017 g, 0.07 mmol) and 1,4-cyclohexadiene (0.014 ml, 0.15 mmol). The resulting mixture was heated at 80 ^{o}C for 18 hours before the addition of saturated sodium thiosulfate solution (4 ml). The organic layer was separated and the aqueous layer extracted with Et_2O (3 x 2 ml). The combined organic layers were then washed with brine (2 ml), dried with $MgSO_4$, filtered and the solvent removed *in vacuo.*

The resulting mixture was purified by flash column chromatography using 10% EtOAc in hexanes to give benzothiophene **219** as a yellow oil (0.015 g, 0.064 mmol, 64%). δ_H (400 MHz, $CDCl_3$) 0.9 (3 H, t, *J* = 6.8 Hz, CH_3), 1.3 - 1.4 (4 H, m, 2 x CH_2), 1.8 (2 H, quin, *J* = 7.3 Hz, CH_2), 2.9 (2 H, t, *J* = 7.5 Hz, CH_2), 6.9 (1 H, s, ArC*H*), 7.2 (1 H, dd, *J* = 8.6, 2.0 Hz, ArC*H*), 7.6 - 7.7 (2 H, m, 2 x ArC*H*); δ_C (100 MHz, $CDCl_3$) 14.0 (*C*H_3), 22.4 (*C*H_2), 30.7 (*C*H_2), 30.8 (*C*H_2), 31.2 (*C*H_2), 119.8 (Ar*C*H), 122.2 (Ar*C*H), 123.0 (Ar*C*H), 123.7 (Ar*C*H), 130.2 (Ar*C*), 137.3 (Ar*C*), 141.3 (Ar*C*), 149.1 (Ar*C*); ν_{max} (neat)/cm^{-1} 574, 597, 667, 734, 803, 882, 903, 1074, 1180, 1206, 1375, 1417, 1465, 1560 1580, 2857, 2925, 2952; **HRMS** (GCMS): Calcd. for $C_{13}H_{15}SCl$ $(M)^+$, 238.0578; found 238.0578.

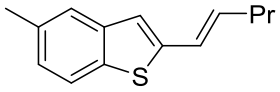
3.2.8 General Procedure H: Iodine-Mediated Cyclisations to Give Alkenes

(*E*)-2-(Pent-1-en-1-yl)benzo[*b*]thiophene 220



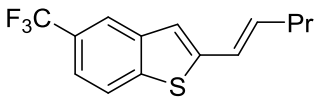
Under an Ar atmosphere, a solution of iodine (55.6 mg, 0.22 mmol) in Ar flushed 1,2-dichloroethane (2 ml) was added to a solution of (2-(hept-2-yn-1-yl)phenyl)(methyl)sulfide (43.6 mg, 0.2 mmol) in Ar flushed 1,2-dichloroethane (18 ml) at room temperature. The reaction mixture was stirred for 18 h at 80 °C before quenching with saturated aqueous $Na_2S_2O_3$ (5 ml). The aqueous layer was then extracted with EtOAc (3 x 5 ml) and the combined organic layers washed with brine (5 ml), dried (Na_2SO_4) and concentrated *in vacuo*. The crude product was purified by preparative thin-layer chromatography on silica gel eluting with *n*-hexane to yield **220** (37.5 mg, 0.18 mmol, 92 % yield) as a yellow solid; **mp**: 38-40 ^oC; δ_H (500 MHz, C_6D_6) 0.82 (3 H, t, *J* = 7.3, CH_3), 1.29 (2 H, sxt, *J* = 7.3, CH_2CH_3), 1.95 (2 H, qd, *J* = 7.2, 1.4, CHCH_2), 6.14 (1 H, dt, *J* = 15.7, 7.0, CCH=C*H*), 6.44 (1 H, dt, *J* = 15.7, 1.2, CC*H*=CH), 6.81 (1 H, s, ArC*H*), 7.03 (1 H, td, *J* = 7.6, 1.3, ArC*H*), 7.12 (1 H, td, *J* = 7.5, 1.2, ArC*H*), 7.45 - 7.52 (2 H, m, 2 × ArC*H*); δ_C (125 MHz, C_6D_6) 14.1 (*C*H_3), 22.9 (*C*H_2CH_3), 35.6 (CH*C*H_2), 122.1 (Ar*C*H), 122.8 (Ar*C*H), 123.9 (Ar*C*H), 124.9 (C*C*H=CH), 125.0 (2 × Ar*C*H), 134.1 (CCH=*C*H), 139.5 (Ar*C*), 141.2 (Ar*C*), 143.9 (Ar*C*); ν_{max} (neat)/cm^{-1} 725, 743, 839, 950, 1012, 1148, 1224, 1436, 1456, 2871, 2926, 2957; **HRMS** (GCMS): Calcd. for $C_{13}H_{14}S$ $(M)^+$, 202.0811; found 202.0802.

(*E*)-5-Methyl-2-(pent-1-en-1-yl)benzo[*b*]thiophene 221



As described in general procedure **H**, (2-(hept-2-yn-1-yl)-4-methylphenyl)(methyl)sulfide (46.4 mg, 0.2 mmol), iodine (55.6 mg, 0.22 mmol) in 1,2-dichloroethane (20 ml), after purification by column chromatography on silica gel eluting with *n*-hexane, gave **221** (34.7 mg, 0.16 mmol, 80 % yield) as a yellow solid; **mp:** 47-50 °C; $\boldsymbol{\delta_H}$ (400 MHz, $CDCl_3$) 0.98 (3 H, t, *J* = 7.3 Hz, CH_3), 1.53 (2 H, sxt, *J* = 7.4 Hz, CH_2CH$_3$), 2.22 (2 H, qd, *J* = 7.2, 1.5 Hz, CHCH_2), 2.44 (3 H, s, CH_3), 6.15 (1 H, dt, *J* = 15.4, 7.0 Hz, CCH=C*H*), 6.60 (1 H, dd, *J* = 15.4, 0.5 Hz, CC*H*=CH), 6.98 (1 H, s, ArC*H*), 7.10 (1 H, dd, *J* = 8.2, 1.1 Hz, ArC*H*), 7.46 (1 H, s, ArC*H*), 7.62 (1 H, d, *J* = 8.1 Hz, ArC*H*); $\boldsymbol{\delta_C}$ (100 MHz, $CDCl_3$) 13.4 (*C*H$_3$), 21.0 (*C*H$_2$CH$_3$), 22.0 (*C*H$_3$), 34.7 (CH*C*H$_2$), 120.6 (Ar*C*H), 121.4 (Ar*C*H), 122.8 (Ar*C*H), 123.7 (C*C*H=CH), 125.6 (Ar*C*H), 133.2 (Ar*C*), 133.6 (CCH=*C*H), 135.2 (Ar*C*), 140.2 (Ar*C*), 143.1 (Ar*C*); $\boldsymbol{\nu_{max}}$ (neat)/cm^{-1} 694, 725, 744, 803, 889, 951, 1008, 1044, 1065, 1138, 1169, 1209, 1230, 1259, 1301, 1378, 1443, 2867, 2924, 2954, 3012; **HRMS** (GCMS): Calcd. for $C_{14}H_{17}S$ (M + H), 217.1051; found 217.1050.

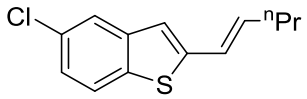
(E)-2-(3-Methylbut-1-en-1-yl)-5-(trifluoromethyl)benzo[b]thiophene 222



As described in general procedure **H**, (2-(hept-2-yn-1-yl)-4-trifluoromethylphenyl)(methyl)sulfide (57.2 mg, 0.2 mmol), iodine (55.6 mg, 0.22 mmol) in 1,2-dichloroethane (20 ml), after purification by column chromatography on silica gel eluting with 1% EtOAc in *n*-hexane, gave **222** (18.0 mg, 0.09 mmol, 47 % yield) as a yellow oil; $\boldsymbol{\delta_H}$ (400 MHz, $CDCl_3$) 0.99 (3 H, t, *J* = 7.4 Hz, CH_3), 1.54 (2 H, sxt, *J* = 7.3 Hz, CH_2CH$_3$), 2.18 - 2.29 (2 H, q, *J* = 6.9, CHCH_2), 6.18 - 6.28 (1 H, m, CCH=C*H*), 6.62 (1 H, d, *J* = 15.8 Hz, CC*H*=CH), 7.10 (1 H, s, ArC*H*), 7.48 (1 H, d, *J* = 8.5 Hz, ArC*H*), 7.83 (1 H, d, *J* = 8.5 Hz, ArC*H*), 7.91 (1 H, s, ArC*H*); $\boldsymbol{\delta_C}$ (100 MHz, $CDCl_3$13.8 (*C*H$_3$), 22.2 (*C*H$_2$CH$_3$), 35.1 (CH*C*H$_2$), 120.1 (q, *J* = 4.2 Hz, Ar*C*H), 120.4 (q, *J* = 3.7 Hz, Ar*C*H), 120.8 (Ar*C*H), 122.5 (Ar*C*H), 123.5 (C*C*H=CH), 124.5 (q, *J* = 272.9 Hz, *C*F$_3$), 126.9 (q, *J*=32.3 Hz, Ar*C*CF$_3$), 135.3 (CCH=*C*H), 139.9 (Ar*C*), 141.6 (Ar*C*), 145.4 (Ar*C*); $\boldsymbol{\nu_{max}}$ (neat)/cm^{-1} 650, 668, 709, 729, 812,

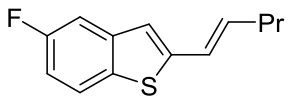
892, 906, 953, 1054, 1073, 1120, 1144, 1169, 1217, 1262, 1332, 1433, 1528, 1607, 2929, 2959; **HRMS** (GCMS): Calcd. for $C_{14}H_{13}F_3S$ $(M)^+$, 270.0685; found 270.0681.

(*E*)-5-Chloro-2-(pent-1-en-1-yl)benzo[*b*]thiophene 223



As described in general procedure **G**, (2-(hept-2-yn-1-yl)-4-chlorophenyl)(methyl)sulfide (49.7 mg, 0.2 mmol), iodine (55.6 mg, 0.22 mmol) in 1,2-dichloroethane (2 ml), after purification by column chromatography on silica gel eluting with *n*-hexane, gave **223** (19.0 mg, 0.08 mmol, 40 % yield) as a yellow solid; **mp:** 85 - 87 °C; $\boldsymbol{\delta_H}$ (400 MHz, C_6D_6) 0.81 (3 H, t, *J* = 7.3, C*H*$_3$), 1.27 (2 H, sxt, *J* = 7.3, C*H*$_2$CH$_3$), 1.93 (2 H, qd, *J* = 7.2, 1.4, CHC*H*$_2$), 6.09 (1 H, dt, *J* = 15.4, 7.1, CCH=C*H*), 6.34 (1 H, dt, *J* = 15.6, 1.1, CC*H*=CH), 6.53 (1 H, s, ArC*H*), 6.98 (1 H, dd, *J* = 8.6, 2.0, ArC*H*), 7.10 (1 H, d, *J* = 8.6, ArC*H*), 7.42 (1 H, d, *J* = 2.0, ArC*H*); $\boldsymbol{\delta_C}$ (100 MHz, C_6D_6) 14.1 (*C*H$_3$), 22.8 (*C*H$_2$CH$_3$), 35.5 (CH*C*H$_2$), 121.3 (Ar*C*H), 123.4 (Ar*C*H), 123.8 (Ar*C*H), 124.6 (C*C*H=CH), 125.3 (Ar*C*H), 131.3 (Ar*C*), 134.9 (CCH=*C*H), 137.4 (Ar*C*), 142.3 (Ar*C*), 145.9 (Ar*C*Cl); $\boldsymbol{\nu_{max}}$ (neat)/cm^{-1} 705, 749, 764, 799, 874, 906, 954, 1077, 1145, 1262, 1275, 1416, 1438, 1582, 2928, 2960; **HRMS** (EI): Calcd. for $C_{13}H_{14}S$ (M-Cl), 202.0811; found 202.0802.

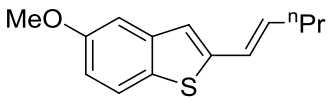
(E)-5-Fluoro-2-(3-methylbut-1-en-1-yl)benzo[b]thiophene 224



As described in general procedure **G**, (2-(hept-2-yn-1-yl)-4-fluorophenyl)(methyl)sulfide (47.2 mg, 0.2 mmol), iodine (55.6 mg, 0.22 mmol) in 1,2-dichloroethane (20 ml), after purification by column chromatography on silica gel eluting with *n*-hexane, gave **224** (30.4 mg, 0.13 mmol, 65 % yield) as a yellow solid; **mp:** 55-58 ^{0}C; $\boldsymbol{\delta_H}$ (400 MHz, $CDCl_3$) 0.98 (3 H, t, *J* = 7.4 Hz, C*H*$_3$), 1.47 - 1.58 (2 H, m, C*H*$_2$CH$_3$), 2.18 - 2.26 (2 H, m, CHC*H*$_2$), 6.19 (1 H, dt, *J* = 15.5, 7.0 Hz, CCH=C*H*), 6.59 (1 H, d, *J* = 15.7 Hz, CC*H*=CH), 6.99 - 7.05 (2 H, m, ArC*H*), 7.32 (1 H, dd, *J* = 9.5, 2.4 Hz, ArC*H*), 7.65 (1 H, dd, *J* = 8.8, 4.9 Hz, ArC*H*); $\boldsymbol{\delta_C}$ (100 MHz, $CDCl_3$) 13.7 (*C*H$_3$), 22.2 (*C*H$_2$CH$_3$), 35.0 (CH*C*H$_2$), 108.6 (d, *J* = 23.5, Ar*C*H), 112.7 (d, *J* = 29.3, Ar*C*H), 120.7 (d, *J* = 4.4 Hz, Ar*C*H), 123.1 (d, *J*

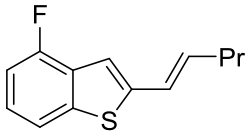
= 9.5 Hz, Ar*C*), 123.7 (C*C*H=CH), 133.7 (Ar*C*), 134.6 (CCH=*C*H), 141.2 (d, *J* = 9.5 Hz, Ar*C*), 145.7 (Ar*C*), 160.8 (dd, *J* = 248.7, 1.0 Hz, Ar*C*F); ν_{max} (neat)/cm^{-1} 715, 725, 803, 836, 889, 951, 1045, 1066, 1121, 1170, 1209, 1230, 1379, 1443, 1595, 2925, 2954; **HRMS** (GCMS): Calcd. for $C_{13}H_{13}SF$ (M-H), 220.0717; found 220.0719.

(*E*)-5-Methoxy-2-(pent-1-en-1-yl)benzo[*b*]thiophene 225



As described in general procedure **H**, (2-(hept-2-yn-1-yl)-4-methoxyphenyl)(methyl)sulfide (49.6 mg, 0.2 mmol), iodine (55.6 mg, 0.22 mmol) in 1,2-dichloroethane (20 ml), after purification by column chromatography on silica gel eluting with 5% EtOAc in *n*-hexane, gave **225** (35.2 mg, 0.15 mmol, 76 % yield) as a yellow solid; **mp:** 79-81 ^{o}C; δ_H (400 MHz, C_6D_6) 0.83 (3 H, t, *J* = 7.4, CH_3), 1.30 (2 H, sxt, *J* = 7.3, CH_2CH$_3$), 1.97 (2 H, qd, *J* = 7.2, 1.3, CHCH_2), 6.17 (1 H, dt, *J* = 15.6, 7.0, CCH=C*H*), 6.48 (1 H, dt, *J* = 15.5, 1.2, CC*H*=CH), 6.81 (1 H, s, ArC*H*), 6.87 (1 H, dd, *J* = 8.6, 2.5, ArC*H*), 7.01 (1 H, d, *J* = 2.5, ArC*H*), 7.34 (1 H, d, *J* = 8.8, ArC*H*); δ_C (100 MHz, C_6D_6) 14.4 (*C*H$_3$), 22.9 (*C*H$_2$CH$_3$), 35.6 (CH*C*H$_2$), 55.4 (O*C*H$_3$), 106.4 (Ar*C*H), 115.0 (Ar*C*H), 122.0 (Ar*C*H), 123.5 (Ar*C*H), 125.1 (C*C*H=CH), 131.7 (Ar*C*), 133.9 (CCH=*C*H), 142.3 (Ar*C*), 145.2 (Ar*C*), 158.6 (Ar*C*); ν_{max} (neat)/cm^{-1} 680, 719, 751, 764, 806, 854, 951, 1001, 1024, 1069, 1098, 1151, 1171, 1203, 1216, 1258, 1331, 1456, 1519, 1599, 1571, 2850, 2872, 2921, 2957; **HRMS** (EI): Calcd. for $C_{14}H_{16}OS$ $(M)^+$, 232.0916; found 232.0915.

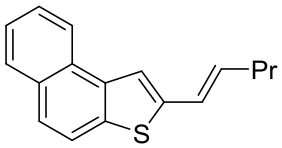
(E)-4-Fluoro-2-(3-methylbut-1-en-1-yl)benzo[b]thiophene 226



As described in general procedure **H**, (2-(hept-2-yn-1-yl)-5-fluorophenyl)(methyl)sulfide (47.2 mg, 0.2 mmol), iodine (55.6 mg, 0.22 mmol) in 1,2-dichloroethane (20 ml), after purification by column chromatography on silica gel eluting with *n*-hexane, gave **226** (40.3 mg, 0.18 mmol, 92 % yield) as a yellow solid: **mp:** 64-65 ^{o}C; δ_H (400 MHz, $CDCl_3$) 0.97 (3 H, t, *J* = 7.4 Hz, CH_3), 1.45 - 1.58 (2 H, m, CH_2CH$_3$), 2.21 (2 H, qd, *J* = 7.2, 1.5 Hz, CHCH_2), 6.13 (1 H, dt, *J* = 15.6, 7.0 Hz, CCH=C*H*), 6.58 (1 H,

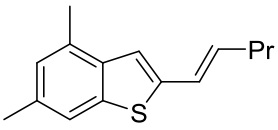
d, *J* = 15.6 Hz, CC*H*=CH), 7.00 (1 H, s, ArC*H*), 7.04 (1 H, td, *J* = 8.9, 2.4 Hz, ArC*H*), 7.43 (1 H, dd, *J* = 8.8, 2.3 Hz, ArC*H*), 7.58 (1 H, dd, *J* = 8.7, 5.2 Hz, ArC*H*); **δ_C** (100 MHz, $CDCl_3$); 13.7 (*C*H_3), 22.3 (*C*H_2CH_3), 35.0 (*C*HCH_2), 108.3 (d, *J* = 24.9 Hz, Ar*C*H), 113.1 (d, *J* = 23.5 Hz, Ar*C*H), 120.3 (Ar*C*H), 123.6 (CH=*C*HCH_2), 123.9 (d, *J* = 8.8 Hz, Ar*C*H), 133.9 (d, *J* = 1.5 Hz, *C*H=$CHCH_2$), 136.7 (d, *J* = 1.5 Hz, Ar*C*), 139.4 (d, *J* = 10.3 Hz, Ar*C*), 143.0 (d, *J* = 3.7 Hz, Ar*C*), 160.5 (d, *J* = 243.6 Hz, Ar*C*F); **ν_{max}** (neat)/cm^{-1} 586, 718, 807, 819, 851, 938, 957, 1046, 1111, 1146, 1188, 1233, 1248, 1378, 1401, 1464, 1520, 1565, 1589, 2872, 2929, 2958; **HRMS** (GCMS): Calcd. for $C_{13}H_{13}SF$ $(M)^+$, 220.0717; found 220.0721.

(E)-2-(3-Methylbut-1-en-1-yl)naphtho[2,1-b]thiophene 227



As described in general procedure **H**, (1-(hept-2-yn-1-yl)naphthalen-2-yl)(methyl)sulfide (53.6 mg, 0.2 mmol), iodine (55.6 mg, 0.22 mmol) in 1,2-dichloroethane (20 ml), after purification by column chromatography on silica gel eluting with *n*-hexane, gave **227** (40.3 mg, 0.16 mmol 80 % yield) as a white solid; **mp:** 83-85 ^oC; **δ_H** (400 MHz, $CDCl_3$) 1.01 (3 H, t, *J* = 7.4 Hz, C*H*$_3$), 1.57 (2 H, m, C*H*$_2$CH$_3$), 2.26 (2 H, m, CHC*H*$_2$), 6.25 (1 H, dt, *J* = 15.5, 7.0 Hz, CCH=C*H*), 6.72 (1 H, d, *J* = 15.5Hz, CC*H*=CH), 7.52 (1 H, m, *J* = 6.8 Hz, ArC*H*), 7.59 (1 H, t, *J* = 7.0 Hz, ArC*H*), 7.73 (3 H, m, 3 x ArC*H*), 7.92 (1 H, d, *J* = 7.9 Hz, ArC*H*), 8.25 (1 H, d, *J* = 8.2 Hz, ArC*H*); **δ_C** (100 MHz, $CDCl_3$) 13.8 (*C*H_3), 22.3 (*C*H_2CH_3), 35.0 (CH*C*H_2), 119.2 (Ar*C*H), 120.5 (Ar*C*H), 123.5 (Ar*C*H), 123.9 (C*C*H=CH), 124.8 (Ar*C*H), 125.1 (Ar*C*H), 126.3 (Ar*C*H), 128.5 (Ar*C*H), 128.9 (Ar*C*), 131.0 (Ar*C*), 133.0 (CCH=*C*H), 135.8 (Ar*C*), 136.2 (Ar*C*), 143.1 (Ar*C*); **ν_{max}** (neat)/cm^{-1} 712, 770, 843, 868, 955, 1025, 1062, 1092, 1159, 1200, 1253, 1340, 1406, 1465, 1502, 1555, 2833, 2869, 2950, 2962; **HRMS** (GCMS): Calcd. for $C_{17}H_{16}S$ $(M)^+$, 253.1050; found 253.1056.

(E)-4,6-Dimethyl-2-(3-methylbut-1-en-1-yl)benzo[b]thiophene 228

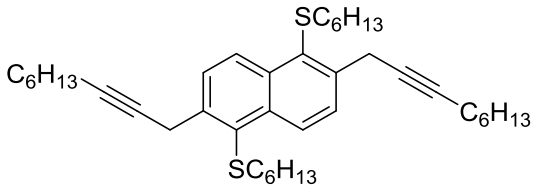


As described in general procedure **H**, (2-(hept-2-yn-1-yl)-3,5-dimethylphenyl)(methyl)sulfide (49.2 mg, 0.2 mmol), iodine (55.6 mg, 0.22 mmol) in

1,2-dichloroethane (20 ml), after purification by column chromatography on silica gel eluting in *n*-hexane, gave **228** (42.4 mg, 0.18 mmol, 92 % yield) as a yellow oil; δ_H (400 MHz, $CDCl_3$) 1.00 (3 H, t, *J* = 7.4 Hz, C*H*$_3$), 1.54 (2 H, sxt, *J* = 7.4 Hz, C*H*$_2$CH$_3$), 2.23 (2 H, q, *J* = 6.9 Hz, CHC*H*$_2$), 2.43 (3 H, s, C*H*$_3$), 2.52 - 2.55 (3 H, s, C*H*$_3$), 6.14 (1 H, dt, *J* = 15.4, 7.0 Hz, CCH=C*H*), 6.63 (1 H, d, *J* = 15.5 Hz, CC*H*=CH), 6.94 (1 H, s, ArC*H*), 7.08 (1 H, s, ArC*H*), 7.40 (1 H, s, ArC*H*); δ_C (100 MHz, $CDCl_3$) 13.8 (*C*H$_3$), 19.4 (*C*H$_2$CH$_3$), 21.5 (*C*H$_3$), 22.3 (*C*H$_3$), 35.0 (CH*C*H$_2$), 119.3 (Ar*C*H), 119.5 (Ar*C*H), 124.1 (Ar*C*H), 126.6 (C*C*H=CH), 132.0 (Ar*C*), 132.9 (CCH=*C*H), 134.3 (Ar*C*), 137.4 (Ar*C*), 138.7 (Ar*C*), 141.5 (Ar*C*); ν_{max} (neat)/cm^{-1} 657, 757, 843, 950, 1032, 1113, 1160, 1204, 1221, 1301, 1376, 1454, 1504, 1567, 1600, 1671, 2869, 2924, 2957; **HRMS** (GCMS): Calcd. for $C_{15}H_{18}S$ $(M)^+$, 230.1124; found 230.1119.

3.2.9 General Procedure I: Two-Directional Propargylations

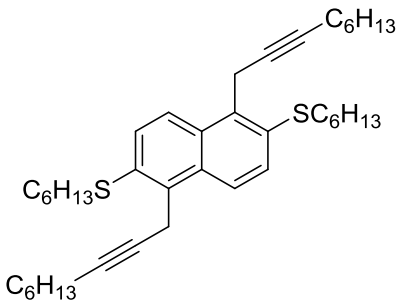
(2,6-Di(non-2-yn-1-yl)naphthalene-1,5-diyl)bis(hexylsulfide) 230



A solution containing 1,5-*bis*(hexylsulfinyl)naphthalene (1.50 g, 3.82 mmol) and trimethyl(non-2-yn-1-yl)silane (2.25 g, 11.5 mol) in MeCN (180 ml) was added to an oven dried tube flushed with N_2. Triflic anhydride (1.93 ml, 11.5 mmol) and 2,6-lutidine (1.55 ml, 13.4 mmol) were added sequentially at room temperature and the reaction mixture was then heated for 24 h at 80 °C. After cooling to room temperature, the solution was quenched with aqueous saturated $NaHCO_3$ (100 ml) and the aqueous layer was extracted with EtOAc (3 × 75 ml). The combined organic layer was washed successively with aqueous HCl 1.0 M (2 × 20 ml) and brine (100 ml), dried (Na_2SO_4) and concentrated *in vacuo*. The crude product was purified by column chromatography on silica gel eluting with 2% EtOAc in *n*-hexane to yield **230** (1.76 g, 2.90 mmol, 76% yield) as a bown solid; **mp:** 39 - 41 °C; δ_H (500 MHz, $CDCl_3$) 0.84 - 0.92 (12 H, m, 4 × C*H*$_3$), 1.18 - 1.45 (24 H, m, 12 × C*H*$_2$), 1.54 (8 H, m, 4 × C*H*$_2$), 2.23 (4 H, tt, *J* = 7.1, 2.5, 2 × CC*H*$_2$), 2.75 (4 H, t, *J* = 7.6, 2 × SC*H*$_2$), 4.14 (4 H, t, *J* = 2.4, 2 × CC*H*$_2$C), 7.85 (2 H, d, *J* = 8.8, ArC*H*), 8.74 (2 H, d, *J* = 8.8, ArC*H*); δ_C (125 MHz, $CDCl_3$) 14.0 (4 × *C*H$_3$), 18.9 (2 × C*C*H$_2$), 22.5 (2 × *C*H$_2$), 22.6 (2 × *C*H$_2$), 25.2 (2 × CC*H*$_2$C), 28.6 (4 × *C*H$_2$), 29.0 (2 × *C*H$_2$), 29.8 (2 × *C*H$_2$), 31.4 (4 ×

CH_2), 36.9 (2 × S*C*H_2), 78.1 (2 x *C*≡C), 82.7 (2 x C≡*C*), 127.7 (2 × Ar*C*H), 128.0 (2 × Ar*C*H), 131.0 (2 × Ar*C*), 135.1 (2 × Ar*C*), 140.7 (2 × Ar*C*); ν_{max} (neat)/cm^{-1} 726, 755, 764, 795, 813, 890, 956, 1182, 1206, 1217, 1259, 1267, 1278, 1302, 1368, 1412, 1440, 1457, 1464, 1486, 1589, 2850, 2868, 2923, 2955; **HRMS** (ES): Calcd. for $C_{40}H_{60}S_2$ $(M)^+$, 604.4131; found 604.4108.

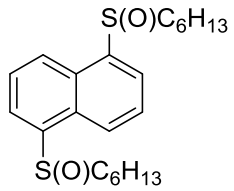
(1,5-Di(non-2-yn-1-yl)naphthalene-2,6-diyl)bis(hexylsulfide) 232



As described in general procedure **I**, 2,6-*bis*(hexylsulfinyl)naphthalene (29.4 mg, 0.075 mmol), trimethyl(non-2-yn-1-yl)silane (44.5 mg, 0.225 mol), triflic anhydride (38 µl, 0.225 mmol), 2,6-lutidine (31 µl, 0.263 mmol) and MeCN (7.50 ml), after purification by preparative thin-layer chromatography eluting with 2% EtOAc in *n*-hexane gave **232** (34.8 mg, 0.17 mmol, 77% yield) as a yellow solid; **mp:** 56 - 57 °C; δ_H (500 MHz, $CDCl_3$) 0.82 - 0.92 (12 H, m, 4 × C*H*$_3$), 1.18 - 1.35 (20 H, m, 10 × C*H*$_2$), 1.37 - 1.48 (8 H, m, 2 × SCH$_2$CH$_2$C*H*$_2$, 2 × CCH$_2$C*H*$_2$), 1.64 (4 H, quin, *J* = 7.5, 2 × SCH$_2$C*H*$_2$), 2.09 (4 H, tt, *J* = 7.1, 2.2, 2 × CC*H*$_2$), 3.00 (4 H, t, *J* = 7.3, 2 × SC*H*$_2$), 4.22 (4 H, t, *J* = 2.2, 2 × CC*H*$_2$C), 7.62 (2 H, d, *J* = 8.8, ArC*H*), 8.06 (2 H, d, *J* = 8.8, ArC*H*); δ_C (125 MHz, $CDCl_3$) 14.0 (4 × *C*H$_3$), 18.9 (2 × C*C*H$_2$), 20.5 (2 × C*C*H$_2$C), 22.5 (2 × *C*H$_2$), 22.6 (2 × *C*H$_2$), 28.5 (4 × *C*H$_2$), 28.9 (2 × *C*H$_2$), 29.6 (2 × SCH$_2$*C*H$_2$), 31.3 (2 × *C*H$_2$), 31.4 (2 × *C*H$_2$), 35.2 (2 × S*C*H$_2$), 77.9 (2 x *C*C), 81.6 (2 x C*C*), 124.2 (2 × Ar*C*H), 129.5 (2 × Ar*C*H), 131.5 (2 × Ar*C*), 132.6 (2 × Ar*C*), 135.4 (2 × Ar*C*); ν_{max} (neat)/cm^{-1} 722, 750, 764, 789, 798, 922, 941, 1112, 1260, 1275, 1377, 1433, 1459, 1468, 1567, 2854, 2870, 2920, 2955; **HRMS** (ES): Calcd. for $C_{40}H_{60}S_2$ $(M)^+$, 604.4131; found 604.4108.

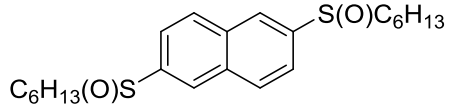
3.2.10 General Procedure J: Oxidation to bis-sulfoxide

1,5-*bis*(Hexylsulfinyl)naphthalene 229



To a solution of 1,5-*bis*(hexylthio)naphthalene **234** (3.0 g, 8.32 mmol) in dichloromethane (42.0 ml) a solution of *m*-CPBA (2.05 g, 9.15 mmol) in dichloromethane (183 ml) was added at -78 °C over 30 min. The reaction was warmed to room temperature over 1 h before adding a second portion of *m*-CPBA (2.05 g, 9.15 mmol) in dichloromethane (183 ml) over 30 min at -78 °C. After allowing the reaction mixture to reach room temperature over 1 h it was stirred for a further 1 h before quenching with aqueous $NaHCO_3$ (100 ml) and extraction with dichloromethane (2 × 75 ml). The combined organic layers were dried (Na_2SO_4) and concentrated *in vacuo*. The crude product was purified by column chromatography on silica gel (30% Et_2O in $CHCl_3$) to yield **229** (2.98 g, 7.57 mmol, 91% yield) as a white solid; **mp:** 103 - 107 °C; $\boldsymbol{\delta_H}$ (500 MHz, $CDCl_3$) 0.79 - 0.91 (6 H, m, 2 × C*H*$_3$), 1.19 - 1.31 (8 H, m, 4 × C*H*$_2$), 1.32 - 1.53 (4 H, m, 2 × C*H*$_2$), 1.59 - 1.74 (2 H, m, 2 × $SCH_2CH_aCH_b$), 1.79 - 1.95 (2 H, m, 2 × $SCH_2CH_aCH_b$), 2.75 - 2.88 (2 H, m, 2 × SCH_aCH_b), 2.94 - 3.07 (2 H, m, 2 × SCH_aCH_b), 7.71 - 7.82 (2 H, m, 2 × ArC*H*), 8.03 - 8.13 (2 H, m, 2 × ArC*H*), 8.16 - 8.27 (2 H, m, 2 × ArC*H*); $\boldsymbol{\delta_C}$ (125 MHz, $CDCl_3$) 14.1 (2 × *C*H_3), 22.5 (2 × SCH_2CH_2, 2 × *C*H_2), 28.4 (2 × $SCH_2CH_2CH_2$), 31.5 (2 × *C*H_2), 56.4 (2 × S*C*H_2), 123.9 (2 × Ar*C*H), 124.5 (2 × Ar*C*H), 127.1 (2 × Ar*C*H), 129.1 (2 × Ar*C*), 141.8 (2 × Ar*C*); $\boldsymbol{\nu_{max}}$ (neat)/cm^{-1} 724, 750, 764, 791, 970, 1036, 1074, 1113, 1155, 1193, 1261, 1275, 1338, 1390, 1403, 1466, 1498, 2856, 2921, 2949; **HRMS** (ES): Calcd. for $C_{22}H_{32}S_2O_2Na$ (M+Na), 415.1736; found 415.1741.

2,6-*bis*(Hexylsulfinyl)naphthalene 232

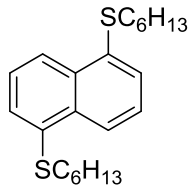


As described in general procedure **J**, 2,6-*bis*(hexylthio)naphthalene **236** (6.70 g, 18.6 mmol), *m*-CPBA (9.25 g, 41.3 mmol) and dichloromethane (832 ml) after purification by column chromatography on silica gel (30% Et_2O in $CHCl_3$) gave **232** (6.49

g, 16.5 mmol, 89% yield) as a white solid; **mp:** 155 - 157 °C; δ_H (400 MHz, $CDCl_3$) 0.87 (6 H, t, *J* = 7.1, 2 × C*H*$_3$), 1.21 - 1.34 (8 H, m, 4 × C*H*$_2$), 1.36 - 1.53 (4 H, m, 2 × C*H*$_2$), 1.58 - 1.71 (2 H, m, 2 × $SCH_2CH_aCH_b$), 1.77 - 1.91 (2 H, m, 2 × $SCH_2CH_aCH_b$), 2.80 - 2.97 (4 H, m, 2 × SC*H*$_2$), 7.66 (2 H, dd, *J* = 8.4, 1.4, 2 × ArC*H*), 8.07 (2H, d, *J* = 8.6, 2 × ArC*H*), 8.27 (2H, d, *J* = 1.5, 2 × ArC*H*); δ_C (100 MHz, $CDCl_3$) 14.2 (2 × *C*H$_3$), 22.2 (2 × SCH_2CH_2), 22.6 (2 × *C*H$_2$), 28.6 (2 × $SCH_2CH_2CH_2$), 31.5 (2 × *C*H$_2$), 57.2 (2 × S*C*H$_2$), 121.6 (2 × Ar*C*H), 124.8 (2 × Ar*C*H), 130.0 (2 × Ar*C*H), 134.1 (2 × Ar*C*), 143.6 (2 × Ar*C*); ν_{max} (neat)/cm^{-1} 638, 646, 706, 728, 749, 824, 909, 970, 1030, 1061, 1076, 1379, 1458, 2857, 2925, 2955; **HRMS** (ES): Calcd. for $C_{22}H_{33}S_2O_2$ (M+H), 393.1916; found 393.1931.

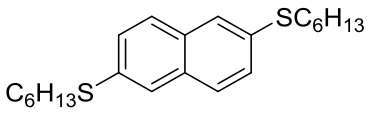
3.2.11 General procedure K: Bis-sulfide Formation

1,5-bis(Hexylthio)naphthalene 234



A solution containing naphthalene-1,5-diol **233** (3.20 g, 20.0 mmol), 1-hexanethiol (6.21 ml, 44.0 mmol) and p-toluenesulfonic acid (1.90 g, 10.0 mmol) in toluene (115 ml) were relfuxed in a flask equipped with a Dean-Stark for 48h. The reaction was then quenched with saturated aqueous $NaHCO_3$ (50 ml) and extracted with Et_2O (3 × 75 ml) and the combined organic layers dried (Na_2SO_4) and concentrated *in vacuo*. The crude product was purified by column chromatography on silica gel eluting with 2% EtOAc in *n*-hexane to yield **234** (5.18 g, 14.6 mmol, 73% yield) as a yellow solid; **mp:** 48 - 52 °C; δ_H (500 MHz, $CDCl_3$) 0.88 (6 H, t, *J* = 6.9, 2 × C*H*$_3$), 1.24 - 1.34 (8 H, m, 4 × C*H*$_2$), 1.45 (4 H, quin, *J* = 7.6, 2 × $SCH_2CH_2CH_2$), 1.67 (4 H, quin, *J* = 7.5, 2 × SCH_2CH_2), 2.98 (4 H, t, *J* = 7.6, 2 × SC*H*$_2$), 7.47 (2 H, t, *J* = 8.0, 2 × ArC*H*), 7.57 (2H, d, *J* = 7.3, 2 × ArC*H*), 8.31 (2H, d, *J* 8.4, 2 × ArC*H*); δ_C (125 MHz, $CDCl_3$) 14.3 (2 × *C*H$_3$), 22.8 (2 × *C*H$_2$), 28.8 (2 × $SCH_2CH_2CH_2$), 29.3 (2 × SCH_2CH_2), 31.6 (2 × *C*H$_2$), 34.5 (2 × S*C*H$_2$), 123.9 (2 × Ar*C*H), 126.2 (2 × Ar*C*H), 127.8 (2 × Ar*C*H), 133.4 (2 × Ar*C*), 135.1 (2 × Ar*C*); ν_{max} (neat)/cm^{-1} 729, 746, 770, 1063, 1151, 1193, 1219, 1311, 1374, 1389, 1431, 1465, 1492, 1575, 2853, 2924, 2951; **HRMS** (EI): Calcd. for $C_{22}H_{32}S_2$ $(M)^+$, 360.1940; found 360.1946.

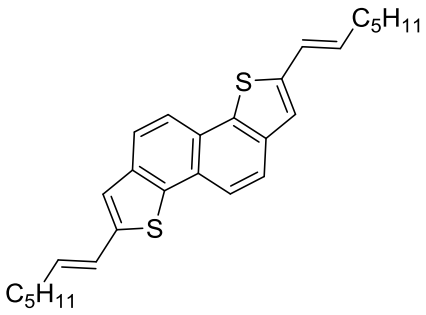
2,6-bis(Hexylthio)naphthalene 236



As described in general procedure **K**, naphthalene-2,6-diol **235** (5.00 g, 31.2 mmol), 1-hexanethiol (9.70 ml, 68.7 mmol), p-toluenesulfonic acid (2.97 g, 15.6 mmol) and toluene (160 ml) gave **236** (11.1 g, 28.3 mmol, 91% yield) as a grey solid; **mp:** 49 - 52 °C; δ_H (500 MHz, $CDCl_3$) 0.92 (6 H, t, *J* = 6.9, 2 × C*H*$_3$), 1.28 - 1.37 (8 H, m, 4 × C*H*$_2$), 1.47 (4 H, quin, *J* = 7.5, 2 × SCH$_2$CH$_2$C*H*$_2$), 1.71 (4 H, quin, *J* = 7.5, 2 × SCH$_2$C*H*$_2$), 3.02 (4 H, t, *J* = 7.6, 2 × SC*H*$_2$), 7.42 (2 H, dd, *J* = 8.5, 1.9, 2 × ArC*H*), 7.65 (2 H, d, *J* = 8.5, 2 × ArC*H*), 7.68 (2 H, d, *J* = 1.9, 2 × ArC*H*); δ_C (125 MHz, $CDCl_3$) 14.2 (2 × *C*H$_3$), 22.7 (2 × *C*H$_2$), 28.7 (2 × SCH$_2$CH$_2$*C*H$_2$), 29.2 (2 × SCH$_2$*C*H$_2$), 31.5 (2 × *C*H$_2$), 33.7 (2 × S*C*H$_2$), 126.3 (2 × Ar*C*H), 127.5 (2 × Ar*C*H), 128.0 (2 × Ar*C*H), 132.1 (2 × Ar*C*), 134.3 (2 × Ar*C*); ν_{max} (neat)/cm^{-1} 638, 732, 763, 806, 860, 883, 1063, 1146, 1179, 1207, 1367, 1435, 1448, 1459, 1479, 1580, 2854, 2927, 2944, 2955; **HRMS** (EI): Calcd. for $C_{22}H_{32}S_2$ $(M)^+$, 360.1940; found 360.1923.

3.2.12 General Procedure L: Two-Directional Eliminative Cyclisation

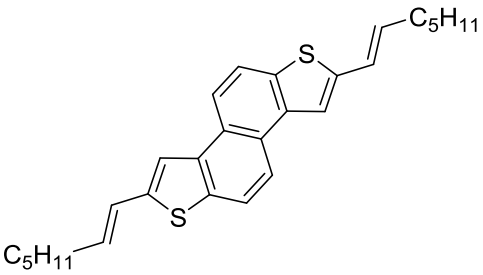
2,7-Di((E)-hept-1-en-1-yl)naphtho[1,2-b:5,6-b']dithiophene 237



To a solution of 2,6-di(non-2-yn-1-yl)naphthalene-1,5-diyl)bis(hexylsulfide **230** (30.2 mg, 0.05 mmol) in Ar flushed 1,2-dichloroethane (8 ml) was added a solution of iodine (27.8 mg, 0.11 mmol) in 1,2-dichloroethane (2 ml) at room temperature with methanol (0.81 ml, 5 mmol) and stirred for 1 h at 80 °C before quenching with saturated aqueous $Na_2S_2O_3$ (10 ml). The aqueous layer was then extracted with Dichloromethane (2 × 10 ml), dried ($MgSO_4$) and concentrated *in vacuo*. The crude product was purified by column chromatography on neutralised silica gel eluting with hexanes to yield **237** (18.1 mg, 0.042 mmol, 84% yield) as a white solid; **mp:** 145-147 °C; δ_H (400 MHz, $CDCl_3$)

0.90 - 0.99 (6 H, m, 2 × CH_3), 1.29 - 1.45 (8 H, m, 4 × CH_2) 1.47 - 1.61 (4 H, m, 2 × CH_2) 2.27 (4 H, q, *J* = 6.8 Hz, 2 × CH=CHCH_2) 6.26 (2 H, dt, *J* = 15.4, 7.0 Hz, 2 × CH=C*H*) 6.65 (2 H, d, *J* = 15.65 Hz, 2 × C*H*=CH) 7.18 (2 H, s, 2 × ArC*H*) 7.75 (2 H, d, *J* = 8.5 Hz, 2 × ArC*H*) 7.90 (2 H, d, *J* = 8.6 Hz, 2 × ArC*H*); **δ_C** (100 MHz, $CDCl_3$) 14.1 (2 × *C*H_3), 22.6 (2 × *C*H_2CH_3), 28.9 (2 × *C*$H_2CH_2CH_3$), 31.5 (2 × $CHCH_2$*C*H_2), 33.0 (2 × CH=CH*C*H_2), 121.1 (2 × Ar*C*H), 122.2 (2 × Ar*C*H), 122.3 (2 × Ar*C*H), 123.6 (2 × *C*H=CH), 125.8 (2 × ArC), 133.7 (2 × CH=*C*H), 136.8 (2 × Ar*C*), 137.6 (2 × Ar*C*), 142.4 (2 × Ar*C*); **ν_{max}** (neat)/cm^{-1} 651, 669, 709, 729, 812, 893, 907, 953, 1055, 1074, 1121, 1145, 1169, 1263, 1332, 2483, 2930, 2960; **HRMS** (APCI): Calcd. for $C_{28}H_{32}S_2O_2$ $(M+H)^+$, 433.2024; found 433.2009.

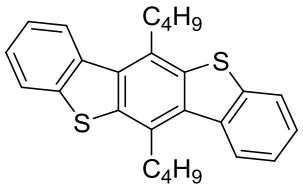
2,7-Di((E)-hept-1-en-1-yl)naphtho[2,1-b:6,5-b']dithiophene 238



As described in general procedure **L**, 2,7-di((E) hept-1-en-1-yl)naphtho[2,1-b:6,5-b']dithiophene **232** (40.9 mg, 0.088 mmol), I_2 (55.7 mg, 0.022 mmol), 1,2-dichloroethane (20.0 ml) and methanol (0.40 ml, 8.8 mmol were heated for 1 h at 80 ^oC. Purification by column chromatography on neutralised silica gel (1 % Et_2O in hexanes) gave **238** (24.6 mg, 0.057 mmol 65% yield) as a white solid; **mp:** decomp. T > 235 °C; **δ_H** (400 MHz,$CDCl_3$) 0.91 - 0.96 (6 H, m, 2 × CH_3), 1.37 (8 H, dq, *J* = 7.2, 3.5 Hz, 4 × CH_2), 1.49 - 1.57 (4 H, m, 2 × CH_2), 2.27 (4 H, q, *J* = 6.9 Hz, 2 × CH=CHCH_2), 6.26 (2 H, dt, *J* = 15.4, 7.0 Hz, 2 × CH=C*H*), 6.72 (2 H, d, *J* = 15.5 Hz, 2 × C*H*=CH), 7.72 (2 H, s, 2 × ArC*H*), 7.87 (2 H, d, *J* = 8.8 Hz, 2 × ArC*H*), 8.12 (2 H, d, *J* = 8.6 Hz, 2 × ArC*H*); **δ_C** (100 MHz, $CDCl_3$) 14.4 (2 × *C*H_3), 22.9 (2 × *C*H_2), 29.1 (2 × *C*H_2), 31.8 (2 × *C*H_2), 33.3 (2 × *C*H_2), 119.7 (2 × Ar*C*H), 120.8 (2 × Ar*C*H), 121.0 (2 × Ar*C*H), 124.1 (2 × C*C*H=CH_2), 126.6 (2 × Ar*C*), 134.1 (2 × CCH=*C*H), 135.5 (2 × Ar*C*), 137.3 (2 × Ar*C*), 143.8 (2 × Ar*C*); **ν_{max}** (neat)/cm^{-1} 677, 725, 796, 806,837, 876, 955, 1171, 1190, 1362, 1455, 1465, 2849, 2922, 2952; **HRMS** (APCI): Calcd. for $C_{28}H_{32}S_2O_2$ (M+H), 433.2024; found 433.2009.

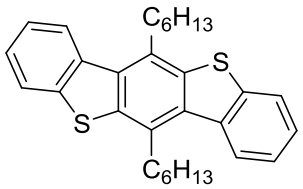
3.2.13 General Procedure M: Iodine-Mediated Dimerisations

6,12-Dibutylbenzo[1,2-*b*:4,5-*b*']bis[*b*]benzothiophene 251



Under an Ar atmosphere, a solution of (*E*)-2-pent-1-en-1-yl)benzo[*b*]thiophene **220** (40.4 mg, 0.2 mmol) in Ar sparged 1,2-dichloroethane (2 ml) was added to a solution of iodine (506 mg, 2 mmol) in argon sparged 1,2-dichloroethane (18 ml). The reaction mixture was stirred for 18 h at 80 °C before quenching with saturated aqueous $Na_2S_2O_3$ (5 ml). The aqueous layer was then extracted with EtOAc (3 × 5 ml) and the combined organic layers washed with brine (5 ml), dried (Na_2SO_4) and concentrated *in vacuo*. The crude product was washed with cold ethanol (3 ml) to yield **251** (34.8 mg, 86.0 µmol, 86 % yield) as a white solid; **mp:** 151 - 155 °C; δ_H (400 MHz, $CDCl_3$) 1.09 (6 H, t, *J* = 7.3, 2 × C*H*$_3$), 1.69 (4 H, sxt, *J* = 7.1, 2 × C*H*$_2$CH$_3$), 1.93 (4 H, quin, *J* = 7.5, 2 × C*H*$_2$), 3.46 - 3.57 (4 H, m, 2 × CC*H*$_2$), 7.44 - 7.57 (4 H, m, 4 × ArC*H*), 7.88 - 7.97 (2 H, m, 2 × ArC*H*), 8.25 - 8.37 (2 H, m, 2 × ArC*H*); δ_C (100 MHz, $CDCl_3$) 14.2 (2 × *C*H$_3$), 23.5 (2 × *C*H$_2$CH$_3$), 30.6 (2 × CCH$_2$*C*H$_2$), 33.9 (2 × C*C*H$_2$), 123.1 (2 × Ar*C*H), 124.7 (2 × Ar*C*H), 125.1 (2 × Ar*C*H), 126.3 (2 × Ar*C*H), 131.3 (4 × Ar*C*), 136.2 (2 × Ar*C*), 139.1 (2 × Ar*C*), 140.2 (2 × Ar*C*); ν_{max} (neat)/cm^{-1} 670, 724, 751, 764, 927, 1043, 1074, 1106, 1164, 1267, 1275, 1364, 1424, 1468, 2850, 2923, 2953; **HRMS** (EI): Calcd. for $C_{26}H_{26}S_2$ $(M)^+$, 402.1470; found 402.1483.

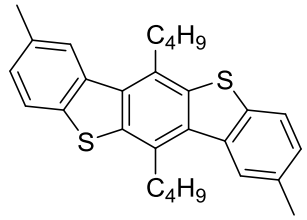
6,12-Dihexylbenzo[1,2-*b*:4,5-*b*']bis[*b*]benzothiophene 252



As in general procedure **M**, (*E*)-2-hex-1-en-1-yl)benzo[*b*]thiophene (41.2 mg, 0.17 mmol) in 1,2-dichloroethane (2 ml) was added to a solution of iodine (450 mg, 1.78 mmol) in 1,2-dichloroethane (15 ml). The reaction mixture was stirred for 18 h at 80 °C before quenching. The crude product was washed with cold ethanol (2 ml) to yield **252** (30.7 mg, 69.0 µmol, 81 % yield) as a white solid; **mp:** 155-157 °C; δ_H (500 MHz, $CDCl_3$)

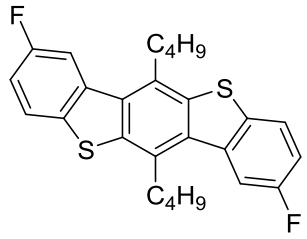
0.96 (6 H, t, *J* = 7.1 Hz, 2 x C*H*$_3$), 1.36 - 1.49 (8 H, m, 4 x C*H*$_2$), 1.68 (4 H, quin, *J* = 7.4 Hz, 2 x C*H*$_2$), 1.89 - 1.97 (4 H, m, 2 x C*H*$_2$), 3.47 - 3.52 (4 H, m, 2 x CC*H*$_2$), 7.50 (4 H, quin, *J* = 6.5 Hz, 4 x ArC*H*), 7.93 (2 H, d, *J* = 8.7 Hz, 2 x ArC*H*), 8.30 (2 H, d, *J* = 7.5 Hz, 2 x ArC*H*); **δ_C** (100 MHz, $CDCl_3$) 14.1 (2 x *C*H$_3$), 22.6 (2 x *C*H$_2$CH$_3$), 28.1 (2 x *C*H$_2$), 29.7 (*C*H$_2$), 31.6 (2 x CCH$_2$*C*H$_2$), 33.9 (2 x C*C*H$_2$CH$_2$), 122.8 (2 x Ar*C*H), 124.4 (2 x Ar*C*H), 124.8 (2 x Ar*C*H), 126.0 (2 x Ar*C*H), 131.0 (2 x Ar*C*), 131.0 (2 x Ar*C*), 135.9 (2 x Ar*C*), 138.8 (2 x Ar*C*), 139.9 (2 x Ar*C*); **ν_{max}** (neat)/cm^{-1} 660, 700, 723, 756, 801, 843, 927, 1049, 1072, 1103, 1163, 1260, 1365, 1424, 1467, 1725, 2854, 2923, 2948; **HRMS** (APCI): Calcd. for $C_{30}H_{35}S_2$ (M+H), 459.2180; found 459.2200.

6,12-Dibutylbenzo[1,2-*b*:4,5-*b*']bis[*b*]5-methylbenzothiophene 253



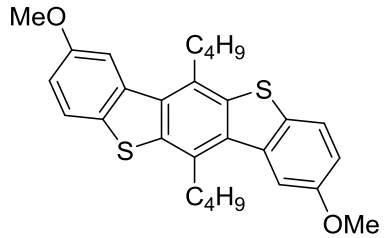
As for general procedure **M**, (*E*)-5-methyl-2-(pent-1-en-1-yl)benzo[*b*]thiophene **221** (43.2 mg, 0.2 mmol) in 1,2-dichloroethane (2 ml) was added to a solution of iodine (506 mg, 2 mmol) in 1,2-dichloroethane (18 ml). The reaction mixture was stirred for 18 h at 80 °C before quenching. The crude product was washed with cold ethanol (3 ml) to yield **253** (27.1 mg, 63.0 μmol, 63 % yield) as a white solid; **mp:** 260-262 °C; **δ_H** (400 MHz, $CDCl_3$) 1.11 (6 H, t, *J* = 7.3 Hz, 2 x C*H*$_3$), 1.70 (4 H, sxt, *J* = 7.3 Hz, 2 x C*H*$_2$), 1.87 - 1.97 (4 H, m, 2 x C*H*$_2$), 2.58 (6 H, s, 2 x C*H*$_3$), 3.45 - 3.54 (4 H, m, 2 x CC*H*$_2$), 7.32 (2 H, dd, *J* = 8.0, 0.6 Hz, 2 x ArC*H*), 7.80 (2 H, d, *J* = 8.0 Hz, ArC*H*), 8.13 (2 H, s, ArC*H*); **δ_C** (100 MHz, $CDCl_3$) 14.0 (2 x *C*H$_3$), 22.0 (2 x *C*H$_2$CH$_3$), 23.2 (2 x ArC*C*H$_3$), 30.2 (2 x CCH$_2$*C*H$_2$), 33.5 (2 x C*C*H$_2$CH$_2$), 122.4 (2 X Ar*C*H), 125.3 (2 X Ar*C*H), 127.4 (2 X Ar*C*H), 130.9 (2 X Ar*C*), 131.0 (2 X Ar*C*), 133.9 (2 X Ar*C*), 136.2 (2 X Ar*C*), 136.8 (2 X Ar*C*), 139.2 (2 X Ar*C*); **ν_{max}** (neat)/cm^{-1} 567, 613, 626, 687, 793, 861, 1017, 1258, 1412, 1568, 2961; **HRMS** (APCI): Calcd. for $C_{28}H_{30}S_2$ (M+H), 431.1867; found 459.1858.

6,12-Dibutylbenzo[1,2-*b*:4,5-*b*']bis[*b*]5-fluorobenzothiophene 254



As for general procedure **M**, (*E*)-5-fluoro-2-(pent-1-en-1-yl)benzo[*b*]thiophene **224** (44.0 mg, 0.2 mmol) in 1,2-dichloroethane (2 ml) was added to a solution of iodine (506 mg, 2 mmol) in 1,2-dichloroethane (18 ml). The reaction mixture was stirred for 18 h at 80 °C before quenching. The crude product was washed with cold ethanol (3 ml) to yield **254** (25.4 mg, 58.0 µmol, 58 % yield) as a white solid; **mp:** 209-211 °C; **δ_H** (400 MHz, $CDCl_3$) 1.09 (6 H, t, *J* = 7.34 Hz, 2 x CH_3), 1.69 (4 H, sxt, *J* = 7.3 Hz, 2 x CH_2), 1.84 - 1.94 (4 H, m, 2 x CH_2), 3.40 - 3.46 (4 H, m, 2 x CCH_2), 7.26 (2 H, td, *J* = 8.5, 2.3 Hz, 2 x ArC*H*), 7.84 (2 H, dd, *J* = 8.7, 5.2 Hz, , ArC*H*), 7.97 (2 H, dd, *J* = 11.0, 2.3 Hz, ArC*H*); **δ_C** (100 MHz, $CDCl_3$) 13.9 (2 x *C*H_3), 23.1 (2 x *C*H_2CH_3), 30.3 (2 x CCH_2*C*H_2), 33.3 (2 x C*C*H_2CH_2), 111.0 (d, *J* = 28.2 Hz, 2 x Ar*C*H), 114.1 (d, *J* = 24.5 Hz, 2 x Ar*C*H), 123.6 (d, *J* = 9.1 Hz, 2 x Ar*C*H), 131.0 (d, *J* = 3.6 Hz, 2 x Ar*C*) 131.4 (2 x Ar*C*), 135.1 (2 x Ar*C*), 136.9 (d, *J* = 9.1 Hz, 2 x Ar*C*), 140.1 (2 x Ar*C*), 158.9 (d, *J* = 240.7 Hz, 2 x ArCF); **ν_{max}** (neat)/cm^{-1} 613, 656, 793, 850, 939, 1020, 1096, 1183, 1258, 1293, 1356, 1414, 1472, 1569, 1601, 1770, 2870, 2960; **HRMS** (APCI): Calcd. for $C_{26}H_{24}S_2F_2$ $(M)^+$, 439.1366; found 439.1356.

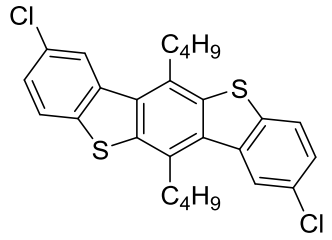
6,12-Dibutylbenzo[1,2-*b*:4,5-*b*']bis[*b*]5-methoxybenzothiophene 255



As in general procedure **M**, (*E*)-5-methoxy-2-(pent-1-en-1-yl)benzo[*b*]thiophene **225** (49.6 mg, 0.2 mmol) in 1,2-dichloroethane (2 ml) was added to a solution of iodine (506 mg, 2 mmol) in 1,2-dichloroethane (18 ml). The reaction mixture was stirred for 18 h at 80 °C before quenching. The crude product was washed with cold ethanol (3 ml) to yield **255** (27.6 mg, 55.0 µmol, 55 % yield) as a white solid; **mp:** 175-177 °C; **δ_H** (500 MHz, $CDCl_3$) 1.09 (6 H, t, *J* = 7.3 Hz, 2 x CH_3), 1.70 (4 H, sxt, *J* = 7.4 Hz, 2 x CH_2), 1.90 -

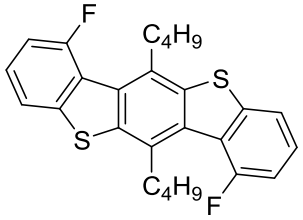
1.98 (4 H, m, 2 x CH_2), 3.46 - 3.50 (4 H, m, 2 x CCH_2), 3.97 (6 H, s, 2 x OCH_3), 7.14 (2 H, dd, *J* = 8.7, 2.3 Hz, 2 x ArC*H*), 7.79 (2 H, d, *J* = 8.7 Hz, 2 x ArC*H*), 7.84 (2 H, d, *J* = 2.3 Hz, 2 x ArC*H*); **δ_C** (100 MHz, $CDCl_3$) 14.1 (2 x *C*H_3), 23.4 (2 x *C*H_2CH_3), 30.5 (2 x CCH_2CH_2), 33.7 (2 x CCH_2CH_2), 55.7 (2 x O*C*H_3), 109.2 (2 x Ar*C*H), 114.6 (2 x Ar*C*H), 123.2 (2 x Ar*C*H), 131.1 (2 x Ar*C*), 131.1 (2 x Ar*C*), 131.8 (2 x Ar*C*), 136.9 (2 x Ar*C*), 139.9 (2 x Ar*C*), 157.5 (2 x $ArCOCH_3$); **ν_{max}** (neat)/cm^{-1} 663, 794, 894, 1020, 1184, 1213, 1308, 1428, 1470, 1564, 1596, 1874, 2872, 2930, 2959; **HRMS** (APCI): Calcd. for $C_{28}H_{31}S_2O_2$ (M+H), 463.1765; found 463.1751.

6,12-Dibutylbenzo[1,2-*b*:4,5-*b*']bis[*b*]5-chlorobenzothiophene 256



As in general procedure **M**, (*E*)-5-chloro-2-(pent-1-en-1-yl)benzo[*b*]thiophene **233** (33.7 mg, 0.14 mmol) in 1,2-dichloroethane (2 ml) was added to a solution of iodine (359 mg, 1.42 mmol) in 1,2-dichloroethane (12 ml). The reaction mixture was stirred for 18 h at 80 °C before quenching. The crude product was washed with cold ethanol (2 ml) to yield **256** (19.0 mg, 46.0 µmol, 64 % yield) as a white solid: **mp:** 196-198 °C; **δ_H** (500 MHz, $CDCl_3$) 1.11 (6 H, t, *J* = 7.4 Hz, 2 x CH_3), 1.70 (4 H, sxt, *J* = 7.3 Hz, 2 x CH_2), 1.85 - 1.96 (4 H, m, 2 x CH_2), 3.39 - 3.51 (4 H, m, 2 x CCH_2), 7.47 (2 H, dd, *J* = 8.4, 1.9 Hz, 2 x ArC*H*), 7.83 (2 H, d, *J* = 8.3 Hz, 2 x ArC*H*), 8.27 (2 H, d, *J* = 1.8 Hz, 2 x ArC*H*); **δ_C** (100 MHz, $CDCl_3$) 13.9 (2 x *C*H_3), 23.1 (2 x *C*H_2CH_3), 30.1 (2 x CCH_2CH_2), 33.4 (2 x CCH_2CH_2), 123.6 (2 x Ar*C*H), 124.8 (2 x Ar*C*H), 126.4 (2 x Ar*C*H), 130.6 (2 x Ar*C*), 130.6 (2 x Ar*C*), 131.4 (2 x Ar*C*), 137.0 (2 x Ar*C*), 138.1 (2 x Ar*C*), 139.7 (2 x ArCCl); **ν_{max}** (neat)/cm^{-1} 732, 783, 800, 855, 865, 1040, 1102, 1143, 1289, 1320, 1375, 1409, 1431, 1474, 1548, 1583, 1873, 2851, 2870, 2928, 2957; **HRMS** (APCI): Calcd. for $C_{26}H_{25}S_2Cl_2$ (M+H), 471.0775; found 471.0789.

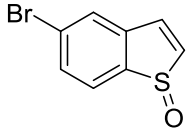
6,12-Dibutylbenzo[1,2-*b*:4,5-*b'*]bis[*b*]6-fluorobenzothiophene 257



As in general procedure **M**, (*E*)-4-fluoro-2-(pent-1-en-1-yl)benzo[*b*]thiophene **226** (32.8 mg, 0.14 mmol) in 1,2-dichloroethane (2 ml) was added to a solution of iodine (374 mg, 1.48 mmol) in 1,2-dichloroethane (12 ml). The reaction mixture was stirred for 18 h at 80 °C before quenching. The crude product was washed with cold ethanol (3 ml) to yield **257** (14.7 mg, 33.0 µmol, 43 % yield) as a white solid; **mp:** 213-215 °C; δ_H (500 MHz, $CDCl_3$) 1.07 (6 H, t, *J* = 7.4 Hz, 2 x CH_3), 1.67 (4 H, sxt, *J* = 7.4 Hz, 2 x CH_2), 1.82 - 1.93 (4 H, m, 2 x CH_2), 3.38 - 3.48 (4 H, m, 2 x CCH_2), 7.23 (2 H, td, *J* = 8.8, 2.4 Hz, 2 x ArC*H*), 7.59 (2 H, dd, *J* = 8.4, 2.4 Hz, 2 x ArC*H*), 8.21 (2 H, dd, *J* = 9.0, 5.0 Hz, 2 x ArC*H*); δ_C (100 MHz, $CDCl_3$) 13.9 (2 x *C*H_3), 23.1 (2 x *C*H_2CH$_3$), 30.2 (2 x CCH_2*C*H_2), 33.3 (2 x C*C*H_2CH$_2$), 109.1 (d, *J* = 22.7 Hz, 2 x Ar*C*H), 112.7 (d, *J* = 22.7 Hz, 2 x Ar*C*H), 125.8 (d, *J* = 9.1 Hz, 2 x Ar*C*H), 130.1 (2 x Ar*C*), 130.4 (2 x Ar*C*), 132.3 (2 x Ar*C*), 138.9 (2 x Ar*C*), 141.4 (d, *J* = 10.0 Hz, 2 x Ar*C*), 161.1 (d, *J* = 248.0 Hz, 2 x Ar*C*F); ν_{max} (neat)/cm^{-1} 720, 735, 767, 800, 842, 900, 925, 1034, 1104, 1195, 1252, 1274, 1315, 1365, 1408, 1457, 1485, 1596, 1597, 2858, 2873, 2934, 2955; **HRMS** (APCI): Calcd. for $C_{26}H_{25}S_2F_2$ (M+H), 439.1366; found 439.1351.

3.2.14 General Procedure N: Oxidation of Benzothiophenes

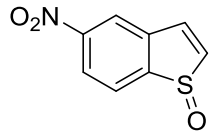
5-Bromobenzo[b]thiophene *S*-oxide 272



To an oven dried vial under nitrogen was added 5-bromobenzo[b]thiophene (213 mg, 1.0 mmol) in Dichloromethane and trifluoroacetic acid (1:1) and H_2O_2 (0.1 ml, 1.0 mmol) was added to the solution at room temperature and the reaction monitored by TLC (5% EtOAc in $CHCl_3$). More H_2O_2 was added until complete consumption of the starting material was observed. The reaction was then quenched with $NaHCO_3$ at 0 °C and the aqueous phase extracted with Dichloromethane. The combined organic layers

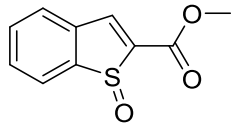
were dried with $MgSO_4$ and concentrated *in vacuo*. The crude mixture was purified by column chromatography (5% EtOAc in $CHCl_3$) to give **272** as a white solid (171 mg, 0.74 mmol, 74%); δ_H (400 MHz, $CDCl_3$) 7.12 - 7.20 (2 H, m, ArC*H*), 7.60 - 7.64 (1 H, m, ArC*H*), 7.67 (1 H, d, *J* = 1.8 Hz, ArC*H*), 7.79 (1 H, d, *J* = 8.0 Hz, ArC*H*); δ_C (101 MHz, $CDCl_3$) 126.6 (Ar*C*Br), 127.4 (Ar*C*H), 128.1 (Ar*C*H), 131.8 (Ar*C*H), 133.6 (Ar*C*H), 138.9 (Ar*C*), 139.4 (Ar*C*H), 144.0 (Ar*C*); ν_{max} (neat)/cm^{-1} 705, 772, 810, 894, 940, 1023, 1095, 1189, 1290, 1313, 1442, 1528, 1573, 3002, 3053, 3074; **HRMS** (APCI): Calcd. for C_8H_6SO $(M+H)^+$, 228.9317; found 228.9317.

5-Nitrobenzo[b]thiophene *S*-oxide



As described in general procedure **N**, 5-nitrobenzo[b]thiophene (179 mg, 1.0 mmol) and H_2O_2 (0.1 ml, 1.0 mmol) in dichloromethane and trifluoroacetic acid (1:1), gave the product (146 mg, 0.73 mmol, 73%) as a yellow solid; δ_H (400 MHz, $CDCl_3$) 7.34 (2 H, s, ArC*H*), 8.09 - 8.15 (1 H, m, ArC*H*), 8.37 (2 H, dq, *J* = 4.4, 2.1 Hz, ArC*H*); δ_C (101 MHz, $CDCl_3$) 120.2 (Ar*C*H), 124.2 (Ar*C*H), 127.4 (Ar*C*H), 133.5 (Ar*C*), 138.8 (Ar*C*), 141.2 (Ar*C*H), 150.8 (Ar*C*), 151.4 (Ar*C*H); ν_{max} (neat)/cm^{-1} 736, 843, 953, 1021, 1045, 1094, 1200, 1290, 1347, 1526, 3060, 3077; **HRMS** (APCI): Calcd. for $C_8H_6SO_3N$ $(M+H)^+$, 196.0063; found 196.0063.

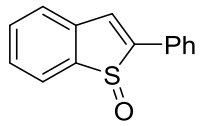
Methyl benzo[*b*]thiophene-2-carboxylate 1-oxide[87]



As described in general procedure **N**, methyl benzo[*b*]thiophene-2-carboxylate (96.1 mg, 0.5 mmol) and H_2O_2 (0.05 ml, 0.5 mmol) in Dichloromethane and trifluoroacetic acid (1:1), gave the product (76.4 mg, 0.36 mmol, 72%) as a yellow solid; δ_H (400 MHz, $CDCl_3$) 3.98 (3 H, s, CH_3), 7.57 - 7.66 (3 H, m, ArC*H*), 7.94 - 7.98 (2 H, m, ArC*H*); δ_C (101 MHz, $CDCl_3$) 53.3 (*C*H_3), 127.2 (Ar*C*H), 127.3 (Ar*C*H), 131.9 (Ar*C*H), 132.7 (Ar*C*H), 135.4 (Ar*C*), 142.8 (Ar*C*H), 143.5 (Ar*C*), 147.0 (Ar*C*), 161.8 (*C*=O); ν_{max} (neat)/cm^{-1}

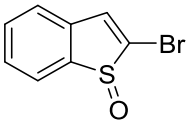
756, 850, 947, 1032, 1068, 1175, 1234, 1341, 1434, 1561, 1714, 2959, 3046; **HRMS** (APCI): Calcd. for $C_{10}H_9SO_3$ $(M+H)^+$, 209.0267; found 209.0260.

2-Phenylbenzo[b]thiophene *S*-oxide



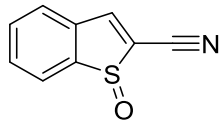
As described in general procedure **N**, 2-phenylbenzo[b]thiophene (186 mg, 1.0 mmol) and H_2O_2 (0.1 ml, 1.0 mmol) in Dichloromethane and trifluoroacetic acid (1:1), gave the product (153 mg, 0.76 mmol, 76%) as a yellow solid; δ_H (400 MHz, $CDCl_3$) 7.28 (1 H, s, ArC*H*), 7.39 - 7.56 (6 H, m, ArC*H*), 7.78 - 7.84 (2 H, m, ArC*H*), 7.94 (1 H, dd, *J* = 7.5, 0.8 Hz, ArC*H*); δ_C (101 MHz, $CDCl_3$) 124.5 (Ar*C*H), 126.4 (Ar*C*H), 126.6 (Ar*C*H), 127.0 (Ar*C*H), 128.4 (Ar*C*H), 129.2 (Ar*C*H), 129.5 (Ar*C*H), 130.8 (Ar*C*), 132.3 (Ar*C*H), 137.7 (Ar*C*), 144.2 (Ar*C*), 152.4 (Ar*C*); ν_{max} (neat)/cm^{-1} 682, 731, 894, 996, 1061, 1447, 1585, 3050; **HRMS** (APCI): Calcd. for $C_{14}H_{11}SO$ $(M)^+$, 227.0525; found 227.0524.

2-Bromobenzo[b]thiophene *S*-oxide



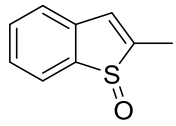
As described in general procedure **N**, 2-bromobenzo[b]thiophene (0.21 g, 1.0 mmol) and H_2O_2 (0.1 ml, 1.0 mmol) in Dichloromethane and trifluoroacetic acid (1:1), gave the product (0.13 g, 0.57 mmol, 57%) as an orange oil; δ_H (400 MHz, $CDCl_3$) 7.23 (1 H, d, *J* = 0.5 Hz, ArC*H*), 7.36 - 7.49 (3 H, m, ArC*H*), 7.82 (1 H, dt, *J* = 7.4, 0.6 Hz, ArC*H*); δ_C (101 MHz, $CDCl_3$) 123.9 (Ar*C*H), 126.3 (Ar*C*H), 128.5 (Ar*C*H), 131.6 (Ar*C*), 132.4 (Ar*C*H), 134.3 (Ar*C*H), 137.3 (Ar*C*), 145.2 (Ar*C*); ν_{max} (neat)/cm^{-1} 700, 772, 819, 888, 942, 1023, 1078, 1190, 1278, 1308, 1441, 1519, 1599, 3017; **HRMS** (EI): Calcd. for C_8H_5SBrO $(M)^+$, 227.9244; found 227.9240.

2-Cyanobenzo[b]thiophene *S*-oxide



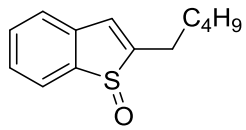
As described in general procedure **N**, 2-cyanobenzo[b]thiophene (159 mg, 1.0 mmol) and H_2O_2 (0.1 ml, 1.0 mmol) in Dichloromethane and trifluoroacetic acid (1:1), gave the product (87.4 mg, 0.5 mmol, 50%) as an orange oil; δ_H (400 MHz, $CDCl_3$) 7.64 - 7.74 (3 H, m, ArC*H*), 7.83 (1 H, d, *J* = 0.5 Hz, ArC*H*), 7.97 (1 H, d, *J* = 7.1 Hz, ArC*H*); δ_C (101 MHz, $CDCl_3$) 112.3 (Ar*C*), 125.0 (*C*N), 126.9 (Ar*C*H), 127.1 (Ar*C*H), 132.2 (Ar*C*H), 133.1 (Ar*C*H), 134.7 (Ar*C*), 145.7 (Ar*C*), 145.9 (Ar*C*H); ν_{max} (neat)/cm^{-1} 773, 919, 1040, 1065, 1078, 1198, 1442, 1548, 2220, 3050, 3058, 3082; **HRMS** (APCI): Calcd. for C_9H_6SON $(M+H)^+$, 176.0165; found 176.0160.

2-Methylbenzo[b]thiophene *S*-oxide



As described in general procedure **N**, 2-methylbenzo[b]thiophene (296 mg, 2.0 mmol) and H_2O_2 (0.2 mg, 2.0 mmol) in Dichloromethane and trifluoroacetic acid (1:1), gave the product (283 mg, 0.17 mmol, 86%) as a yellow solid; δ_H (400 MHz, $CDCl_3$) 2.39 (3 H, d, *J* = 1.5 Hz, CH_3), 6.78 (1 H, s, ArC*H*), 7.33 - 7.40 (2 H, m, ArC*H*), 7.42 - 7.49 (1 H, m, ArC*H*), 7.85 (1 H, d, *J* = 7.5 Hz, ArC*H*); δ_C (101 MHz, $CDCl_3$) 13.0 (CH_3), 123.6 (Ar*C*H), 126.2 (ArC*H*), 127.6 (ArC*H*), 128.6 (ArC*H*), 132.0 (ArC*H*), 138.1 (ArC), 144.5 (ArC), 150.4 (ArC); ν_{max} (neat)/cm^{-1} 762, 901, 1021, 1057, 1447, 1459, 1587, 1711, 2911, 3047; **HRMS** (APCI): Calcd. for C_9H_9SO $(M+H)^+$, 165.0369; found 165.0370.

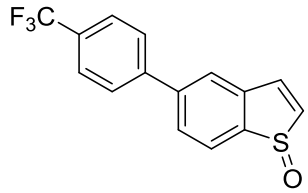
2-Pentylbenzo[b]thiophene *S*-oxide



As described in general procedure **N**, 2-pentylbenzo[b]thiophene (0.37 g, 1.79 mmol) and H_2O_2 (0.18 ml, 1.79 mmol) in Dichloromethane and trifluoroacetic acid (1:1), gave the product (0.30 g, 1.37 mmol, 76%) as an orange oil; δ_H (400 MHz, $CDCl_3$) 0.93 (3

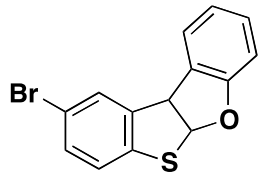
H, t, *J* = 7.1 Hz, C*H*$_3$), 1.34 - 1.47 (4 H, m, 2 × C*H*$_2$), 1.67 - 1.85 (2 H, m, C*H*$_2$), 2.74 (2 H, td, *J* = 7.6, 1.5 Hz, C*H*$_2$), 6.77 (1 H, d, *J* = 0.6 Hz, ArC*H*), 7.34 - 7.41 (2 H, m, ArC*H*), 7.44 - 7.51 (1 H, m, ArC*H*), 7.84 - 7.90 (1 H, m, ArC*H*); **δ_C** (101 MHz, $CDCl_3$) 14.0 (*C*H_3), 22.3 (*C*H_2), 27.3 (*C*H_2), 28.4 (*C*H_2), 31.3 (*C*H_2), 123.7 (Ar*C*H), 126.2 (Ar*C*H), 127.5 (Ar*C*H), 127.6 (Ar*C*H), 132.0 (Ar*C*H), 138.1 (Ar*C*), 144.3 (Ar*C*), 155.5 (Ar*C*); **ν_{max}** (neat)/cm^{-1} 692, 734, 878, 976, 1069, 1444, 1582, 2846, 2968, 3050; **HRMS** (APCI): Calcd. for $C_{13}H_{16}SO$ $(M)^+$, 220.0922; found 220.0920.

5-[4-(Trifluoromethyl)phenyl]benzo[b]thiophene *S*-oxide



As described in general procedure **N**, to 5-(4-(trifluoromethyl)phenyl)benzo[b]thiophene (59.2 mg, 0.21 mmol) and H_2O_2 (0.02 ml, 0.21 mmol) in Dichloromethane and trifluoroacetic acid (1:1), gave the product (50.1 mg, 0.17 mmol, 85%) as a brown solid; **δ_H** (400 MHz, $CDCl_3$) 7.18 (1 H, d, *J* = 6.0 Hz, ArC*H*), 7.30 (1 H, dd, *J* = 6.1, 0.6 Hz, ArC*H*), 7.67 - 7.77 (6 H, m, ArC*H*), 8.03 (1 H, d, *J* = 7.8 Hz, ArC*H*); **δ_C** (101 MHz, $CDCl_3$) 124.0 (q, *J* = 271.9 Hz, *C*F_3), 123.8 (Ar*C*H), 126.0 (q, *J* = 3.6 Hz, Ar*C*H), 126.7 (Ar*C*H), 127.7 (Ar*C*H), 127.9 (Ar*C*H), 130.5 (q, *J* = 32.8 Hz, Ar*C*CF_3), 134.5 (Ar*C*H), 138.0 (Ar*C*), 138.7 (Ar*C*H), 143.0 (Ar*C*), 143.9 (Ar*C*), 144.8 (Ar*C*); **ν_{max}** (neat)/cm^{-1} 770, 841, 942, 1013, 1069, 1108, 1177, 1323, 1596, 1617, 3049; **HRMS** (APCI): Calcd. for $C_{15}H_{10}SOF_3$ $(M+H)^+$, 295.0399; found 295.0389.

9-Bromo-5a,10b-dihydrobenzo[4,5]thieno[2,3-b]benzofuran 273

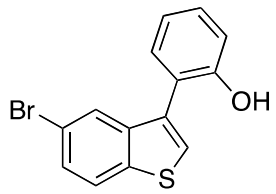


5-Bromo-benzo[b]thiophene *S*-oxide **272** (0.2 mmol) was dissolved in Dichloromethane (1 ml, 0.2 M) in an oven-dried tube flushed with N_2. TFAA (41 µl, 0.3 mmol) was then added at -40 ºC. After 5 min, phenol (29 mg, 0.3 mmol), dissolved in Dichloromethane (1 ml), was added at the same temperature. The mixture was then

allowed to warm to room temperature and stirred overnight. The solution was quenched with H_2O (3 ml) and the aqueous layer was extracted with Dichloromethane (3 x 5 ml). The combined organic layers were dried ($MgSO_4$) and concentrated in vacuo. Purification by column chromatography on silica gel eluting with 5% AcOEt in *n*-hexanes, gave **273** (41 mg, 0.134 mmol, 67%) as white solid; δ_H (400 MHz, $CDCl_3$) 5.23 (1 H, d, *J* = 8.0 Hz, C*H*), 6.88 (2 H, d, *J* = 8.0 Hz, C*H* + ArC*H*), 6.98 (1 H, td, *J* = 7.5, 0.9 Hz, ArC*H*), 7.05 (1 H, d, *J* = 8.5 Hz, ArC*H*), 7.17 - 7.24 (1 H, m, ArC*H*), 7.29 (1 H, ddd, *J* = 8.3, 1.9, 0.8 Hz, ArC*H*), 7.41 (1 H, d, *J* = 7.5 Hz, ArC*H*), 7.51 (1 H, dd, *J* = 1.9, 0.9 Hz, ArC*H*); δ_C (101 MHz, $CDCl_3$) 56.5 (*C*H), 95.2 (*C*H), 110.7 (Ar*C*H), 118.6 (Ar*C*Br), 122.1 (Ar*C*H), 123.5 (Ar*C*H), 124.2 (Ar*C*H), 127.0 (Ar*C*), 127.7 (Ar*C*H), 129.6 (Ar*C*H), 131.7 (Ar*C*H), 138.4 (Ar*C*), 141.8 (Ar*C*), 158.4 (Ar*C*). **HRMS** (ESI): Calcd. for $C_{14}H_9OSBr$ $(M-H)^+$, 303.9550; found 303.9952.

3.2.15 General Procedure O: Arylation of Benzothiophene *S*-Oxides

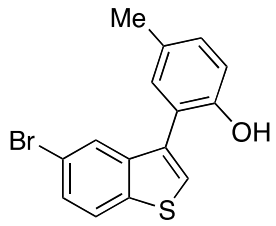
2-(5-Bromobenzo[*b*]thiophen-3-yl)phenol 274



5-bromo-benzo[b]thiophene *S*-oxide (46 mg, 0.2 mmol), was dissolved in Dichloromethane (1 ml, 0.2 M) in an oven-dried tube flushed with N_2. Trifluoroacetic anhydride (41 µl, 0.3 mmol) was then added at −40 ºC. After 5 min, phenol (29 mg, 0.3 mmol) dissolved in Dichloromethane (1 ml) was added and the mixture stirred for 15 min at −40ºC before removing the cooling bath and stirring the mixture at room temperature overnight (16 h). *p*TsOH (69 mg, 0.4 mmol), was then added, and the mixture was heated at 45 ºC for 5 h. The solution was quenched with H_2O (3 ml), and the aqueous layer was extracted with Dichloromethane (3 x 5 ml). The combined organic layers were dried ($MgSO_4$) and concentrated *in vacuo*. The crude product was purified by column chromatography on silica gel eluting with toluene to give **274** as a colourless oil (44 mg, 0.145 mmol, 75 %); δ_H (400 MHz, $CDCl_3$) 5.03 (1 H, s, O*H*), 7.04 - 7.10 (2 H, m, ArC*H*), 7.29 - 7.33 (1 H, m, ArC*H*), 7.35 - 7.40 (1 H, m, ArC*H*), 7.50 - 7.56 (2 H, m, ArC*H*), 7.78 (1 H, d, *J* = 1.5 Hz, ArC*H*), 7.80 (1 H, d, *J* = 8.5 Hz, ArC*H*); δ_C (101 MHz, $CDCl_3$) 116.1 (Ar*C*H), 119.0 (Ar*C*Br), 120.9 (Ar*C*H), 121.0 (Ar*C*), 124.2 (Ar*C*H), 125.9 (Ar*C*H), 127.1 (Ar*C*H), 128.1 (Ar*C*H), 130.0 (Ar*C*H), 130.8 (Ar*C*H), 131.8 (Ar*C*), 139.1 (Ar*C*),

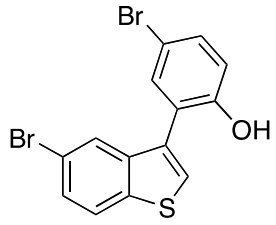
140.0 (Ar*C*), 153.3 (Ar*C*OH); ν_{max} (neat)/cm^{-1} 753, 789, 906, 1064, 1177, 1211, 1420, 1478, 1578, 2849, 2919, 3087, 3520; **HRMS** (ESI): Calcd. for $C_{14}H_8OSBr$ $(M-H)^+$, 302.9484; found 302.9484.

2-(5-Bromobenzo[*b*]thiophen-3-yl)-4-methylphenol 276



As described in general procedure **O**, 5-bromo-benzo[b]thiophene *S*-oxide **272** (46 mg, 0.2 mmol), *p*-cresol (32 mg, 0.3 mmol), trifluoroacetic anhydride (41 µl, 0.3 mmol) and *p*TsOH (69 mg, 0.4 mmol), gave **276** (49 mg, 0.154 mmol, 77%) as a colourless oil; δ_H (500 MHz, $CDCl_3$) 2.35 (3H, s, CH_3) , 4.85 (1 H, s, O*H*), 6.95 (1 H, d, *J* = 8.2 Hz, ArC*H*), 7.09 (1 H, d, *J* = 2.1 Hz, ArC*H*), 7.17 - 7.14 (1 H, m, ArC*H*), 7.51 (2 H, d, *J* = 8.9 Hz, ArC*H*), 7.80 - 7.76 (2 H, m, ArC*H*); δ_C (126 MHz, $CDCl_3$) 20.6 (*C*H_3), 116.0 (Ar*C*H), 119.0 (Ar*C*), 120.9 (Ar*C*), 124.3 (Ar*C*H), 126.0 (Ar*C*H), 127.1 (Ar*C*H), 128.1 (Ar*C*H), 130.2 (Ar*C*), 130.7 (Ar*C*H), 131.3 (Ar*C*H), 132.2 (Ar*C*), 139.2 (Ar*C*), 140.1 (Ar*C*), 151.1 (Ar*C*); ν_{max} (neat)/cm^{-1} 729, 779, 820, 872, 1063, 1181, 1275, 1494, 1579, 2919, 3090, 3520. **HRMS** (ESI): Calcd. for $C_{15}H_{10}OBrS$ $(M-H)^+$, 316.9641; found 316.9633.

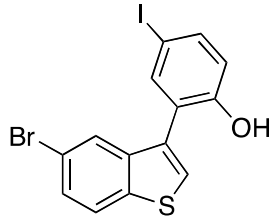
4-Bromo-2-(5-bromobenzo[*b*]thiophen-3-yl)phenol 277



As described in general procedure **O**, 5-bromo-benzo[b]thiophene *S*-oxide **272** (46 mg, 0.2 mmol), 4-bromophenol (52 mg, 0.3 mmol), trifluoroacetic anhydride (41 µl, 0.3 mmol) and *p*TsOH (69 mg, 0.4 mmol), gave **277** (54 mg, 0.14 mmol, 70%) as a white solid; **mp**: 115-116 ^{o}C; δ_H (400 MHz, $CDCl_3$) 6.94 (1 H, d, *J* = 8.6 Hz, ArC*H*), 7.41 (1 H, d, *J* = 2.4 Hz, ArC*H*), 5.02 (1 H, s, O*H*), 7.45 (1 H, dd, *J* = 8.6, 2.5 Hz, ArC*H*), 7.49 - 7.55 (2 H, m, ArC*H*), 7.73 (1 H, d, *J* = 1.8 Hz, ArC*H*), 7.79 (1 H, d, *J* = 8.6 Hz, ArC*H*); δ_C (101 MHz, $CDCl_3$)

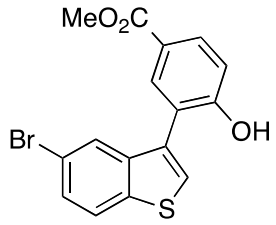
112.9 (Ar*C*), 118.0 (Ar*C*H), 119.3 (Ar*C*), 123.2 (Ar*C*), 124.4 (Ar*C*H), 125.7 (Ar*C*H), 128.0 (Ar*C*H), 128.4 (Ar*C*H), 130.5 (Ar*C*), 132.9 (Ar*C*H), 133.3 (Ar*C*H), 139.2 (Ar*C*), 139.5 (Ar*C*), 152.6 (Ar*C*); ν_{max} (neat)/cm^{-1} 665, 753, 1063, 1209, 1268, 1392, 1426, 1472, 2923, 3089, 3512; **HRMS** (ESI): Calcd. for $C_{14}H_7OBr_2S$ $(M-H)^+$, 380.8579; found 380.8584.

2-(5-Bromobenzo[*b*]thiophen-3-yl)-4-iodophenol 278



As described in general procedure **O**, 5-bromo-benzo[b]thiophene *S*-oxide **272** (46 mg, 0.2 mmol), 4-iodophenol (66 mg, 0.3 mmol), trifluoroacetic anhydride (41 µl, 0.3 mmol) and TFA (61 µl, 0.8 mmol), gave **278** (49 mg, 0.112 mmol, 56%) as a white solid; **mp**: 112-114 ^{o}C; δ_H (500 MHz, $CDCl_3$) 4.97 (s, 1H, O*H*), 6.83 (1 H, d, *J* = 8.6 Hz, ArC*H*), 7.51 - 7.54 (2 H, m, ArC*H*), 7.59 (1 H, d, *J* = 2.2 Hz, ArC*H*), 7.63 (1 H, dd, *J* = 8.6, 2.2 Hz, ArC*H*), 7.72 (1 H, dd, *J* = 1.9, 0.6 Hz, ArC*H*), 7.79 (1 H, dd, *J* = 8.6, 0.6 Hz, ArC*H*); δ_C (126 MHz, $CDCl_3$) 82.7 (Ar*C*), 118.5 (Ar*C*H), 119.3 (Ar*C*), 123.8 (Ar*C*), 124.4 (Ar*C*H), 125.8 (Ar*C*H), 128.0 (Ar*C*H), 128.5 (Ar*C*H), 130.4 (Ar*C*), 138.9 (Ar*C*H), 139.2 (Ar*C*H), 139.6 (Ar*C*), 153.5 (Ar*C*); ν_{max} (neat)/cm^{-1} 753, 791, 1063, 1168, 1209, 1268, 1425, 1471, 1579, 3088, 3509; **HRMS** (ESI): Calcd. for $C_{14}H_7OBrIS$ $(M-H)^+$, 428.8451; found 428.8442.

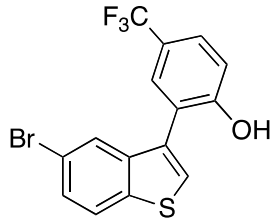
Methyl 3-(5-bromobenzo[*b*]thiophen-3-yl)-4-hydroxybenzoate 279



As described in general procedure **O**, 5-bromo-benzo[b]thiophene *S*-oxide **272** (46 mg, 0.2 mmol), methyl 4-hydroxybenzoate (46 mg, 0.3 mmol), trifluoroacetic anhydride (41 µl, 0.3 mmol) and TFA (61 µl, 0.8 mmol), gave **279** (56 mg, 0.154 mmol, 77%) as a white solid; **mp**: 177-179 ^{o}C; δ_H (500 MHz, $CDCl_3$) 3.89 (3 H, d, *J* = 1.0 Hz, OCH_3), 5.72 (1 H, s, O*H*), 7.09 (1 H, d, *J* = 8.5 Hz, ArC*H*), 7.51 (1 H, dd, *J* = 8.6, 1.7 Hz,

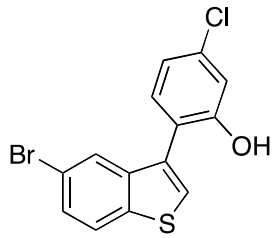
ArC*H*), 7.54 (1 H, s, ArC*H*), 7.70 (1 H, d, *J* = 1.7 Hz, ArC*H*), 7.79 (1 H, d, *J* = 8.6 Hz, ArC*H*), 8.00 (1 H, d, *J* = 2.1 Hz, ArC*H*), 8.04 (1 H, dd, *J* = 8.5, 2.0 Hz, ArC*H*); **δ_C** (126 MHz, $CDCl_3$) 52.2 (O*C*H_3), 116.2 (Ar*C*H), 119.2 (Ar*C*), 121.3 (Ar*C*), 123.0 (Ar*C*), 124.4 (Ar*C*H), 125.8 (Ar*C*H), 128.0 (Ar*C*H), 128.3 (Ar*C*H), 130.9 (Ar*C*), 132.0 (Ar*C*H), 133.0 (Ar*C*H), 139.2 (Ar*C*), 139.8 (Ar*C*), 157.6 (Ar*C*), 166.8 (C=O); **ν_{max}** (neat)/cm^{-1} 769, 831, 1067, 1123, 1277, 1403, 1428, 1597, 1687, 3278; **HRMS** (APCI): Calcd. for $C_{16}H_{12}O_3BrS$ $(M+H)^+$, 362.9685; found 362.9682.

Methyl 3-(5-bromobenzo[*b*]thiophen-3-yl)-4-hydroxybenzoate 280



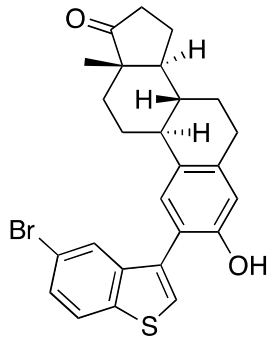
As described in general procedure **O**, 5-bromo-benzo[b]thiophene *S*-oxide **272** (46 mg, 0.2 mmol), 4-(trifluoromethyl)phenol (49 mg, 0.3 mmol), trifluoroacetic anhydride (41 µl, 0.3 mmol) and *p*TsOH (69 mg, 0.4 mmol), gave **280** (60 mg, 0.16 mmol, 80%) as a white solid; **mp**: 113-114 ^oC; **δ_H** (400 MHz, $CDCl_3$) 5.31 (1 H, d, *J* = 3.4 Hz, O*H*), 7.15 (1 H, d, *J* = 8.6 Hz, ArC*H*), 7.54 (1 H, dd, *J* = 8.6, 1.8 Hz, ArC*H*), 7.58 (2 H, d, *J* = 3.4 Hz, ArC*H*), 7.63 (1 H, dd, *J* = 8.6, 2.3 Hz, ArC*H*), 7.69 (1 H, dd, *J* = 1.9, 0.5 Hz, ArC*H*), 7.82 (1 H, d, *J* = 8.5 Hz, ArC*H*); **δ_C** (101 MHz, $CDCl_3$) 116.5 (Ar*C*H), 119.4 (Ar*C*), 121.6 (Ar*C*), 123.5 (q, *J* = 33.0 Hz, Ar*C*), 124.2 (q, *J* = 273 Hz, *C*F_3), 124.5 (Ar*C*H), 125.6 (Ar*C*H), 127.5 (q, *J* = 3.7 Hz, Ar*C*H), 128.3 (q, *J* = 3.7 Hz, Ar*C*H), 128.4 (Ar*C*H), 128.6 (Ar*C*H), 130.4 (Ar*C*), 139.3 (Ar*C*), 139.5 (Ar*C*), 156.1 (Ar*C*); **δ_F** (376 MHz, $CDCl_3$) -61.5; **ν_{max}** (neat)/cm^{-1} 753, 832, 1066, 1108, 1206, 1277, 1316, 1431, 1499, 1587, 1625, 3094, 3446; **HRMS** (ESI): Calcd. for $C_{15}H_7OBrF_3S$ $(M-H)^+$, 370.9359; found 370.9351.

2-(5-Bromobenzo[*b*]thiophen-3-yl)-5-chlorophenol 281



As described in general procedure **O**, 5-bromo-benzo[b]thiophene *S*-oxide **272** (46 mg, 0.2 mmol), 3-chlorophenol (38 mg, 0.3 mmol), trifluoroacetic anhydride (41 µl, 0.3 mmol) and I_2 (102 mg, 0.4 mmol), gave **281** (45 mg, 0.134 mmol, 67%) as a white solid; **mp**: 94-96 ^{o}C; δ_H (500 MHz, $CDCl_3$) 5.13 (1 H, s, O*H*), 7.04 (1 H, dd, *J* = 8.1, 2.1 Hz, ArC*H*), 7.08 (1 H, d, *J* = 2.1 Hz, ArC*H*), 7.22 (1 H, d, *J* = 8.1 Hz, ArC*H*), 7.51 - 7.54 (2 H, m, ArC*H*), 7.73 (1 H, d, *J* = 1.8 Hz, ArC*H*), 7.79 (1 H, d, *J* = 8.7 Hz, ArC*H*); δ_C (126 MHz, $CDCl_3$) 116.6 (Ar*C*H), 119.3 (Ar*C*), 119.7 (Ar*C*), 121.3 (Ar*C*H), 124.4 (Ar*C*H), 125.8 (Ar*C*H), 127.7 (Ar*C*H), 128.4 (Ar*C*H), 130.8 (Ar*C*), 131.7 (Ar*C*H), 135.4 (Ar*C*), 139.3 (Ar*C*), 139.8 (Ar*C*), 154.1 (Ar*C*); ν_{max} (neat)/cm^{-1} 752, 785, 892, 1065, 1173, 1211, 1298, 1477, 1567, 3089, 3513; **HRMS** (ESI): Calcd. for $C_{14}H_7OBrClS$ $(M-H)^+$, 336.9084; found 336.9091.

(8*R*,9*S*,13*S*,14*S*)-2-(5-Bromobenzo[*b*]thiophen-3-yl)-3-hydroxy-13-methyl-7,8,9,11,12,13,15,16-octahydro-6*H*-cyclopenta[*a*]phenanthren-17(14*H*)-one 282

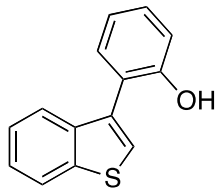


As described in general procedure **O**, 5-bromo-benzo[b]thiophene *S*-oxide **272** (23 mg, 0.1 mmol), estrone (60 mg, 0.125 mmol), trifluoroacetic anhydride (20 µl, 0.15 mmol) and I_2 (51 mg, 0.2 mmol), gave **282** (33 mg, 0.069 mmol, 69%) as a white solid; **mp**: 136-138 ^{o}C; δ_H (400 MHz, $CDCl_3$) 0.93 (3 H, s, CH_3), 1.38 - 1.73 (6 H, m), 1.90 - 1.96 (1 H , m), 2.02 - 2.21 (3 H, m), 2.30 - 2.38 (2 H, m), 2.52 (1 H, dd, *J* = 18.6, 8.7 Hz), 2.96 (2 H, dd, *J* = 9.1, 4.2 Hz), 4.94 (1 H, s, O*H*), 6.80 (1 H, s, ArC*H*), 7.19 (1 H, d, *J* = 1.0 Hz, ArC*H*), 7.47 (1 H, s, ArC*H*), 7.50 (1 H, dd, *J* = 8.6, 1.9 Hz, ArC*H*), 7.80 - 7.76 (2H, m, ArC*H*); δ_C (101

MHz, $CDCl_3$) 14.0 (CH_3), 21.7 (CH_2), 26.1 (CH_2), 26.6 (CH_2), 29.5 (CH_2), 31.6 (CH_2), 36.0 (CH_2), 38.4 (CH), 44.1 (CH), 48.1 (*C*), 50.5 (CH), 116.0 (Ar*C*H), 118.8 (Ar*C*), 119.1 (Ar*C*), 124.3 (Ar*C*H), 126.1 (Ar*C*H), 127.1 (Ar*C*H), 128.0 (Ar*C*H), 128.1 (Ar*C*H), 132.5 (Ar*C*), 138.9 (Ar*C*), 139.2 (Ar*C*), 140.2 (Ar*C*), 151.3 (Ar*C*), 221.2 (Ar*C*); $\boldsymbol{\nu_{max}}$ (neat)/cm^{-1} 749, 871, 1063, 1214, 1404, 1721, 2927, 3346; **HRMS** (ESI): Calcd. for $C_{26}H_{24}O_2BrS$ $(M\text{-}H)^+$, 479.0686; found 579.0675.

3.2.16 General Procedure P: Arylation of Benzothiophenes with *in-situ* Oxidation

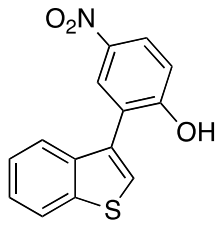
2-(Benzo[*b*]thiophen-3-yl)phenol 283



Benzo[b]thiophene (67 mg, 0.5 mmol) was dissolved in Dichloromethane (2 ml) in an oven-dried tube flushed with N_2 at −20 °C and $BF_3{\cdot}OEt_2$ (8 equiv.) was added. *m*CPBA (1.2 equiv.) in Dichloromethane (1 ml) was then added in portions over 1.5 h at the same temperature. The reaction was monitored by TLC, and after the disappearance of the starting material, saturated Na_2CO_3 (0.2 ml) was added to the mixture, followed by K_2CO_3 (100 mg) at −20 °C. The mixture was then filtered through a plug loaded with $MgSO_4$ and K_2CO_3, washing with Dichloromethane (5 ml). The resulting solution was cooled to −40 °C and trifluoroacetic anhydride (105 µl, 0.75 mmol) was added. After 5 min, phenol (90 mg, 0.75 mmol) dissolved in Dichloromethane (1 ml) was added, and the mixture stirred for 15 min at −40 °C before removing the cooling bath and stirring the mixtures at ambient temperature overnight (16 h). *p*TsOH (172 mg, 1 mmol) was then added, and the mixture was heated at 45 °C for 5h. The solution was quenched with H_2O (8 ml) and the aqueous layer was extracted with Dichloromethane (3 × 5 ml). The combined organic layers were dried ($MgSO_4$) and concentrated *in vacuo*. The crude product was purified by column chromatography on silica gel eluting with toluene giving **283** (58 mg, 0.395 mmol, 79 %) as a white solid; **mp**: 82-83 °C; $\boldsymbol{\delta_H}$ (400 MHz, $CDCl_3$) 5.12 (s, 1H, O*H*), 7.02 - 7.10 (2 H, m, ArC*H*), 7.32 - 7.39 (2 H, m, ArC*H*), 7.46 - 7.39 (2 H, m, ArC*H*), 7.51 (1 H, s, ArC*H*), 7.64 - 7.69 (1 H, m, ArC*H*), 7.93 - 7.98 (1 H, m, ArC*H*); $\boldsymbol{\delta_C}$ (101 MHz, $CDCl_3$) 116.0 (Ar*C*H), 120.8 (Ar*C*H), 121.7 (Ar*C*), 123.0 (Ar*C*H), 123.2 (Ar*C*H), 124.8 (Ar*C*H), 125.1 (Ar*C*H), 125.7 (Ar*C*H), 129.9 (Ar*C*H), 130.9 (Ar*C*H), 132.4 (Ar*C*), 138.2 (Ar*C*),

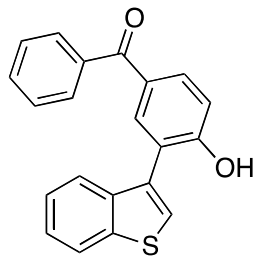
140.7 (Ar*C*), 153.5 (Ar*C*); ν_{max} (neat)/cm^{-1} 729, 752, 839, 1176, 1212, 1345, 1447, 1476, 1576, 3058, 3521; **HRMS** (ESI): Calcd. for $C_{14}H_9OS$ $(M-H)^+$, 225.0369; found 225.0366.

2-(Benzo[*b*]thiophen-3-yl)-4-nitrophenol 284



As described in general procedure **P**, benzo[b]thiophene (67 mg, 0.5 mmol), 4-nitrophenol (104 mg, 0.75 mmol), trifluoroacetic anhydride (105 µl, 0.75 mmol) and *p*TsOH (172 mg, 1 mmol), gave **284** (115 mg, 0.375 mmol, 85 %) as a yellow solid; **mp**: 122-123 ^{o}C; δ_H (500 MHz, $CDCl_3$) 5.84 (1 H, s, O*H*), 7.16 (1 H, d, *J* = 8.9 Hz, ArC*H*), 7.42 - 7.51 (2 H, m, ArC*H*), 7.57 - 7.62 (2 H, m, ArC*H*), 7.95 - 8.01 (1 H, m, ArC*H*), 8.23 - 8.30 (2 H, m, ArC*H*); δ_C (126 MHz, $CDCl_3$) 116.53 (Ar*C*H), 122.43 (Ar*C*), 122.61 (Ar*C*H), 123.33 (Ar*C*H), 125.35 (Ar*C*H), 125.64 (Ar*C*H), 125.94 (Ar*C*H), 127.02 (Ar*C*H), 127.34 (Ar*C*H), 129.61 (Ar*C*), 137.35 (Ar*C*H), 140.84 (Ar*C*), 141.71 (Ar*C*), 159.04 (Ar*C*); ν_{max} (neat)/cm^{-1} 752, 763, 1082, 1274, 1328, 1480, 1534, 1581, 3095, 3336; **HRMS** (ESI): Calcd. for $C_{14}H_8O_3NS$ $(M-H)^+$, 270.0230; found 270.0220.

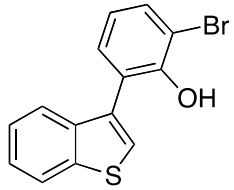
[3-(Benzo[*b*]thiophen-3-yl)-4-hydroxyphenyl](phenyl)methanone 285



As described in general procedure **P**, benzo[b]thiophene (67 mg, 0.5 mmol), 4-hydroxybenzophenone (148 mg, 0.75 mmol), trifluoroacetic anhydride (105 µl, 0.75 mmol) and *p*TsOH (172 mg, 1 mmol), gave **285** (152 mg, 0.46 mmol, 92 %) as a white solid; **mp**: 180-183 ^{o}C; δ_H (400 MHz, $CDCl_3$) 5.68 - 5.75 (1 H, m, O*H*), 7.14 - 7.17 (1 H, m, ArC*H*), 7.42 - 7.44 (2 H, m, ArC*H*), 7.47 (2 H, t, *J* = 7.6 Hz, ArC*H*), 7.56 (2 H, d, *J* = 5.9 Hz, ArC*H*), 7.64 (1 H, dd, *J* = 6.9, 2.1 Hz, ArC*H*), 7.79 - 7.82 (2 H, m, ArC*H*), 7.86 - 7.89 (2 H, m,

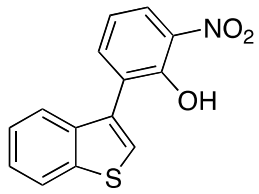
ArC*H*), 7.95 (1 H, dd, *J* = 6.9, 2.0 Hz, ArC*H*); **δ_C** (101 MHz, $CDCl_3$) 115.9 (Ar*C*H), 121.8 (Ar*C*), 123.0 (Ar*C*H), 123.2 (Ar*C*H), 125.0 (Ar*C*H), 125.3 (Ar*C*H), 126.5 (Ar*C*H), 128.4 (Ar*C*H), 129.9 (Ar*C*H), 130.5 (Ar*C*), 131.1 (Ar*C*), 132.2 (Ar*C*H), 132.7 (Ar*C*H), 133.8 (Ar*C*H), 137.8 (Ar*C*), 138.2 (Ar*C*), 140.8 (Ar*C*), 157.5 (Ar*C*), 195.6 (C=O); **ν_{max}** (neat)/cm^{-1} 701, 718, 835, 922, 1112, 1232, 1273, 1428, 1552, 1626, 3068; **HRMS** (APCI): Calcd. for $C_{21}H_{15}O_2S$ $(M+H)^+$, 331.0787; found 331.0785.

2-(Benzo[*b*]thiophen-3-yl)-6-bromophenol 286



As described in general procedure **P**, benzo[b]thiophene (67 mg, 0.5 mmol), 2-bromophenol (130 mg, 0.75 mmol), trifluoroacetic anhydride (105 µl, 0.75 mmol) and *p*TsOH (172 mg, 1 mmol), gave **286** (78 mg, 0.255 mmol, 51 %) as a colourless oil; **δ_H** (400 MHz, $CDCl_3$) 5.66 (s, 1H, O*H*), 6.93 (1 H, t, *J* = 7.7 Hz, ArC*H*), 7.34 (1 H, dd, *J* = 7.7, 1.6 Hz, ArC*H*), 7.34 - 7.46 (2 H, m, ArC*H*), 7.52 (1 H, s, ArC*H*), 7.56 (1 H, dd, *J* = 8.0, 1.6 Hz, ArC*H*), 7.64 - 7.69 (1 H, m, ArC*H*), 7.91 - 7.97 (1 H, m, ArC*H*); **δ_C** (101 MHz, $CDCl_3$) 110.9 (Ar*C*), 121.7 (Ar*C*H), 123.0 (Ar*C*H), 123.3 (Ar*C*H), 123.6 (Ar*C*), 124.6 (Ar*C*H), 124.8 (Ar*C*H), 125.8 (Ar*C*H), 130.8 (Ar*C*H), 132.3 (Ar*C*H), 132.5 (Ar*C*), 138.2 (Ar*C*), 140.3 (Ar*C*), 150.2 (Ar*C*); **ν_{max}** (neat)/cm^{-1} 731, 840, 953, 1112, 1162, 1215, 1234, 1318, 1438, 3055, 3447; **HRMS** (ESI): Calcd. for $C_{14}H_8OBrS$ $(M-H)^+$, 302.9485; found 302.9477.

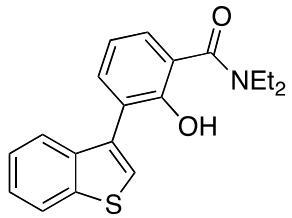
2-(Benzo[*b*]thiophen-3-yl)-6-nitrophenol 287



As described in general procedure **P**, benzo[b]thiophene (67 mg, 0.5 mmol), 2-nitrophenol (104 mg, 0.75 mmol), trifluoroacetic anhydride (105 µl, 0.75 mmol) and *p*TsOH (172 mg, 1 mmol), gave **287** (102 mg, 0.375 mmol, 75 %) as a yellow solid; **mp**: 122-123 ^oC; **δ_H** (400 MHz, $CDCl_3$) 7.11 - 7.44 (1 H, dd, *J* = 8.5, 7.4 Hz, ArC*H*), 7.36 (2 H, m, ArC*H*), 7.57 (1H, s, ArC*H*), 7.62 - 7.65 (1 H, m, ArC*H*), 7.75 (1 H, dd, *J* = 7.4, 1.6 Hz, ArC*H*),

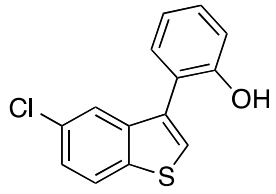
7.91 - 7.97 (1 H, m, ArC*H*), 8.21 (1 H, dd, *J* = 8.5, 1.6 Hz, ArC*H*), 11.07 (1 H, s, O*H*); **δ_C** (101 MHz, $CDCl_3$) 119.9 (Ar*C*H), 123.0 (Ar*C*H), 123.1 (Ar*C*H), 124.5 (Ar*C*H), 124.7 (Ar*C*H), 124.8 (Ar*C*H), 126.5 (Ar*C*H), 127.5 (Ar*C*), 131.2 (Ar*C*), 134.4 (Ar*C*), 138.1 (Ar*C*), 139.1 (Ar*C*H), 140.0 (Ar*C*), 153.4 (Ar*C*); **ν_{max}** (neat)/cm^{-1} 733, 755, 1217, 1276, 1442, 1540, 1603, 3125; **HRMS** (ESI): Calcd. for $C_{14}H_8O_3NS$ $(M-H)^+$, 270.0230; found 270.0221.

3-(Benzo[*b*]thiophen-3-yl)-*N*,*N*-diethyl-2-hydroxybenzamide 288



As described in general procedure **P**, benzo[b]thiophene (67 mg, 0.5 mmol), *N*,*N*-diethyl-2-hydroxybenzamide (145 mg, 0.75 mmol), trifluoroacetic anhydride (105 µl, 0.75 mmol) and *p*TsOH (172 mg, 1 mmol), gave **288** (90 mg, 0.275 mmol, 55 %) as a yellow oil; **δ_H** (400 MHz, $CDCl_3$) 1.31 (6 H, t, *J* = 7.1 Hz, CH_3), 3.57 (4 H, q, *J* = 7.1 Hz, CH_2), 6.98 (1 H, t, *J* = 7.6 Hz, ArC*H*), 7.33 - 7.39 (3H, m, ArC*H*), 7.46 (1 H, dd, *J* = 7.6, 1.6 Hz, ArC*H*), 7.52 (1 H, s, ArC*H*), 7.70 - 7.74 (1 H, m, ArC*H*), 7.89 - 7.94 (1 H, m, ArC*H*), 9.60 (1 H, s, O*H*); **δ_C** (101 MHz, $CDCl_3$) 13.6 (*C*H_3), 42.3 (*C*H_2), 118.6 (Ar*C*H), 119.4 (Ar*C*), 122.8 (Ar*C*H), 123.5 (Ar*C*H), 124.2 (Ar*C*H), 124.4 (Ar*C*), 124.9 (Ar*C*H), 125.4 (Ar*C*H), 127.2 (Ar*C*H), 133.2 (Ar*C*), 133.7 (Ar*C*H), 138.5 (Ar*C*), 140.2 (Ar*C*), 155.9 (Ar*C*), 171.4 (C=O); **ν_{max}** (neat)/cm^{-1} 729, 760, 908, 1117, 1250, 1345, 1431, 1573, 1599, 2973; **HRMS** (ESI+): Calcd. for $C_{19}H_{20}O_2NS$ $(M+H)^+$, 326.1209; found 326.1201.

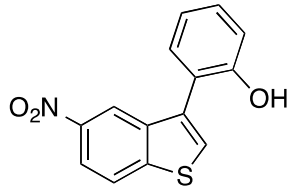
2-(5-Chlorobenzo[b]thiophen-3-yl)phenol 289



As described in general procedure **C**, 5-chloro-benzo[b]thiophene (85 mg, 0.5 mmol), phenol (73 mg, 0.75 mmol), trifluoroacetic anhydride (105 µl, 0.75 mmol) and *p*TsOH (172 mg, 1 mmol), gave **289** (77 mg, 0.3 mmol, 60 %) as a colourless oil; **δ_H** (400 MHz, $CDCl_3$) 5.07 (1 H, s, O*H*), 7.04 - 7.10 (2 H, m, ArC*H*), 7.29 - 7.42 (3 H, m, ArC*H*), 7.56

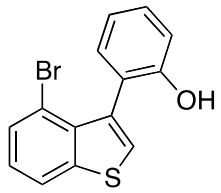
(1 H, s, ArC*H*), 7.63 (1 H, d, *J* = 2.0 Hz, ArC*H*), 7.85 (1 H, d, *J* = 8.5 Hz, ArC*H*); δ_C (101 MHz, $CDCl_3$) 115.7 (Ar*C*H), 120.5 (Ar*C*H), 120.7 (Ar*C*), 122.5 (Ar*C*H), 123.5 (Ar*C*H), 125.1 (Ar*C*H), 126.9 (Ar*C*H), 129.6 (Ar*C*H), 130.5 (Ar*C*H), 130.8 (Ar*C*), 131.5 (Ar*C*Cl), 138.3 (Ar*C*), 139.2 (Ar*C*), 152.9 (Ar*C*OH); $\boldsymbol{\nu_{max}}$ (neat)/cm^{-1} 753, 832,906, 1075, 1172, 1212, 1277, 1423, 1479, 1579, 3087, 3525; **HRMS** (ESI): Calcd. for $C_{14}H_{10}OSCl$ $(M+H)^+$, 261.0135; found 261.0134.

2-(5-Nitrobenzo[*b*]thiophen-3-yl)phenol 290



As described in general procedure **O**, 5-nitro-benzo[b]thiophene *S*-oxide (39 mg, 0.2 mmol), phenol (28 mg, 0.3 mmol), trifluoroacetic anhydride (41 µl, 0.3 mmol) and *p*TsOH (69 mg, 0.4 mmol), gave **290** (50 mg, 0.186 mmol, 93%) as a yellow solid; **mp**: 202-204 °C; $\boldsymbol{\delta_H}$ (500 MHz, $CDCl_3$) 5.00 (s, 1H, O*H*), 7.03 - 7.14 (2 H, m, ArC*H*), 7.31 - 7.42 (2 H, m, ArC*H*), 7.69 (1 H, s, ArC*H*), 8.04 (1 H, d, *J* = 8.8 Hz, ArC*H*), 8.23 - 8.29 (1 H, m, ArC*H*), 8.54 (1 H, d, *J* = 2.3 Hz, ArC*H*); $\boldsymbol{\delta_C}$ (126 MHz, $CDCl_3$) 116.5 (Ar*C*H), 119.3 (Ar*C*H), 119.5 (Ar*C*H), 120.6 (Ar*C*), 121.4 (Ar*C*H), 123.6 (Ar*C*H), 128.6 (Ar*C*H), 130.5 (Ar*C*H), 131.2 (Ar*C*H), 134.3 (Ar*C*), 138.6 (Ar*C*), 145.9 (Ar*C*), 146.3 (Ar*C*), 153.2 (Ar*C*); $\boldsymbol{\nu_{max}}$ (neat)/cm^{-1} 738, 754, 1052, 1097, 1184, 1284, 1325, 1451, 1484, 1529, 3093, 3427; **HRMS** (APCI): Calcd. for $C_{14}H_{10}O_3NS$ $(M+H)^+$, 272.0376; found 272.0373.

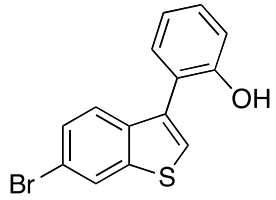
2-(4-Bromobenzo[*b*]thiophen-3-yl)phenol 291



As described in general procedure **P**, 4-bromo-benzo[b]thiophene (106 mg, 0.5 mmol), phenol (71 mg, 0.75 mmol), trifluoroacetic anhydride (105 µl, 0.75 mmol) and I_2 (500 mg, 1 mmol), gave **291** (104 mg, 0.35 mmol, 70 %) as a white solid; **mp**: 120-122 °C; $\boldsymbol{\delta_H}$ (400 MHz, $CDCl_3$) 4.75 (s, 1H, O*H*), 6.95 - 7.01 (2 H, m, ArC*H*), 7.21 - 7.26 (2 H, m, ArC*H*), 7.35 (1 H, td, *J* = 8.0, 1.7 Hz, ArC*H*), 7.51 (1 H, s, ArC*H*), 7.58 (1 H, dd, *J* = 7.6, 1.0

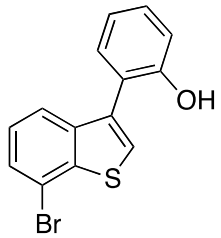
Hz, ArC*H*), 7.90 (1 H, dd, *J* = 8.0, 1.0 Hz, ArC*H*); **δ_C** (101 MHz, $CDCl_3$) 115.2 (Ar*C*H), 117.5 (Ar*C*), 120.2 (Ar*C*H), 122.5 (Ar*C*H), 123.7 (Ar*C*), 125.8 (Ar*C*H), 129.1 (Ar*C*H), 130.1 (Ar*C*H), 130.3 (Ar*C*H), 131.9 (Ar*C*H), 132.8 (Ar*C*), 135.53 (Ar*C*), 142.6 (Ar*C*), 154.5 (Ar*C*); **ν_{max}** (neat)/cm^{-1} 753, 792, 844, 1074, 1100, 1199, 1227, 1322, 1438, 1579, 3260; **HRMS** (ESI): Calcd. for $C_{14}H_8OBrS$ $(M-H)^+$, 302.9485; found 302.9478.

2-(6-Bromobenzo[*b*]thiophen-3-yl)phenol 292



As described in general procedure **P**, 6-bromo-benzo[b]thiophene (106 mg, 0.5 mmol), phenol (71 mg, 0.75 mmol), trifluoroacetic anhydride (105 µl, 0.75 mmol) and *p*TsOH (172 mg, 1 mmol), gave **292** (109 mg, 0.36 mmol, 72 %) as a colourless oil; **δ_H** (400 MHz, $CDCl_3$) 5.04 (1 H, s, O*H*), 7.01 - 7.08 (2 H, m, ArC*H*), 7.30 (1 H, dd, *J* = 7.5, 1.7 Hz, ArC*H*), 7.34 - 7.37 (1 H, m, ArC*H*), 7.46 - 7.51 (3 H, m, ArC*H*), 8.06 - 8.10 (1H, m, ArC*H*); **δ_C** (101 MHz, $CDCl_3$) 116.1 (Ar*C*H), 119.2 (Ar*C*), 120.9 (Ar*C*H), 121.2 (Ar*C*), 124.5 (Ar*C*H), 125.5 (Ar*C*H), 126.0 (Ar*C*H), 128.2 (Ar*C*H), 130.1 (Ar*C*H), 131.0 (Ar*C*H), 132.3 (Ar*C*), 137.1 (Ar*C*), 142.1 (Ar*C*), 153.4 (Ar*C*); **ν_{max}** (neat)/cm^{-1} 746, 887, 1069, 1206, 1286, 1470, 1560, 3080, 3520; **HRMS** (ESI): Calcd. for $C_{14}H_8OBrS$ $(M-H)^+$, 302.9474; found 302.9477.

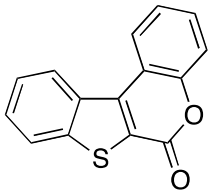
2-(7-Bromobenzo[*b*]thiophen-3-yl)phenol 293



As described in general procedure **P**, 7-bromo-benzo[b]thiophene *S*-oxide (106 mg, 0.5 mmol), phenol (71 mg, 0.75 mmol), trifluoroacetic anhydride (105 µl, 0.75 mmol) and *p*TsOH (172 mg, 1 mmol), gave **293** (84 mg, 0.275 mmol, 55%) as a colourless oil; **δ_H** (500 MHz, $CDCl_3$) 5.04 (1 H, s, O*H*), 7.01 - 7.08 (2 H, m, ArC*H*), 7.26 - 7.33 (2 H, m, ArC*H*), 7.35 - 7.37 (1 H, m, ArC*H*), 7.56 - 7.63 (3 H, m, ArC*H*); **δ_C** (126 MHz, $CDCl_3$) 116.1

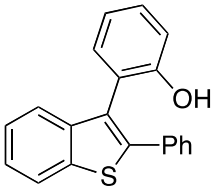
(Ar*C*H), 116.5 (Ar*C*), 120.9 (Ar*C*H), 121.7 (Ar*C*), 122.3 (Ar*C*H), 126.2 (Ar*C*H), 126.6 (Ar*C*H), 127.9 (Ar*C*H), 130.1 (Ar*C*H), 131.0 (Ar*C*H), 133.5 (Ar*C*), 139.4 (Ar*C*), 142.4 (Ar*C*), 153.3 (Ar*C*); ν_{max} (neat)/cm^{-1} 722, 752, 782, 1080, 1176, 1213, 1343, 1383, 1475, 1575, 2923, 3064, 3525; **HRMS** (APCI): Calcd. for $C_{14}H_{10}OBrS$ $(M+H)^+$, 304.9630; found 304.9629.

6H-Benzo[4,5]thieno[2,3-c]chromen-6-one 294[111]



As described in general procedure **O**, methyl benzo[*b*]thiophene-2-carboxylate 1-oxide (24.8 mg, 0.12 mmol), phenol (16.9 mg, 0.18 mmol), trifluoroacetic anhydride (105 µl, 0.75 mmol) and I_2 (61 mg, 0.24 mmol), gave **294** (22.1 mg, 8.2 mmol, 68%) as a white solid; **mp**: 199-200 ^{o}C; δ_H (500 MHz, $CDCl_3$) 7.44-7-47 (1 H, m, ArC*H*), 7.55 (2 H, m, ArC*H*), 8.03 (1 H, m, ArC*H*), 7.64 (2 H, m, ArC*H*), 8.50 (1 H, m, ArC*H*), 8.64 (1 H, m, ArC*H*); δ_C (126 MHz, $CDCl_3$) 118.1 (Ar*C*H), 118.4 (Ar*C*), 123.5 (Ar*C*H), 124.0 (Ar*C*H), 124.8 (Ar*C*H), 125.7 (Ar*C*H), 126.1 (Ar*C*H), 126.2 (Ar*C*), 128.4 (Ar*C*H), 130.0 (Ar*C*H), 135.0 (Ar*C*), 138.6 (Ar*C*), 143.7 (Ar*C*), 152.7 (Ar*C*), 158.0 (*C*=O); ν_{max} (neat)/cm^{-1} 674, 736, 943, 1028, 1161, 1272, 1374, 1441, 1590, 1718, 2923, 3058. **HRMS** (HESI): Calcd. for $C_{15}H_9O_2S$ $(M+H)^+$, 253.0318; found 253.0308.

2-(2-Phenylbenzo[b]thiophen-3-yl)phenol 295

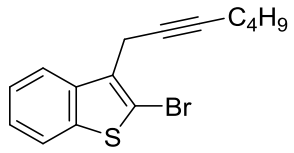


As described in general procedure **O**, 2-phenylbenzo[b]thiophene 1-oxide (25.7 mg, 0.11 mmol), phenol (15.5 mg, 0.17 mmol), trifluoroacetic anhydride (105 µl, 0.75 mmol) and *p*TsOH (38 mg, 0.22 mmol), gave **295** (10.8 mg, 3.6 mmol, 40%) as a colourless oil; δ_H (500 MHz, $CDCl_3$) 4.91 (1 H, s, OH), 6-97-7.03 (2 H, m, ArC*H*), 7.20-7.23 (1 H, m, ArC*H*), 7.28 (3 H, m, ArC*H*), 7.37 (5 H, m, ArC*H*), 7.45 (1 H, d, *J* = 7.8 Hz, ArC*H*), 7.91 (1 H, d, *J* = 7.8 Hz, ArC*H*); δ_C (126 MHz, $CDCl_3$) 115.8 (Ar*C*H), 120.8 (Ar*C*H), 121.3 (Ar*C*), 122.1 (Ar*C*H), 123.2 (Ar*C*H), 124.8 (Ar*C*H), 125.0 (Ar*C*H), 126.9 (Ar*C*), 128.3 (Ar*C*H),

128.5 (Ar*C*H), 128.6 (Ar*C*H), 129.8 (Ar*C*H), 131.3 (Ar*C*H), 133.3 (Ar*C*), 139.0 (Ar*C*), 140.5 (Ar*C*), 141.9 (Ar*C*), 153.4 (Ar*C*); $\boldsymbol{\nu}_{max}$ (neat)/cm^{-1} 3524, 3057, 693, 732, 751, 1068, 1192, 1286, 1331, 1492, 1578, 2924; **HRMS** (HESI): Calcd. for $C_{20}H_{13}OS$ $(M-H)^+$, 301.0682; found 301.0682.

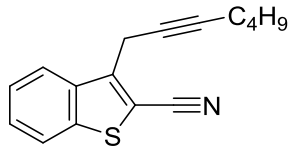
3.2.17 General Procedure Q: Propargylation/Allyation of Benzothiophene *S*-Oxides

2-Bromo-3-(hept-2-yn-1-yl)benzo[b]thiophene 311



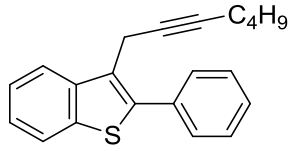
To an oven dried tube under nitrogen was added 2-bromobenzo[b]thiophene *S*-oxide (45 mg, 0.2 mmol), hept-2-yn-1-yltrimethylsilane (50.0 mg, 0.3 mmol) and MeCN (2 ml). The solution was cooled to 0 ^oC, and trifluoroacetic anhydride (56 µl, 0.4 mmol). The cooling bath was then removed and the mixture stirred at room temperature for 3 hours. Saturated $NaHCO_3$ (aq) (3 ml) was added and the aqueous layer was extracted with EtOAc (3 × 5 ml). The combined organic extracts dried with $MgSO_4$. The solvent was removed *in vacuo* before purification by column chromatography eluting with hexane, to give **311** (60 mg, 0.19 mmol, 98%) as a brown oil; $\boldsymbol{\delta_H}$ (400 MHz, $CDCl_3$) 0.89 (3 H, t, *J* = 7.3 Hz, C*H*$_3$), 1.33 - 1.52 (4 H, m, 2 × C*H*$_2$), 2.14 (2 H, tt, *J* = 7.0, 2.4 Hz, C*H*$_2$), 3.74 (2 H, t, *J* = 2.4 Hz, C*H*$_2$), 7.32 - 7.42 (2 H, m, ArC*H*), 7.73 (1 H, ddd, *J* = 7.8, 1.4, 0.7 Hz, ArC*H*), 7.88 - 7.96 (1 H, m, ArC*H*); $\boldsymbol{\delta_C}$ (101 MHz, $CDCl_3$) 13.6 (*C*H$_3$), 18.2 (*C*H$_2$), 18.4 (*C*H$_2$), 21.9 (*C*H$_2$), 30.9 (*C*H$_2$), 75.2 (*C*C), 81.6 (C*C*), 113.3 (Ar*C*Br), 121.7 (Ar*C*H), 122.2 (Ar*C*H), 124.5 (Ar*C*H), 124.6 (Ar*C*H), 131.2 (Ar*C*), 137.8 (Ar*C*), 139.7 (Ar*C*); $\boldsymbol{\nu}_{max}$ (neat)/cm^{-1} 764, 824, 1025, 1067, 1149, 1247, 1263, 1347, 1418, 1498, 1662, 1706, 2858, 2928, 2952; **HRMS** (EI): Calcd. for $C_{15}H_{15}SBr$ $(M)^+$, 306.0072; found 306.0070.

3-(Hept-2-yn-1-yl)benzo[b]thiophene-2-carbonitrile 312



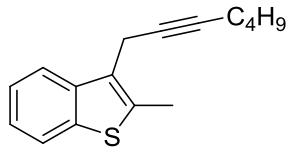
As described in general procedure **Q**, 2-carbonitrile-benzo[b]thiophene *S*-oxide (35 mg, 0.2 mmol), hept-2-yn-1-yltrimethylsilane (50.0 mg, 0.3 mmol) and trifluoroacetic anhydride (56 µl, 0.4 mmol), gave **312** (46 mg, 0.18 mmol, 91 %) as a brown oil; δ_H (400 MHz, $CDCl_3$) 0.89 (3 H, t, *J* = 7.3 Hz, CH_3), 1.34 - 1.49 (4 H, m, 2 x CH_2), 2.16 (2 H, tt, *J* = 7.0, 2.4 Hz, CH_2), 3.93 (2 H, t, *J* = 2.4 Hz, CH_2), 7.44 - 7.62 (2 H, m, ArC*H*), 7.84 (1 H, dt, *J* = 8.3, 0.8 Hz, ArC*H*), 8.09 (1 H, dq, *J* = 7.9, 0.7 Hz, ArC*H*); δ_C (101 MHz, $CDCl_3$) 12.9 (CH_3), 18.4 (*C*H_2), 18.8 (*C*H_2), 21.7 (*C*H_2), 30.6 (*C*H_2), 74.1 (*C*C), 83.4 (C*C*), 106.3 (Ar*C*CN), 113.9 (ArC*C*N), 122.6 (Ar*C*H), 124.2 (Ar*C*H), 125.3 (Ar*C*H), 127.9 (Ar*C*H), 136.5 (Ar*C*), 140.9 (Ar*C*), 143.8 (Ar*C*); ν_{max} (neat)/cm^{-1} 730, 755, 853, 1129, 1157, 1173, 1428, 1688, 2216, 2930, 2956; **HRMS** (EI): Calcd. for $C_{16}H_{16}NS$ $(M+H)^+$, 254.0998; found 254.0993.

3-(Hept-2-yn-1-yl)-2-phenylbenzo[b]thiophene 313



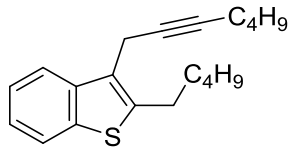
As described in general procedure **Q**, 2-phenylbenzo[b]thiophene *S*-oxide (45 mg, 0.2 mmol), hept-2-yn-1-yltrimethylsilane (50.0 mg, 0.3 mmol) and trifluoroacetic anhydride (56 µl, 0.4 mmol), gave **313** (58 mg, 0.19 mmol, 95 %) as a yellow oil; δ_H (400 MHz, $CDCl_3$) 0.88 - 0.95 (3 H, d, *J* = 7.5 Hz, CH_3), 1.38 - 1.53 (4 H, m, 2 × CH_2), 2.19 (2 H, tt, *J* = 6.9, 2.4 Hz, CH_2), 3.74 (2 H, t, *J* = 2.4 Hz, CH_2), 7.36 - 7.53 (5 H, m, ArC*H*), 7.64 - 7.70 (2 H, m, ArC*H*), 7.86 (1 H, dt, *J* = 7.7, 0.9 Hz, ArC*H*), 7.98 (1 H, dd, *J* = 8.0, 0.5 Hz, ArC*H*); δ_C (101 MHz, $CDCl_3$) 13.6 (*C*H_3), 17.4 (*C*H_2), 18.5 (*C*H_2), 21.9 (*C*H_2), 31.0 (*C*H_2), 77.2 (*C*C), 81.5 (C*C*), 122.1 (Ar*C*H), 122.6 (Ar*C*H), 124.2 (Ar*C*H), 124.4 (Ar*C*H), 127.2 (Ar*C*), 128.1 (Ar*C*H), 128.7 (Ar*C*H), 129.6 (Ar*C*H), 134.1 (Ar*C*), 139.0 (Ar*C*), 139.3 (Ar*C*), 140.1 (Ar*C*); ν_{max} (neat)/cm^{-1} 697, 715, 730, 751, 907, 1028, 1079, 1323, 1434, 1601, 2859, 2869, 2928, 2955; **HRMS** (EI): Calcd. for $C_{21}H_{21}S$ $(M+H)^+$, 305.1357; found 305.1358.

3-(Hept-2-yn-1-yl)-2-methylbenzo[b]thiophene 314



As described in general procedure **Q**, 2-methylbenzo[b]thiophene *S*-oxide (32 mg, 0.2 mmol), hept-2-yn-1-yltrimethylsilane (50.0 mg, 0.3 mmol) and trifluoroacetic anhydride (56 µl, 0.4 mmol), gave **314** (35 mg, 0.14 mmol, 72 %) as a yellow oil; δ_H (400 MHz, $CDCl_3$) 0.89 (3 H, t, *J* = 7.3 Hz, C*H*$_3$), 1.34 - 1.50 (4 H, m, 2 x C*H*$_2$), 2.14 (2 H, tt, *J* = 7.0, 2.4 Hz, C*H*$_2$), 2.56 (3 H, s, ArC*H*$_3$), 3.64 (2 H, t, *J* = 2.4 Hz, C*H*$_2$), 7.25 - 7.31 (1 H, m, ArC*H*), 7.37 (1 H, td, *J* = 7.5, 1.3 Hz, ArC*H*), 7.75 (1 H, d, *J* = 8.0 Hz, ArC*H*), 7.80 (1 H, d, *J* = 7.8 Hz, ArC*H*); δ_C (101 MHz, $CDCl_3$) 13.6 (*C*H$_3$), 13.8 (*C*H$_3$), 16.2 (*C*H$_2$), 18.5 (*C*H$_2$), 22.0 (*C*H$_2$), 31.0 (*C*H$_2$), 76.6 (C*C*), 80.9 (*C*C), 121.6 (ArC*H*), 122.0 (ArC*H*), 123.6 (ArC*H*), 123.9 (ArC*H*), 126.8 (ArC), 135.2 (ArC), 138.1 (ArC), 139.8 (ArC); ν_{max} (neat)/cm^{-1} 728, 907, 1025, 1174, 1324, 1435, 1460, 1669, 1708, 2870, 2929, 2956; **HRMS** (EI): Calcd. for $C_{16}H_{18}S$ $(M)^+$, 242.1124; found 242.1134.

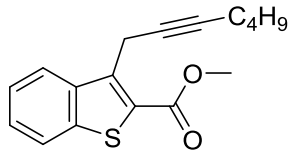
3-(Hept-2-yn-1-yl)-2-pentylbenzo[b]thiophene 315



As described in general procedure **Q**, 2-pentylbenzo[b]thiophene *S*-oxide (42 mg, 0.2 mmol), hept-2-yn-1-yltrimethylsilane (50.0 mg, 0.3 mmol) and trifluoroacetic anhydride (56 µl, 0.4 mmol), gave **315** (39 mg, 0.13 mmol, 65 %) as a yellow oil; δ_H (400 MHz, $CDCl_3$) 0.82 - 0.96 (6 H, m, 2 × C*H*$_3$), 1.30 - 1.47 (8 H, m, 4 × C*H*$_2$), 1.63 - 1.81 (2 H, m, C*H*$_2$), 2.11 (2 H, tt, *J* = 7.0, 2.4 Hz, C*H*$_2$), 2.65 - 2.84 (2 H, m, C*H*$_2$), 3.41 (2 H, q, *J* = 2.3 Hz, C*H*$_2$), 7.41 (1 H, td, *J* = 7.5, 1.2 Hz, ArC*H*), 7.52 (1 H, td, *J* = 7.6, 1.1 Hz, ArC*H*), 7.57 - 7.62 (1 H, m, ArC*H*), 7.88 (1 H, dq, *J* = 7.5, 0.6 Hz, ArC*H*); δ_C (101 MHz, $CDCl_3$) 13.5 (*C*H$_3$), 14.0 (*C*H$_3$), 16.5 (*C*H$_2$), 18.3 (*C*H$_2$), 21.9 (*C*H$_2$), 22.4 (*C*H$_2$), 25.2 (*C*H$_2$), 29.5 (*C*H$_2$), 30.7 (*C*H$_2$), 31.5 (*C*H$_2$), 74.0 (*C*C), 82.6 (C*C*), 122.6 (Ar*C*H), 125.9 (Ar*C*H), 127.7 (Ar*C*H), 131.8 (Ar*C*H), 135.4 (Ar*C*), 138.6 (Ar*C*), 143.6 (Ar*C*), 149.0 (Ar*C*); ν_{max} (neat)/cm^{-1} 757, 934,

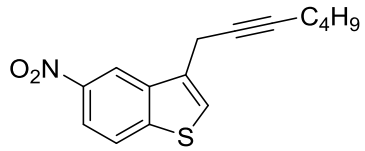
1047, 1097, 1149, 1170, 1214, 1289, 1347, 1456, 1499, 1643, 1787, 2825, 2970, 2979; **HRMS** (EI): Calcd. for $C_{20}H_{26}S$ $(M)^+$, 298.1750; found 298.1748.

Methyl 3-(hept-2-yn-1-yl)benzo[b]thiophene-2-carboxylate 316



As described in general procedure **Q**, 2-methylcarboxylate-benzo[b]thiophene *S*-oxide (41 mg, 0.2 mmol), hept-2-yn-1-yltrimethylsilane (50.0 mg, 0.3 mmol) and trifluoroacetic anhydride (56 µl, 0.4 mmol), gave **316** (42 mg, 0.14 mmol, 72 %) as a yellow oil; δ_H (400 MHz, $CDCl_3$) 0.86 (3 H, t, *J* = 7.3 Hz, C*H*$_3$), 1.29 - 1.48 (4 H, m, 2 × C*H*$_2$), 2.12 (2 H, tt, *J* = 7.0, 2.4 Hz, C*H*$_2$), 3.95 (3 H, s, C*H*$_3$), 4.27 (2 H, t, *J* = 2.5 Hz, C*H*$_2$), 7.43 - 7.52 (2 H, m, ArC*H*), 7.85 (1 H, s, ArC*H*), 8.10 - 8.14 (1 H, m, ArC*H*); δ_C (101 MHz, $CDCl_3$) 13.5 (*C*H$_3$), 16.9 (*C*H$_2$), 18.4 (*C*H$_2$), 21.8 (*C*H$_2$), 30.8 (*C*H$_2$), 52.2 (*C*H$_3$), 76.1 (*C*C), 81.2 (C*C*), 122.5 (Ar*C*H), 124.4 (Ar*C*H), 124.4 (Ar*C*H), 127.0 (Ar*C*), 127.2 (Ar*C*H), 139.1 (Ar*C*), 139.7 (Ar*C*), 140.4 (Ar*C*), 163.4 (ArC*C*O$_2$Me); ν_{max} (neat)/cm^{-1} 732, 756, 1061, 1104, 1199, 1241, 1327, 1435, 1530, 1676, 1711, 2871, 2931, 2955; **HRMS** (EI): Calcd. for $C_{17}H_{19}O_2S$ $(M+H)^+$, 287.1098; found 287.1100.

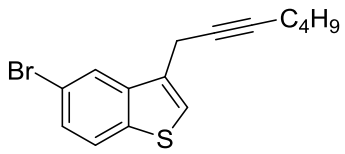
3-(Hept-2-yn-1-yl)-5-nitrobenzo[b]thiophene 317



As described in general procedure, 5-nitrobenzo[b]thiophene *S*-oxide (39 mg, 0.2 mmol), hept-2-yn-1-yltrimethylsilane (50 mg, 0.3 mmol) and trifluoroacetic anhydride (56 µl, 0.4 mmol), gave **317** (42 mg, 0.15 mmol, 76 %) as a yellow oil; δ_H (400 MHz, $CDCl_3$) 0.92 (3 H, t, *J* = 7.3 Hz, C*H*$_3$), 1.40 - 1.56 (4 H, m, 2 × C*H*$_2$), 2.25 (2 H, tt, *J* = 7.0, 2.4 Hz, C*H*$_2$), 3.79 (2 H, td, *J* = 2.4, 1.3 Hz, C*H*$_2$), 7.55 (1 H, t, *J* = 1.0 Hz, ArC*H*), 7.93 - 7.97 (1 H, m, ArC*H*), 8.18 - 8.25 (1 H, m, ArC*H*), 8.67 - 8.74 (1 H, m, ArC*H*); δ_C (101 MHz, $CDCl_3$) 13.6 (*C*H$_3$), 18.4 (*C*H$_2$), 19.2 (*C*H$_2$), 22.0 (*C*H$_2$), 30.9 (*C*H$_2$), 75.3 (*C*C), 83.6 (C*C*), 117.5 (Ar*C*H), 118.7 (Ar*C*H), 123.4 (Ar*C*H), 126.2 (Ar*C*H), 133.4 (Ar*C*), 138.0 (Ar*C*), 145.2

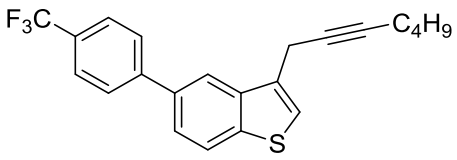
(Ar*C*NO_2), 146.6 (Ar*C*); ν_{max} (neat)/cm^{-1} 729, 819, 907, 1035, 1119, 1247, 1341, 1379, 1510, 1533, 1682, 1708, 2871, 2931, 2957; **HRMS** (EI): Calcd. for $C_{15}H_{16}O_2NS$ $(M+H)^+$, 274.0896; found 274.0887.

5-Bromo-3-(hept-2-yn-1-yl)benzo[b]thiophene 310



As described in general procedure **Q**, 5-bromobenzo[b]thiophene *S*-oxide (46 mg, 0.2 mmol) hept-2-yn-1-yltrimethylsilane (50 mg, 0.3 mmol) and trifluoroacetic anhydride (56 µl, 0.4 mmol), gave **310** (42 mg, 0.13 mmol, 68 %) as a yellow oil; δ_H (400 MHz, $CDCl_3$) 0.94 (3 H, t, *J* = 7.3 Hz, C*H*$_3$), 1.41 - 1.58 (4 H, m, 2 × C*H*$_2$), 2.25 (2 H, tt, *J* = 7.0, 2.3 Hz, C*H*$_2$), 3.68 (2 H, td, *J* = 2.4, 1.3 Hz, C*H*$_2$), 7.38 - 7.41 (1 H, m, ArC*H*), 7.45 (1 H, dt, *J* = 8.5, 1.0 Hz, ArC*H*), 7.71 (1 H, dd, *J* = 8.5, 0.5 Hz, ArC*H*), 7.93 (1 H, d, *J* = 1.8 Hz, ArC*H*); δ_C (101 MHz, $CDCl_3$) 13.6 (*C*H_3), 18.5 (*C*H_2), 19.1 (*C*H_2), 22.0 (*C*H_2), 31.0 (*C*H_2), 75.8 (*C*C), 83.1 (C*C*), 118.1 (Ar*C*Br), 124.2 (Ar*C*H), 124.4 (2 × Ar*C*H), 127.3 (Ar*C*H), 131.5 (Ar*C*), 139.3 (Ar*C*), 139.8 (Ar*C*); ν_{max} (neat)/cm^{-1} 787, 867, 1067, 1247, 1418, 1498, 1662, 1706, 2858, 2928, 2952; **HRMS** (EI): Calcd. for $C_{15}H_{15}SBr$ $(M)^+$, 306.0072; found 306.0065.

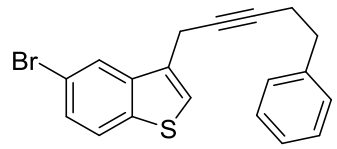
3-(Hept-2-yn-1-yl)-5-(4-(trifluoromethyl)phenyl)benzo[b]thiophene 318



As described in general procedure **Q**, 5-(4-(trifluoromethyl)phenyl)benzo[b]thiophene *S*-oxide (57 mg, 0.2 mmol), hept-2-yn-1-yltrimethylsilane (50.0 mg, 0.3 mmol) and trifluoroacetic anhydride (56 µl, 0.4 mmol), gave **318** (63 mg, 0.17 mmol, 84 %) as a yellow oil; δ_H (400 MHz, $CDCl_3$) 0.91 (3 H, t, *J* = 7.3 Hz, C*H*$_3$), 1.41 - 1.57 (4 H, m, 2 × C*H*$_2$), 2.26 (2 H, tt, *J* = 7.0, 2.3 Hz, C*H*$_2$), 3.76 - 3.82 (2 H, m, C*H*$_2$), 7.45 (1 H, s, ArC*H*), 7.60 (1 H, dd, *J* = 8.4, 1.6 Hz, ArC*H*), 7.71 - 7.80 (4 H, m, ArC*H*), 7.95 (1 H, d, *J* = 8.5 Hz, ArC*H*), 7.98 (1 H, d, *J* = 1.3 Hz, ArC*H*); δ_C (101 MHz, $CDCl_3$) 13.6 (C*H*$_3$), 18.5 (C*H*$_2$), 19.2 (C*H*$_2$), 22.0 (C*H*$_2$), 31.0 (C*H*$_2$), 76.0 (*C*C), 83.0 (C*C*), 120.2

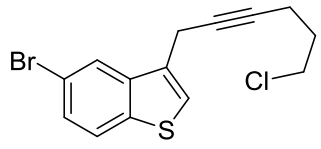
(Ar*C*H), 125.3 (d, *J* = 272.0 Hz, *C*F_3), 123.4 (Ar*C*H), 123.8 (Ar*C*H), 123.8 (Ar*C*H), 127.7 (Ar*C*H), 129.2 (q, *J* = 32.4 Hz, Ar*C*CF_3), 132.3 (Ar*C*), 136.0 (Ar*C*), 138.7 (Ar*C*), 140.6 (Ar*C*), 145.0 (Ar*C*); ν_{max} (neat)/cm^{-1} 731, 808, 907, 1069, 1121, 1272, 1321, 1615, 1709, 2931, 2958; **HRMS** (EI): Calcd. for $C_{22}H_{20}F_3S$ $(M+H)^+$, 373.1232; found 373.1227.

5-Bromo-3-(5-phenylpent-2-yn-1-yl)benzo[b]thiophene 319



As described in general procedure **Q**, 5-bromobenzo[b]thiophene *S*-oxide (46 mg, 0.2 mmol), trimethyl(5-phenylpent-2-yn-1-yl)silane (64 mg, 0.3 mmol) and trifluoroacetic anhydride (56 µl, 0.4 mmol), gave **319** (57 mg, 0.16 mmol, 81 %) as a yellow oil; δ_H (400 MHz, $CDCl_3$) 2.57 (2 H, tt, *J* = 7.4, 2.4 Hz, CH_2), 2.88 (2 H, t, *J* = 7.4 Hz, CH_2), 3.64 (2 H, t, *J* = 2.4 Hz, CH_2), 7.21 - 7.33 (6 H, m, ArC*H*), 7.46 (1 H, dd, *J* = 8.5, 1.8 Hz, ArC*H*), 7.71 (1 H, d, *J* = 8.5 Hz, ArC*H*), 7.88 (1 H, d, *J* = 1.8 Hz, ArC*H*); δ_C (101 MHz, $CDCl_3$) 19.0 (*C*H_2), 20.9 (*C*H_2), 35.2 (*C*H_2), 76.7 (C*C*), 82.3 (*C*C), 118.1 (Ar*C*Br), 124.2 (Ar*C*H), 124.3 (Ar*C*H), 124.6 (Ar*C*H), 126.3 (Ar*C*H), 127.3 (Ar*C*H), 128.4 (2 × Ar*C*H), 128.5 (2 × Ar*C*H), 131.2 (Ar*C*), 139.3 (Ar*C*), 139.7 (Ar*C*), 140.7 (Ar*C*); ν_{max} (neat)/cm^{-1} 731, 860, 907, 1026, 1062, 1149, 1249, 1418, 1494, 1681, 1707, 2922, 3025; **HRMS** (ASAP): Calcd. for $C_{19}H_{16}SBr$ $(M+H)^+$, 355.0151; found 355.0145.

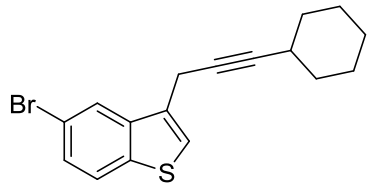
5-Bromo-3-(6-chlorohex-2-yn-1-yl)benzo[b]thiophene 320



As described in general procedure **Q**, 5-bromo-benzo[b]thiophene *S*-oxide (46 mg, 0.2 mmol), (6-chlorohex-2-yn-1-yl)trimethylsilane (56 mg, 0.3 mmol) and trifluoroacetic anhydride (56 µL, 0.4 mmol), gave **320** (55 mg, 0.17 mmol, 84%) as a colourless oil; δ_H (400 MHz, CDCl3) 2.00 (2 H, quin, *J* = 6.6 Hz, CH_2), 2.45 (2 H, tt, *J* = 6.8, 2.4 Hz, CH_2), 3.65 - 3.72 (4 H, m, 2 × CH_2), 7.39 (1 H, s, ArC*H*), 7.46 (1 H, dd, *J* = 8.5, 1.9 Hz, ArC*H*), 7.72 (1 H, d, *J* = 8.5 Hz, ArC*H*), 7.92 (1 H, d, *J* = 1.9 Hz, ArC*H*); δ_C (101 MHz,

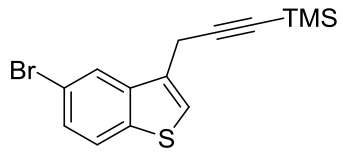
$CDCl_3$) 16.2 (*C*H_2), 19.1 (*C*H_2), 31.5 (*C*H_2), 43.7 (*C*H_2), 77.2 (C*C*CH_2), 81.0 (*C*CCH_2), 118.2 (Ar*C*Br), 124.2 (Ar*C*H), 124.4 (Ar*C*H), 124.5 (Ar*C*H), 127.4 (Ar*C*H), 131.1 (Ar*C*), 139.3 (Ar*C*), 139.7 (Ar*C*); ν_{max} (neat)/cm^{-1} 704, 797, 1037, 1064, 1149, 1207, 1262, 1418, 1498, 1544, 1580, 1678, 1708, 2920, 3093; **HRMS** (APCI): Calcd. for $C_{14}H_{12}BrClS$ (M)+, 325.9532; found 325.9530.

5-Bromo-3-(3-cyclohexylprop-2-yn-1-yl)benzo[b]thiophene 321



As described in general procedure **Q**, 5-bromobenzo[b]thiophene *S*-oxide (46 mg, 0.2 mmol), (3-cyclohexylprop-2-yn-1-yl)trimethylsilane (54 mg, 0.3 mmol) and trifluoroacetic anhydride (56 µl, 0.4 mmol), gave **321** (54 mg, 0.16 mmol, 82 %) as a yellow oil; δ_H (400 MHz, $CDCl_3$) 1.32 - 1.36 (2 H, m, C*H*$_2$), 1.44 - 1.57 (4 H, m, 2 × C*H*$_2$), 1.71 - 1.87 (4 H, m, 2 × C*H*$_2$), 2.44 (1 H, t, *J* = 9.0 Hz, C*H*), 3.70 (2 H, t, *J* = 1.5 Hz, C*H*$_2$), 7.40 (1 H, s, ArC*H*), 7.45 (1 H, dd, *J* = 8.5, 1.8 Hz, ArC*H*), 7.71 (1 H, d, *J* = 8.5 Hz, ArC*H*), 7.94 (1 H, d, *J* = 2.0 Hz, ArC*H*); δ_C (101 MHz, $CDCl_3$) 19.2 (*C*H_2), 24.9 (2 × *C*H_2), 25.9 (2 × *C*H_2), 29.2 (*C*H), 32.9 (*C*H_2), 75.7 (C*C*), 87.5 (*C*C), 118.1 (Ar*C*Br), 124.2 (Ar*C*H), 124.4 (Ar*C*H), 124.5 (Ar*C*H), 127.3 (Ar*C*H), 131.6 (Ar*C*), 139.3 (Ar*C*), 139.8 (Ar*C*); ν_{max} (neat)/cm^{-1} 777, 814, 863, 906, 1026, 1059, 1071, 1149, 1250, 1344, 1421, 1446, 1556, 1580, 2849, 2897, 2930; **HRMS** (EI): Calcd. for $C_{17}H_{17}SBr$ $(M)^+$, 332.0229; found 332.0227.

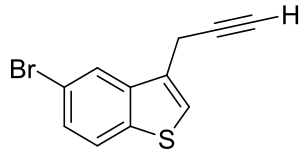
[3-(5-Bromobenzo[b]thiophen-3-yl)prop-1-yn-1-yl]trimethylsilane 322



As described in general procedure **Q**, 5-bromobenzo[b]thiophene *S*-oxide (46 mg, 0.2 mmol), prop-1-yne-1,3-diylbis(trimethylsilane) (55 mg, 0.3 mmol) and trifluoroacetic anhydride (56 µl, 0.4 mmol), gave **322** (59 mg, 0.18 mmol, 91 %) as a yellow oil; δ_H (400 MHz, $CDCl_3$) 0.24 (9 H, s, Si(C*H*$_3$)$_3$), 3.75 (2 H, d, *J* = 1.3 Hz, C*H*$_2$), 7.41

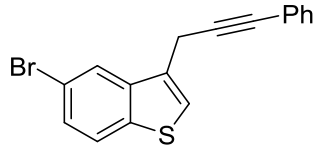
(1 H, s, ArC*H*), 7.46 (1 H, dd, *J* = 8.5, 1.8 Hz, ArC*H*), 7.71 (1 H, d, *J* = 8.5 Hz, ArC*H*), 7.93 (1 H, d, *J* = 1.8 Hz, ArC*H*); **δ_C** (101 MHz, $CDCl_3$) 0.0 (Si(*C*H_3)$_3$), 20.2 (*C*H_2), 87.7 (*C*C Si(*C*H_3)$_3$), 102.3 (C*C* Si(*C*H_3)$_3$), 118.2 (Ar*C*Br), 124.2 (Ar*C*H), 124.4 (Ar*C*H), 124.8 (Ar*C*H), 127.4 (Ar*C*H), 130.1 (Ar*C*), 139.3 (Ar*C*), 139.6 (Ar*C*); **ν_{max}** (neat)/cm^{-1} 730, 777, 815, 999, 1012, 1045, 1149, 1248, 1419, 1581, 2178, 2957; **HRMS** (EI): Calcd. for $C_{14}H_{15}SSiBr$ $(M)^+$, 321.9842; found 321.9842.

5-Bromo-3-(prop-2-yn-1-yl)benzo[b]thiophene 323



As described in general procedure **Q**, 5-bromo-benzo[b]thiophene *S*-oxide (46 mg, 0.2 mmol), propargyl silane (44 µL, 0.3 mmol) and trifluoroacetic anhydride (56 µL, 0.4 mmol), gave **323** (30 mg, 0.11 mmol, 58%) as a white solid; **mp:** 82-84 ^oC; **δ_H** (400 MHz, CDCl3) 2.26 (1 H, t, *J* = 2.8 Hz, CC*H*), 3.72 (2 H, dd, *J* = 2.8, 1.3 Hz, C*H*$_2$), 7.44 - 7.50 (2 H, m, 2 × ArC*H*), 7.72 (1 H, d, *J* = 8.5 Hz, ArC*H*), 7.90 (1 H, d, *J* = 1.8 Hz, ArC*H*); **δ_C** (101 MHz, $CDCl_3$) 18.7 (*C*H_2), 71.0 (C*C*H), 80.1 (*C*CH), 118.3 (Ar*C*Br), 124.2 (ArC*H*), 124.2 (ArC*H*), 124.9 (ArC*H*), 127.5 (ArC*H*), 129.8 (ArC), 139.2 (ArC), 139.5 (ArC); **ν_{max}** (neat)/cm^{-1} 721, 791, 799, 862, 1035, 1061, 1153, 1247, 1307, 1422, 1436, 1580, 1722, 3274; **HRMS** (APCI): Calcd. for $C_{11}H_7BrS$ (M)+, 249.9446; found 249.9446.

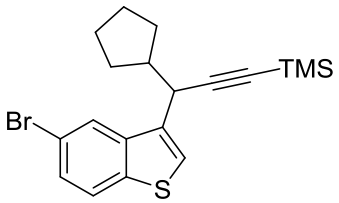
5-Bromo-3-(3-phenylprop-2-yn-1-yl)benzo[b]thiophene 324



As described in general procedure **Q**, 5-bromo-benzo[b]thiophene *S*-oxide (40 mg, 0.17 mmol), trimethyl(3-phenylprop-2-yn-1-yl)silane (49 mg, 0.26 mmol) and trifluoroacetic anhydride (49 µL, 0.34 mmol), gave **324** (33 mg, 0.10 mmol, 59%) as a yellow solid; **mp:** 91-92 ^oC; **δ_H** (400 MHz, CDCl3) 3.95 (2 H, d, *J* = 1.3 Hz, C*H*$_2$), 7.30 - 7.35 (3 H, m, 3 × ArC*H*), 7.45 - 7.52 (4 H, m, 4 × ArC*H*), 7.73 (1 H, d, *J* = 8.5 Hz, ArC*H*), 7.99 (1 H, d, *J* = 1.8 Hz, ArC*H*); **δ_C** (101 MHz, $CDCl_3$) 19.7 (*C*H_2), 83.1 (C*C*Ph), 85.6 (*C*CPh), 118.3

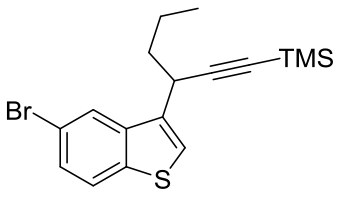
(Ar*C*Br), 123.3 (Ar*C*), 124.3 (Ar*C*H), 124.4 (Ar*C*H), 124.9 (Ar*C*H), 127.5 (Ar*C*H), 128.1 (2 × Ar*C*H), 128.3 (Ar*C*H), 130.5 (Ar*C*), 131.7 (2 × Ar*C*H), 139.3 (Ar*C*), 139.8 (Ar*C*); ν_{max} (neat)/cm^{-1} 721, 813, 871, 910, 968, 1032, 1149, 1245, 1417, 1439, 1555, 1579, 1738, 3055; **HRMS** (APCI): Calcd. for $C_{17}H_{11}BrS$ (M)+, 325.9759; found 325.9759.

[3-(5-Bromobenzo[b]thiophen-3-yl)-3-cyclopentylprop-1-yn-1-yl]trimethylsilane 325



As described in general procedure **Q**, 5-bromobenzo[b]thiophene *S*-oxide (46 mg, 0.2 mmol), (3-cyclopentylprop-1-yne-1,3-diyl)bis(trimethylsilane) (76 mg, 0.3 mmol) and trifluoroacetic anhydride (56 µl, 0.4 mmol), gave **235** (67 mg, 0.17 mmol, 85 %) as a yellow oil; δ_H (400 MHz, $CDCl_3$) 0.21 (9 H, s, Si(CH_3)$_3$), 1.41 - 1.72 (8 H, m, 4 × CH_2), 2.36 - 2.46 (1 H, m, C*H*), 3.94 (1 H, d, *J* = 6.8 Hz, C*H*), 7.36 (1 H, s, ArC*H*), 7.44 (1 H, dd, *J* = 8.5, 1.8 Hz, ArC*H*), 7.71 (1 H, d, *J* = 8.5 Hz, ArC*H*), 8.09 (1 H, d, *J* = 1.8 Hz, ArC*H*); δ_C (101 MHz, $CDCl_3$) 0.1 (Si(*C*H_3)$_3$), 25.3 (*C*H_2), 25.5 (*C*H_2), 29.8 (*C*H_2), 31.3 (*C*H_2), 38.0 (*C*H), 44.1 (*C*H), 87.8 (*C*CSi(CH$_3$)$_3$), 106.2 (C*C*Si(CH$_3$)$_3$), 117.9 (Ar*C*Br), 124.2 (Ar*C*H), 124.6 (Ar*C*H), 125.1 (Ar*C*H), 127.2 (Ar*C*H), 135.3 (Ar*C*), 139.2 (Ar*C*), 139.5 (Ar*C*); ν_{max} (neat)/cm^{-1} 697, 732, 758, 785, 820, 838, 907, 938, 1042, 1066, 1150, 1247, 1415, 1429, 1580, 2170, 2865, 2954; **HRMS** (EI): Calcd. for $C_{19}H_{24}SSiBr$ $(M)^+$, 391.0546; found 391.0544.

[3-(5-Bromobenzo[b]thiophen-3-yl)hex-1-yn-1-yl]trimethylsilane 326

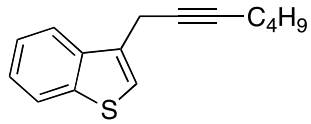


As described in general procedure **Q**, 5-bromobenzo[b]thiophene *S*-oxide (46 mg, 0.2 mmol), hex-1-yne-1,3-diylbis(trimethylsilane) (68 mg, 0.3 mmol) and trifluoroacetic anhydride (56 µl, 0.4 mmol), gave **326** (60 mg, 0.16 mmol, 83 %) as a yellow oil; δ_H (400 MHz, $CDCl_3$) 0.18 - 0.23 (9 H, s, Si(CH_3)$_3$), 0.97 (3 H, t, *J* = 7.4 Hz, CH_3), 1.55 (2 H, m, CH_2), 1.85 (2 H, d, *J* = 8.0 Hz, CH_2), 3.98 (1 H, s, C*H*), 7.36 (1 H, s, ArC*H*), 7.45

(1 H, dd, *J* = 8.7, 1.9 Hz, ArC*H*), 7.71 (1 H, d, *J* = 8.8 Hz, ArC*H*), 8.07 (1 H, d, *J* = 1.8 Hz, ArC*H*); **δ_C** (101 MHz, $CDCl_3$) 0.1 (Si(*C*H_3)$_3$), 13.7 (*C*H_3), 20.5 (*C*H_2), 32.9 (*C*H_2), 37.8 (*C*H), 87.5 (C*C*), 106.9 (*C*C), 118.0 (Ar*C*), 124.2 (Ar*C*H), 124.3 (Ar*C*H), 125.0 (Ar*C*H), 127.2 (Ar*C*H), 135.4 (Ar*C*), 139.1 (Ar*C*), 139.5 (Ar*C*); **ν_{max}** (neat)/cm^{-1} 731, 839, 907, 1068, 1248, 1323, 1431, 1580, 2170, 2932, 2957; **HRMS** (ESI): Calcd. for $C_{17}H_{21}SSi$ $(M)^+$, 364.0311; found 364.0298.

3.2.18 General Procedure R: Propargylation of Benzothiophenes with *in-situ* Oxidation

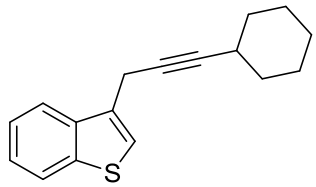
3-(Hept-2-yn-1-yl)benzo[*b*]thiophene 327



To an oven dried vial under nitrogen, was added benzo[b]thiophene (67 mg, 0.5 mmol), Dichloromethane (1 ml) and TFA (1 ml). To this mixture was H_2O_2 (60 µl, 30% aq., 0.5 mmol) at room temperature. The reaction was monitored by TLC (5% EtOAc in $CHCl_3$) and more H_2O_2 was added until complete consumption of the starting material was observed. The reaction was then quenched with $NaHCO_3$ at 0 ^oC and the aqueous layer extracted with Dichloromethane (3 × 1 ml). The combined organic layers were dried with $MgSO_4$ before MeCN was added (10 ml). Dichloromethane was removed under vacuum with no heating to give a solution of benzo[b]thiophene *S*-oxide in MeCN to which was added hept-2-yn-1-yltrimethylsilane (126 mg, 0.75 mmol) and trifluoroacetic anhydride (105 µl, 0.75 mmol) at 0 ^oC. The cooling bath was then removed and the mixture stirred at ambient temperature overnight. Saturated $NaHCO_3$ (aq) (3 ml) was added and the aqueous layer was extracted with EtOAc (3 × 5 ml). The combined organic extracts dried with $MgSO_4$. The solvent was removed *in vacuo* before purification by column chromatography (hexane) to give **327** (68 mg, 0.3 mmol, 60 %) as a colourless oil; **δ_H** (400 MHz, $CDCl_3$) 0.94 (3 H, t, *J* = 7.3 Hz, C*H*$_3$), 1.41 - 1.58 (4 H, m, 2 × C*H*$_2$), 2.25 (2 H, m, C*H*$_2$), 3.73 (2 H,dq, *J* = 2.8, 1.7, 1.3 Hz, C*H*$_2$), 7.34 - 7.42 (3 H, m, ArC*H*), 7.75 - 7.78 (1 H, m, ArC*H*), 7.85 - 7.88 (1 H, m, ArC*H*); **δ_C** (101 MHz, $CDCl_3$) 13.8 (*C*H_3), 18.7 (*C*H_2), 19.3 (*C*H_2), 22.2 (*C*H_2), 31.2 (*C*H_2), 76.4 (C*C*), 83.0 (C*C*), 121.6 (Ar*C*H), 122.8 (Ar*C*H), 123.0 (Ar*C*H), 124.0 (Ar*C*H), 124.4 (Ar*C*H), 132.2 (Ar*C*), 138.2 (Ar*C*), 140.8

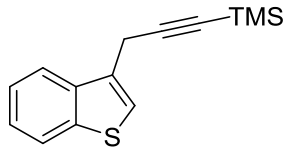
(Ar*C*); ν_{max} (neat)/cm^{-1} 1072, 1252, 1430, 1460, 2870, 2929, 2955; **HRMS** (APCI): Calcd. for $C_{15}H_{17}S$ $(M+H)^+$, 229.1045; found 229.1043.

3-(3-Cyclohexylprop-2-yn-1-yl)benzo[b]thiophene 328



As described in general procedure **R**, benzo[b]thiophene (67 mg, 0.5 mmol) and H_2O_2 (60 µl, 30% aq., 0.5 mmol) in Dichloromethane and TFA (2 ml, 1:1), *then* (3-cyclohexylprop-2-yn-1-yl)trimethylsilane (135 mg, 0.75 mmol) and trifluoroacetic anhydride (0.14 ml, 1.0 mmol), gave **328** (74 mg, 0.30 mmol, 60 %) as a yellow oil; δ_H (400 MHz, $CDCl_3$) 1.25 - 1.58 (6 H, m, 3 × C*H*$_2$), 1.69 - 1.92 (4 H, m, 2 × C*H*$_2$), 2.45 (1 H, t, *J* = 9.0 Hz, C*H*), 3.73 - 3.77 (2 H, m, C*H*$_2$), 7.33 - 7.44 (3 H, m, ArC*H*), 7.77 (1 H, dt, *J* = 7.7, 0.7 Hz, ArC*H*), 7.83 - 7.90 (1 H, m, ArC*H*); δ_C (101 MHz, $CDCl_3$) 19.2 (2 × *C*H$_2$), 24.9 (2 × *C*H$_2$), 25.9 (2 × *C*H$_2$), 29.2 (*C*H), 33.0 (*C*H$_2$), 76.1 (*C*C), 87.2 (C*C*), 121.4 (Ar*C*H), 122.6 (Ar*C*H), 122.9 (Ar*C*H), 123.9 (Ar*C*H), 124.3 (Ar*C*H), 132.1 (Ar*C*), 138.1 (Ar*C*), 140.7 (Ar*C*); ν_{max} (neat)/cm^{-1} 725, 750, 906, 1429, 1447, 1681, 2851, 2926; **HRMS** (EI): Calcd. for $C_{17}H_{19}S$ $(M+H)^+$, 255.1202; found 255.1199.

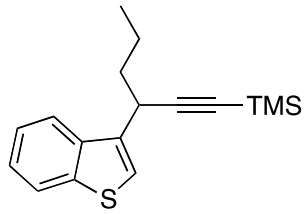
[3-(Benzo[b]thiophen-3-yl)prop-1-yn-1-yl]trimethylsilane 329



As described in general procedure **R** benzo[b]thiophene (67 mg, 0.5 mmol) and H_2O_2 (60 µl, 30% aq., 0.5 mmol) in Dichloromethane and TFA (2 ml, 1:1), *then* prop-1-yne-1,3-diylbis(trimethylsilane) (0.13 g, 0.75 mmol) and trifluoroacetic anhydride (0.14 ml, 1.0 mmol), gave **329** (97 mg, 0.39 mmol, 80 %) as a yellow oil; δ_H (400 MHz, $CDCl_3$) 0.89 (3 H, t, *J* = 7.3 Hz, C*H*$_3$), 1.33 - 1.52 (4 H, m, 2 × C*H*$_2$), 2.14 (2 H, tt, *J* = 7.0, 2.4 Hz, C*H*$_2$), 3.74 (2 H, t, *J* = 2.4 Hz, C*H*$_2$), 7.32 - 7.42 (2 H, m, 2 × ArC*H*), 7.73 (1 H, ddd, *J* = 7.8, 1.4, 0.7 Hz, C*H*$_2$), 7.88 - 7.96 (1 H, m, C*H*$_2$); δ_C (101 MHz, $CDCl_3$) 0.7 (Si(*C*H$_3$)$_3$), 20.2 (*C*H$_2$), 87.3 (*C*CSi(*C*H$_3$)$_3$), 102.9 (C*C*Si(*C*H$_3$)$_3$), 121.3 (ArC*H*), 122.9 (ArC*H*), 123.0 (ArC*H*), 124.0

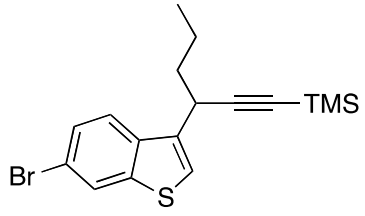
(ArC*H*), 124.4 (ArC*H*), 130.6 (ArC), 137.9 (ArC), 140.6 (ArC); ν_{max} (neat)/cm^{-1} 739, 788, 840, 999, 1021, 1052, 1149, 1237, 1424, 1590, 2163; **HRMS** (EI): Calcd. for $C_{14}H_{15}SSi$ $(M-H)^+$ 244.0746; found 244.0738.

[3-(Benzo[b]thiophen-3-yl)hex-1-yn-1-yl]trimethylsilane 330



As described in general procedure **R**, benzo[b]thiophene (67 mg, 0.5 mmol) and H_2O_2 (60 µl, 30% aq., 0.5 mmol) in Dichloromethane and TFA (2 ml, 1:1), *then* hex-1-yne-1,3-diylbis(trimethylsilane) (167 mg, 0.75 mmol) and trifluoroacetic anhydride (0.14 ml, 1.0 mmol), gave **330** (0.11 g, 0.40 mmol, 80 %) as a colourless oil; δ_H (400 MHz, $CDCl_3$) 0.09 (9 H, s, Si(C*H*$_3$)$_3$), 0.85 (3 H, t, *J* = 7.4 Hz, C*H*$_3$), 1.43 (2 H, m, C*H*$_2$), 1.75 (2 H, m, C*H*$_2$), 3.95 (1 H, ddd, *J* = 8.5, 5.7, 0.7 Hz, C*H*), 7.25 (3 H, m, ArC*H*), 7.74 (2H, ddt, *J* = 8.3, 1.7, 0.8 Hz, ArC*H*); δ_C (126 MHz, $CDCl_3$) 0.31 (Si(*C*H$_3$)$_3$), 13.9 (*C*H$_3$), 20.7 (*C*H$_2$), 33.0 (*C*H), 38.1 (*C*H$_2$), 87.1 (C*C*), 107.7 (C*C*), 122.1 (Ar*C*H), 122.7 (Ar*C*H), 123.1 (Ar*C*H), 123.9 (Ar*C*H), 124.3 (Ar*C*H), 136.2 (Ar*C*), 137.6 (Ar*C*), 141.0 (Ar*C*); ν_{max} (neat)/cm^{-1} 730, 757, 837, 871, 943, 1018, 1072, 1140, 1248, 1458, 2169, 2871, 2956; **HRMS** (APCI): Calc. for $C_{17}H_{23}SSi$ $(M+H^+)$, 287.1284; found 287.1282.

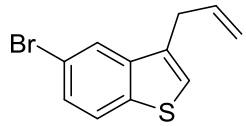
[3-(6-Bromobenzo[*b*]thiophen-3-yl)hex-1-yn-1-yl]trimethylsilane 331



As described in general procedure **R**, 6-bromo-benzo[b]thiophene (106 mg, 0.5 mmol) and H_2O_2 (60 µl, 30% aq., 0.5 mmol) in Dichloromethane and TFA (2 ml, 1:1), *then* hex-1-yne-1,3-diylbis(trimethylsilane (170 mg, 0.75 mmol) and trifluoroacetic anhydride (105 µl, 0.75 mmol), gave **331** (157 mg, 0.3 mmol, 86 %) as a colourless oil; δ_H (400 MHz, $CDCl_3$) 0.18 (9 H, s, Si(C*H*$_3$)$_3$), 0.95 (3 H, t, *J* = 7.4 Hz, C*H*$_3$), 1.49 - 1.56 (2 H, m, C*H*$_2$), 1.80 -

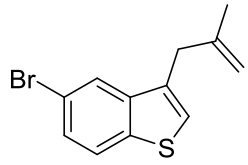
1.86 (2 H, m, CH_2), 3.97 - 4.03 (1 H, m, C*H*), 7.32 (1 H, s, ArC*H*), 7.47 (1 H, dd, *J* = 8.6, 1.7 Hz, ArC*H*), 7.72 (1 H, d, *J* = 8.6 Hz, ArC*H*), 7.89 (1 H, m, *J* = 1.7 Hz, ArC*H*); **δ_C** (101 MHz, $CDCl_3$) 0.3 (Si(*C*H_3)$_3$), 13.9 (*C*H_3), 20.7 (*C*H_2), 33.0 (*C*H), 38.0 (*C*H_2), 87.4 (C*C*), 107.2 (C*C*), 118.3 (Ar*C*), 123.2 (Ar*C*H), 123.3 (Ar*C*H), 125.6 (Ar*C*H), 127.3 (Ar*C*H), 136.0 (Ar*C*), 136.4 (Ar*C*), 142.5 (Ar*C*); **ν_{max}** (neat)/cm^{-1} 758, 808, 838, 942, 1248, 1446, 1584, 2169, 2871, 2956; **HRMS** (ESI): Calcd. for $C_{17}H_{21}SSiBr$ $(M)^+$, 364.0311; found 364.0309.

3-Allyl-5-bromobenzo[b]thiophene 332



As described in general procedure **Q**, 5-bromo-benzo[b]thiophene *S*-oxide (46 mg, 0.2 mmol), trimethyl(2-methylallyl)silane (47 µl, 0.3 mmol) and trifluoroacetic anhydride (56 µl, 0.4 mmol), gave **332** (40 mg, 0.16 mmol, 79%) as a colourless oil; **δ_H** (400 MHz, $CDCl_3$) 3.57 (2 H, dq, *J* = 6.5, 1.3 Hz, CH_2), 5.15 - 5.22 (2 H, m, CH=CH_2), 6.00 - 6.11 (1 H, m, C*H*=CH_2), 7.17 (1 H, s, ArC*H*), 7.45 (1 H, dd, *J* = 8.5, 1.8 Hz, ArC*H*), 7.71 (1 H, d, *J* = 8.5 Hz, ArC*H*), 7.89 (1 H, d, *J* = 2.0 Hz, ArC*H*); **δ_C** (101 MHz, $CDCl_3$) 32.8 (*C*H_2), 117.0 (CH=*C*H_2), 118.1 (Ar*C*Br), 123.9 (Ar*C*H), 124.1 (Ar*C*H), 124.7 (Ar*C*H), 127.2 (Ar*C*H), 134.0 (Ar*C*), 135.0 (*C*H=CH_2), 139.1 (Ar*C*), 140.5 (Ar*C*); **ν_{max}** (neat)/cm^{-1} 730, 77, 815, 992, 1062, 1149, 1247, 1418, 1429, 1579, 1638; **HRMS** (EI): Calcd. for $C_{11}H_9SBr$ $(M)^+$, 251.9603; found 251.9611.

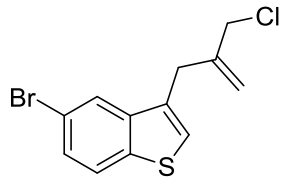
5-Bromo-3-(2-methylallyl)benzo[b]thiophene 333



As described in general procedure **Q**, 5-bromo-benzo[b]thiophene *S*-oxide (46 mg, 0.2 mmol), trimethyl(2-methylallyl)silane (52 µl, 0.3 mmol) and trifluoroacetic anhydride (56 µl, 0.4 mmol), gave **333** (47 mg, 0.17 mmol, 88%) as a colourless oil; **δ_H** (400 MHz, $CDCl_3$) 1.77 (3 H, s, CH_3), 3.53 (2 H, s, CH_2), 4.78 (1 H, s, C=CH_2), 4.91 (1 H, s, C=CH_2), 7.18 (1 H, s, ArC*H*), 7.44 (1 H, dd, *J* = 8.5, 1.8 Hz, ArC*H*), 7.71 (1 H, d, *J* = 8.5 Hz, ArC*H*), 7.89 (1 H, d, *J* = 1.8 Hz, ArC*H*); δ_C (101 MHz, $CDCl_3$) 22.3 (*C*H_3), 37.1 (*C*H_2), 112.7

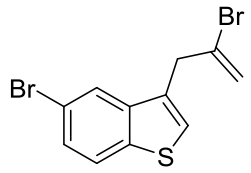
(C=*C*H_2), 118.0 (Ar*C*Br), 124.1 (Ar*C*H), 124.6 (Ar*C*H), 124.9 (Ar*C*H), 127.1 (Ar*C*H), 133.5 (Ar*C*), 139.1 (Ar*C*), 140.8 (Ar*C*), 142.9 (*C*=CH_2); ν_{max} (neat)/cm^{-1} 773, 866, 892, 1062, 1248, 1373, 1417, 1578, 1650, 2903, 2969; **HRMS** (EI): Calcd. for $C_{12}H_{11}SBr$ $(M)^+$, 265.97.59; found 265.9770.

5-Bromo-3-[2-(chloromethyl)allyl]benzo[b]thiophene 334



As described in general procedure **Q**, 5-bromo-benzo[b]thiophene *S*-oxide (46 mg, 0.2 mmol), [2-(chloromethyl)allyl]trimethylsilane (54 µl, 0.3 mmol) and trifluoroacetic anhydride (56 µl, 0.4 mmol), gave **334** (52 mg, 0.17 mmol, 85%) as a colourless oil: δ_H (400 MHz, $CDCl_3$) 3.51 (2 H, s, CH_2Cl), 3.82 (2 H, d, *J* = 0.8 Hz, CH_2), 4.79 (1 H, q, *J* = 1.3 Hz, C=CH_2), 5.05 (1 H, d, *J* = 0.8 Hz, C=CH_2), 7.04 (1 H, s, ArC*H*), 7.23 (1 H, dd, *J* = 8.5, 1.8 Hz, ArC*H*), 7.50 (1 H, d, *J* = 8.5 Hz, ArC*H*), 7.65 (1 H, d, *J* = 2.0 Hz, ArC*H*); δ_C (101 MHz, $CDCl_3$) 32.4 (*C*H_2), 47.7 (*C*H_2Cl), 117.0 (C=*C*H_2), 118.2 (Ar*C*Br), 124.1 (Ar*C*H), 124.8 (Ar*C*H), 125.5 (Ar*C*H), 127.4 (Ar*C*H), 132.0 (Ar*C*), 139.2 (Ar*C*), 140.4 (Ar*C*), 142.5 (*C*=CH_2); ν_{max} (neat)/cm^{-1} 687, 730, 778, 905, 1062, 1149, 1257, 1418, 1579, 1645; **HRMS** (EI): Calcd. for $C_{12}H_{10}SBr$ $(M)^+$, 299.9370; found 299.9374.

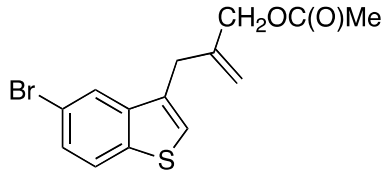
5-Bromo-3-(2-bromoallyl)benzo[b]thiophene 335



As described in general procedure **Q**, 5-bromo-benzo[b]thiophene *S*-oxide (46 mg, 0.2 mmol), trimethyl(2-bromoallyl)silane (57 µL, 0.3 mmol) and trifluoroacetic anhydride (56 µL, 0.4 mmol), gave **335** (53 mg, 0.16 mmol, 80%) as a colourless oil; δ_H (400 MHz, CDCl3) 3.95 (2 H, s, CH_2), 5.57 - 5.61 (2 H, m, C=CH_2), 7.33 (1 H, s, ArC*H*), 7.46 (1 H, dd, *J* = 8.6, 1.9 Hz, ArC*H*), 7.73 (1 H, d, *J* = 8.6 Hz, ArC*H*), 7.86 (1 H, d, *J* = 1.8 Hz, ArC*H*); δ_C (101 MHz, $CDCl_3$) 40.9 (*C*H_2), 118.7 (Ar*C*Br), 119.1 (C=*C*H_2), 124.5 (Ar*C*H), 124.9 (Ar*C*H), 126.6 (Ar*C*H), 127.8 (Ar*C*H), 130.5 (*C*=CH_2), 131.3 (Ar*C*), 139.3 (Ar*C*), 140.4 (Ar*C*);

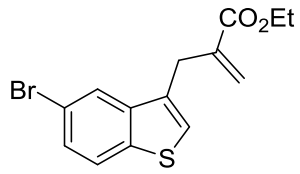
ν_{max} (neat)/cm^{-1} 692, 719, 816, 917, 1032, 1063, 1172, 1212, 1247, 1341, 1413, 1580, 1634, 1837, 2913, 3084; **HRMS** (APCI): Calcd. for $C_{11}H_9Br_2S$ $(M)^+$, 329.8708; found 329.8708.

2-[(5-Bromobenzo[b]thiophen-3-yl)methyl]allyl acetate 336



As described in general procedure **Q**, 5-bromo-benzo[b]thiophene *S*-oxide (46 mg, 0.2 mmol), 2-((trimethylsilyl)methyl)allyl acetate (56 mg, 0.3 mmol) and trifluoroacetic anhydride (56 µL, 0.4 mmol), gave **336** (50 mg, 0.17 mmol, 80%) as a colourless oil; δ_H (400 MHz, CDCl3) 2.10 (3 H, s, CH_3), 3.61 (2 H, s, CH_2), 4.57 (2 H, s, CH_2), 5.00 (1 H, s, C=CH_2), 5.21 (1 H, s, C=CH_2), 7.22 (1 H, s, ArC*H*), 7.45 (1 H, dd, *J* = 8.5, 1.8 Hz, ArC*H*), 7.71 (1 H, d, *J* = 8.5 Hz, ArC*H*), 7.86 (1 H, d, *J* = 1.8 Hz, ArC*H*); δ_C (101 MHz, $CDCl_3$) 20.9 (*C*H$_3$), 32.6 (CH_2), 66.5 (CH_2), 115.5 (C=*C*H$_2$), 118.2 (Ar*C*Br), 124.1 (Ar*C*H), 124.8 (Ar*C*H), 125.2 (Ar*C*H), 127.3 (Ar*C*H), 132.3 (Ar*C*), 139.1 (Ar*C*), 140.5 (Ar*C*), 141.1 (*C*=CH$_2$), 170.6 (*C*=O); ν_{max} (neat)/cm^{-1} 723, 778, 799, 867, 959, 1025, 1040, 1061, 1223, 1371, 1418, 1655, 1734, 2931; **HRMS** (APCI): Calcd. for $C_{14}H_{14}O_2BrS$ $(M+H)^+$, 324.9892; found 324.9891.

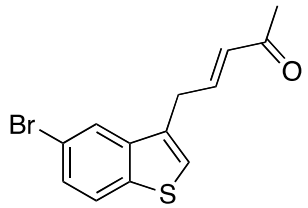
Ethyl 2-((5-bromobenzo[b]thiophen-3-yl)methyl)acrylate 337



As described in general procedure **Q**, 5-bromo-benzo[b]thiophene *S*-oxide (46 mg, 0.2 mmol), ethyl 2-((trimethylsilyl)methyl)acrylate (56 mg, 0.3 mmol) and trifluoroacetic anhydride (56 µL, 0.4 mmol), gave **337** (50 mg, 0.16 mmol, 80%) as a colourless oil; δ_H (400 MHz, CDCl3) 1.30 (3 H, t, *J* = 7.0 Hz, CH_3), 3.83 (2 H, d, *J* = 0.5 Hz, CH_2), 4.24 (2 H, q, *J* = 7.2 Hz, CH_2), 5.44 (1 H, d, *J* = 1.2 Hz, C=CH_2), 6.28 (1 H, d, *J* = 1.2 Hz, C=CH_2), 7.20 (1 H, s, ArC*H*), 7.44 (1 H, dd, *J* = 8.5, 1.8 Hz, ArC*H*), 7.71 (1 H, d, *J* = 8.5 Hz, ArC*H*), 7.84 (1 H, d, *J* = 1.8 Hz, ArC*H*); δ_C (101 MHz, $CDCl_3$) 14.2 (*C*H$_3$), 30.6 (*C*H$_2$), 61.0

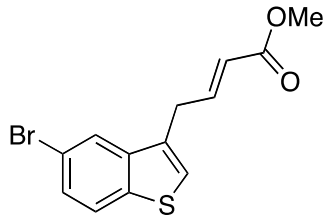
(CH_2), 118.2 (Ar*C*Br), 124.1 (Ar*C*H), 124.7 (Ar*C*H), 125.3 (C=*C*H_2), 126.4 (Ar*C*H), 127.3 (Ar*C*H), 132.7 (*C*=CH_2), 138.2 (Ar*C*), 139.1 (Ar*C*), 140.3 (Ar*C*), 166.7 (*C*=O); ν_{max} (neat)/cm^{-1} 702, 749, 781, 818, 950, 1026, 1092, 1134, 1172, 1199, 1249, 1298, 1418, 1579, 1709, 2978; **HRMS** (APCI): Calcd. for $C_{14}H_{14}O_2BrS$ $(M+H)^+$, 324.9892; found 324.9890.

(*E*)-5-(5-Bromobenzo[*b*]thiophen-3-yl)pent-3-en-2-one 338



As described in general procedure **Q**, 5-bromo-benzo[b]thiophene-*S*-oxide (46 mg, 0.2 mmol), (*E*)-5-(trimethylsilyl)pent-3-en-2-one (47 mg, 0.3 mmol) and trifluoroacetic anhydride (56 µl, 0.4 mmol), gave **338** (34 mg, 0.116 mmol, 58%) as a yellow oil; δ_H (400 MHz, $CDCl_3$) 2.26 (3 H, s, CH_3), 3.72 (2 H, dd, *J* = 6.4, 1.6, Hz, CH_2), 6.11 (1 H, dt, *J* = 15.9, 1.6 Hz, CH=C*H*), 6.97 (1 H, dt, *J* = 15.9, 6.4 Hz, CH=C*H*), 7.21 (1 H, s, ArC*H*), 7.46 (1 H, dd, *J* = 8.5, 1.9 Hz, ArC*H*), 7.72 (1 H, dd, *J* = 8.5, 0.5 Hz, ArC*H*), 7.79 - 7.81 (1 H, m, ArC*H*); δ_C (101 MHz, $CDCl_3$) 27.4 (CH_3), 31.4 (CH_2), 118.5 (Ar*C*), 124.4 (Ar*C*H), 124.5 (Ar*C*H), 125.3 (Ar*C*H), 127.7 (Ar*C*H), 131.6 (Ar*C*), 132.7 (CH=*C*H), 139.2 (Ar*C*), 140.2 (Ar*C*), 143.9 (*C*H=CH), 198.3 (*C*=O); ν_{max} (neat)/cm^{-1} 793, 979, 1066, 1251, 1359, 1418, 1625, 1669, 2919, 3089; **HRMS** (APCI): Calcd. for $C_{13}H_{12}OSBr$ $(M+H)^+$, 294.9787; found 294.9786.

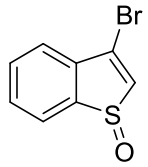
(*E*)-Methyl 4-(5-bromobenzo[*b*]thiophen-3-yl)but-2-enoate 339



As described in general procedure **Q**, 5-bromo-benzo[b]thiophene-*S*-oxide (46 mg, 0.2 mmol), (*E*)-methyl 4-(trimethylsilyl)but-2-enoate (52 mg, 0.3 mmol) and trifluoroacetic anhydride (56 µl, 0.4 mmol), gave **339** (45 mg, 0.146 mmol, 73%) as a yellow oil; δ_H (400 MHz, $CDCl_3$) 3.70 (2 H, dd, *J* = 6.5, 1.7 Hz, CH_2), 3.73 (3 H, s, OCH_3), 5.86 (1 H, dt, *J* = 15.7, 1.7 Hz, CH=C*H*), 7.16 (1 H, dt, *J* = 15.7, 6.5 Hz, C*H*=CH), 7.20 (1 H, s,

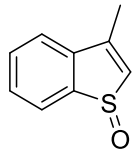
ArC*H*), 7.45 (1 H, dd, *J* = 8.5, 1.8 Hz, ArC*H*), 7.71 (1 H, d, *J* = 8.5 Hz, ArC*H*), 7.80 (1 H, d, *J* = 1.8 Hz, ArC*H*); **δ_C** (101 MHz, $CDCl_3$) 31.2 (CH_2), 51.7 (CH_3), 118.5 (Ar*C*), 123.0 (*C*H=CH), 124.4 (Ar*C*H), 124.5 (Ar*C*H), 125.2 (Ar*C*H), 127.7 (Ar*C*H), 131.7 (Ar*C*), 139.2 (Ar*C*), 140.2 (Ar*C*), 145.3 (CH=*C*H), 166.8 (*C*=O); **ν_{max}** (neat)/cm^{-1} 785, 982, 1067, 1161, 1208, 1271, 1432, 1655, 1715, 2948, 3092; **HRMS** (APCI): Calcd. for $C_{13}H_2OSBr$ $(M+H)^+$, 310.9736; found 310.9734.

3-Bromobenzo[b]thiophene *S*-oxide 349



As described in general procedure **N**, 3-bromobenzo[b]thiophene (213 mg, 1.0 mmol) and H_2O_2 (0.1 ml, 1.0 mmol) in Dichloromethane and trifluoroacetic acid (1:1), gave **349** (171 mg, 0.74 mmol, 74%) as a brown solid; **mp**: 134-136 ^oC; **δ_H** (400 MHz, $CDCl_3$) 7.28 (1 H, s, ArC*H*), 7.55 - 7.59 (1 H, m, ArC*H*), 7.60 - 7.67 (2 H, m, 2 × ArC*H*), 7.92 (1 H, d, *J* = 7.6 Hz, ArC*H*); **δ_C** (101 MHz, $CDCl_3$) 124.5 (Ar*C*H), 125.9 (Ar*C*H), 128.6 (Ar*C*Br), 130.0 (Ar*C*H), 132.4 (Ar*C*H), 135.3 (Ar*C*H), 136.3 (Ar*C*), 144.0 (Ar*C*); **ν_{max}** (neat)/cm^{-1} 680, 699, 754, 915, 1021, 1032, 1052, 1246, 1326, 1520, 1532, 1716, 3082; **HRMS** (ESI): Calcd. for C_8H_6SOBr $(M+H)^+$, 228.9317; found 228.9313.

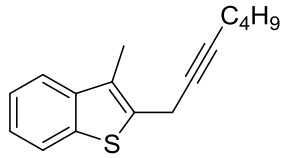
3-Methylbenzo[b]thiophene 1-oxide



As described in general procedure **N**, 3-methylbenzo[b]thiophene (0.52 ml, 4.0 mmol) and H_2O_2 (0.44 ml, 4.0 mmol) in Dichloromethane and trifluoroacetic acid (1:1), gave the product (559 mg, 3.4 mmol, 85%) as a white solid; **mp**: 83-84 ^oC; **δ_H** (400 MHz, $CDCl_3$) 2.29 (3 H, d, *J* = 1.3 Hz, CH_3), 6.78 (1 H, d, *J* = 1.3 Hz, ArC*H*), 7.44 - 7.52 (2 H, m, ArC*H*), 7.54 - 7.59 (1 H, m, ArC*H*), 7.91 (1 H, d, *J* = 7.6 Hz, ArC*H*); **δ_C** (101 MHz, $CDCl_3$) 14.2 (CH_3), 122.5 (Ar*C*H), 126.0 (Ar*C*H), 128.8 (Ar*C*H), 131.8 (Ar*C*H), 132.2 (Ar*C*H), 138.5 (Ar*C*), 145.2 (Ar*C*), 145.9 (Ar*C*); **ν_{max}** (neat)/cm^{-1} 688, 730, 752, 987, 1020, 1051, 1148, 1336, 1382, 1438, 1561, 1602, 3048, 3072; **HRMS** (ESI): Calcd. for $C_{16}H_{18}S$ $(M)^+$, 242.1124; found 242.1121.

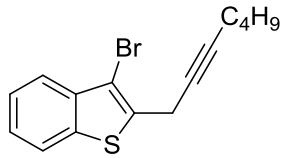
3.2.19 General Procedure S: C2 Propargylation of Benzothiophene *S*-Oxides

2-(Hept-2-yn-1-yl)-3-methylbenzo[b]thiophene 351



To a solution of 3-methylbenzo[b]thiophene *S*-oxide (32.8 mg, 0.2 mmol) and hept-2-yn-1-yltrimethylsilane (50.4 mg, 0.3 mmol) in MeCN (2 ml) at 0 ^{o}C was added trifluoroacetic anhydride (56 µl, 0.4 mmol) and the reaction was heated to 80 ^{o}C for 1 hour. The reaction was cooled to room temperature and a saturated aqueous solution of $NaHCO_3$ was added (2 ml) along with EtOAc (2ml). The organic phase was separated and the aqueous phase washed with EtOAc (3 x 5ml). The combined organic phases were dried ($MgSO_4$), filtered and concentrated *in vacuo* and the resulting crude mixture was purified by flash column chromatography using *n*-hexane to give **351** as a yellow oil (42.1 mg, 0.17 mmol, 87%); $\boldsymbol{\delta_H}$ (400 MHz, $CDCl_3$) 0.91 - 0.97 (3 H, m, C*H*$_3$), 1.40 - 1.58 (4 H, m, 2 × C*H*$_2$), 2.23 (2 H, tt, *J* = 7.0, 2.4 Hz, C*H*$_2$), 2.34 (3 H, s, C*H*$_3$), 3.77 (2 H, t, *J* = 2.1 Hz, C*H*$_2$), 7.28 - 7.40 (2 H, m, 2 × ArC*H*), 7.63 (1 H, dd, *J* = 7.3, 0.6 Hz, ArC*H*), 7.76 - 7.83 (1 H, d, *J* = 7.8 Hz, ArC*H*); $\boldsymbol{\delta_C}$ (101 MHz, $CDCl_3$) 11.4 (*C*H$_3$), 13.6 (*C*H$_3$), 18.4 (*C*H$_2$), 18.7 (*C*H$_2$), 21.9 (*C*H$_2$), 30.9 (*C*H$_2$), 76.5 (*C*C), 82.5 (C*C*), 121.3 (ArC*H*), 122.2 (ArC*H*), 123.7 (ArC*H*), 123.8 (ArC*H*), 127.1 (ArC), 134.9 (ArC), 138.2 (ArC), 140.8 (ArC); $\boldsymbol{\nu_{max}}$ (neat)/cm^{-1} 668, 727, 1016, 1214, 1378, 1460, 1584, 1662, 1711, 2870, 2930, 2956; **HRMS** (ESI): Calcd. for $C_{16}H_{18}S$ $(M)^+$, 242.1124; found 242.1121.

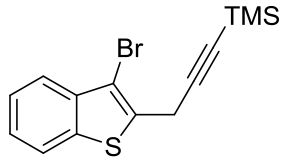
3-Bromo-2-(hept-2-yn-1-yl)benzo[b]thiophene 350



As described in general procedure **S**, 3-bromobenzo[b]thiophene *S*-oxide (45.8 mg, 0.2 mmol), hept-2-yn-1-yltrimethylsilane (50.0 mg, 0.3 mmol) and trifluoroacetic anhydride (56 µl, 0.4 mmol) in MeCN (2 ml) after purification by flash column chromatography using *n*-hexane gave **350** as a yellow oil (57.9 mg, 0.19 mmol, 94%); $\boldsymbol{\delta_H}$ (400 MHz, $CDCl_3$) 0.89 (3 H, t, *J* = 7.3 Hz, C*H*$_3$), 1.34 - 1.49 (4 H, m, 2 × C*H*$_2$), 2.14 (2 H, tt, *J* = 7.0, 2.4 Hz, C*H*$_2$), 3.74 (2 H, t, *J* = 2.4 Hz, C*H*$_2$), 7.37 (2 H, m, 2 × ArC*H*), 7.70 - 7.74 (1 H,

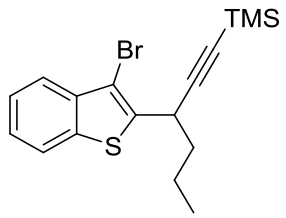
m, ArC*H*), 7.93 (1 H, dt, *J* = 7.9, 0.7 Hz, ArC*H*); **δ_C** (101 MHz, $CDCl_3$) 13.6 (*C*H_3), 18.2 (*C*H_2), 18.4 (*C*H_2), 21.9 (*C*H_2), 30.9 (*C*H_2), 75.2 (*C*C), 81.6 (C*C*), 113.3 (Ar*C*Br), 121.7 (Ar*C*H), 122.2 (Ar*C*H), 124.5 (Ar*C*H), 124.6 (Ar*C*H), 131.2 (Ar*C*), 137.8 (Ar*C*), 139.7 (Ar*C*); **ν_{max}** (neat)/cm^{-1} 728, 751, 923, 1043, 1199, 1258, 1429, 1458, 1676, 1708, 2869, 2928, 2955; **HRMS** (ESI): Calcd. for $C_{15}H_{15}SBr$ $(M)^+$, 306.0078; found 306.0077.

(3-(3-Bromobenzo[b]thiophen-2-yl)prop-1-yn-1-yl)trimethylsilane 352



As described in general procedure **S**, 3-bromobenzo[b]thiophene *S*-oxide (45.8 mg, 0.2 mmol), prop-1-yne-1,3-diylbis(trimethylsilane) (55.2 mg, 0.3 mmol) and trifluoroacetic anhydride (56 µl, 0.4 mmol) in MeCN (2 ml) after purification by flash column chromatography using *n*-hexane gave **352** as a yellow oil (53.6 mg, 0.17 mmol, 83%); **δ_H** (400 MHz, $CDCl_3$) 0.11 - 0.17 (9 H, s, Si(CH_3)$_3$), 3.81 (2 H, s, CH_2), 7.37 (2 H, m, 2 × ArC*H*), 7.73 (1 H, dd, *J* = 7.2, 1.1 Hz, ArC*H*), 7.95 (1 H, dd, *J* = 7.4, 1.4 Hz, ArC*H*); **δ_C** (101 MHz, $CDCl_3$) -0.1 (Si(*C*H_3)$_3$), 19.4 (*C*H_2), 86.1 (*C*C Si(CH$_3$)$_3$), 101.6 (C*C* Si(CH$_3$)$_3$), 113.7 (Ar*C*Br), 121.7 (Ar*C*H), 122.3 (Ar*C*H), 124.5 (Ar*C*H), 124.7 (Ar*C*H), 130.0 (Ar*C*), 137.7 (Ar*C*), 139.7 (Ar*C*); **ν_{max}** (neat)/cm^{-1} 690, 728, 834, 923, 941, 1020, 1095, 1136, 1245, 1412, 1429, 1459, 2172, 2952; **HRMS** (ESI): Calcd. for $C_{14}H_{15}SSiBr$ $(M)^+$, 321.9842; found 321.9842.

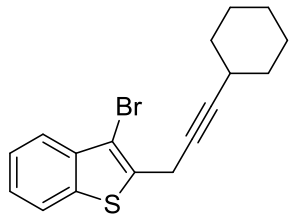
(3-(3-Bromobenzo[b]thiophen-2-yl)hex-1-yn-1-yl)trimethylsilane 353



As described in general procedure **S**, 3-bromobenzo[b]thiophene *S*-oxide (45.8 mg, 0.2 mmol), hex-1-yne-1,3-diylbis(trimethylsilane) (67.0 mg, 0.3 mmol) and trifluoroacetic anhydride (56 µl, 0.4 mmol) in MeCN (2 ml) after purification by flash column chromatography using *n*-hexane gave **353** as a yellow oil (48.2 mg, 0.13 mmol, 65%); **δ_H** (400 MHz, $CDCl_3$) 0.17 (9 H, s, Si(CH_3)$_3$), 0.95 (3 H, t, *J* = 7.4 Hz, CH_3), 1.35 - 1.45 (1 H, m, from CH_2), 1.51 - 1.61 (1 H, m, from CH_2), 1.76 - 1.87 (1 H, m, from CH_2), 1.97 -

2.07 (1 H, m, from CH_2), 4.22 (1 H, s, C*H*), 7.30 - 7.38 (2 H, m, 2 × ArC*H*), 7.70 - 7.74 (1 H, m, ArC*H*), 8.23 - 8.27 (1 H, m, ArC*H*); **δ_C** (101 MHz, $CDCl_3$) 0.0 (Si(*C*H_3)$_3$), 13.7 (*C*H_3), 20.7 (*C*H_2), 32.8 (*C*H_2), 37.7 (C*H*), 87.3 (*C*C Si$(CH_3)_3$), 106.2 (C*C* Si$(CH_3)_3$), 113.0 (Ar*C*Br), 121.7 (Ar*C*H), 123.1 (Ar*C*H), 123.9 (Ar*C*H), 124.4 (Ar*C*H), 134.0 (Ar*C*), 136.8 (Ar*C*), 140.0 (Ar*C*); **ν_{max}** (neat)/cm^{-1} 697, 758, 790, 838, 975, 1122, 1247, 1335, 1426, 1457, 2171, 2871, 2957; **HRMS** (ESI): Calcd. for $C_{17}H_{21}SSiBr$ $(M)^+$, 364.0311; found 364.0305.

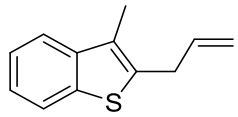
3-Bromo-2-(3-cyclohexylprop-2-yn-1-yl)benzo[b]thiophene 354



As described in general procedure **S**, 3-bromobenzo[b]thiophene *S*-oxide (45.8 mg, 0.2 mmol), (3-cyclohexylprop-2-yn-1-yl)trimethylsilane (58.0 mg, 0.3 mmol) and trifluoroacetic anhydride (56 µl, 0.4 mmol) in MeCN (2 ml) after purification by flash column chromatography using *n*-hexane gave **354** as a yellow oil (39.4 mg, 0.12 mmol, 59%); **δ_H** (400 MHz, $CDCl_3$) 1.19 - 1.79 (10 H, m, 5 × CH_2), 2.27 - 2.36 (1 H, m, C*H*), 3.72 - 3.76 (2 H, m, CH_2), 7.31 - 7.41 (2 H, m, 2 × ArC*H*), 7.70 - 7.74 (1 H, m, ArC*H*), 7.93 - 7.97 (1 H, m, ArC*H*); **δ_C** (101 MHz, $CDCl_3$) 18.3 (*C*H_2), 24.9 (2 × *C*H_2), 25.9 (2 × *C*H_2), 29.1 (*C*H), 32.8 (*C*H_2), 75.2 (*C*C), 85.9 (C*C*), 113.2 (Ar*C*Br), 121.7 (Ar*C*H), 122.3 (Ar*C*H), 124.4 (Ar*C*H), 124.6 (Ar*C*H), 131.3 (Ar*C*), 137.9 (Ar*C*), 139.7 (Ar*C*); **ν_{max}** (neat)/cm^{-1} 70, 777, 798, 863, 906, 994, 1025, 1060, 1071, 1149, 1259, 1257, 1300, 1421, 1445, 1556, 1705, 2849, 2930; **HRMS** (ESI): Calcd. for $C_{17}H_{17}SBr$ $(M)^+$, 332.0234; found 332.0230.

3.2.20 General Procedure T: C2 Allylations of Benzothiophene *S*-Oxides

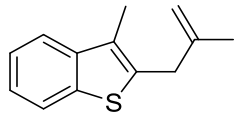
2-Allyl-3-methylbenzo[b]thiophene 355



To an oven dried tube under nitrogen atmosphere was added 3-methylbenzo[b]thiophene *S*- oxide (32.8 mg, 0.2 mmol) and allyltrimethylsilane (47.0 µl, 0.3 mmol) in MeCN (2 ml). This mixture was cooled to 0 ^oC, trifluoroacetic anhydride (57 µl, 0.4 mmol) added and the reaction heated to 80 ^oC for 3 hours. After this period the

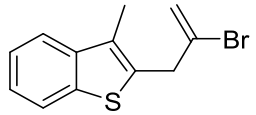
reaction was cooled and a solution of saturated aqueous $NaHCO_3$ (2 ml) added along with EtOAc (2 ml). The organic phase was separated and the aqueous phase washed with EtOAc (3 x 5 ml). The combined organic phases were dried ($MgSO_4$), filtered and concentrated *in vacuo* and the resulting crude mixture was purified by flash column chromatography using *n*-hexane to give **355** as a yellow oil (30.3 mg, 0.16 mmol, 80%); $\boldsymbol{\delta_H}$ (400 MHz, $CDCl_3$) 2.34 (3 H, s, C*H*$_3$), 3.63 (2 H, d, *J* = 6.3 Hz, C*H*$_2$), 5.10 - 5.21 (2 H, m, CH=C*H*$_2$), 6.01 (1 H, ddt, *J* = 16.8, 10.2, 6.3, 6.3 Hz, C*H*=CH$_2$), 7.27 - 7.33 (1 H, m, ArC*H*), 7.37 (1 H, t, *J* = 8.0 Hz, ArC*H*), 7.65 (1 H, d, *J* = 7.8 Hz, ArC*H*), 7.79 (1 H, d, *J* = 8.0 Hz, ArC*H*); $\boldsymbol{\delta_C}$ (101 MHz, $CDCl_3$) 11.1 (*C*H$_3$), 32.3 (*C*H$_2$), 116.0 (CH=*C*H$_2$), 121.0 (Ar*C*H), 121.8 (Ar*C*H), 123.3 (Ar*C*H), 123.5 (Ar*C*H), 127.0 (Ar*C*), 135.2 (*C*H=CH$_2$), 136.1 (Ar*C*), 138.1 (Ar*C*), 140.6 (Ar*C*); $\boldsymbol{\nu_{max}}$ (neat)/cm^{-1} 727, 914, 987, 1054, 1153, 1434, 1460, 1639, 1661, 1722, 2913, 3060; **HRMS** (ESI): Calcd. for $C_{12}H_{13}S$ $(M+H)^+$, 189.0732; found 189.0728.

3-Methyl-2-(2-methylallyl)benzo[b]thiophene 356



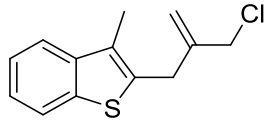
As described in general procedure **T**, 3-methylbenzo[b]thiophene *S*- oxide (32.8 mg, 0.2 mmol), trimethyl(2-methylallyl)silane (52 µl, 0.3 mmol) and trifluoroacetic anhydride (56 µl, 0.4 mmol) in MeCN (2 ml) after purification by flash column chromatography using *n*-hexane gave **356** as a yellow oil (23.2 mg, 0.11 mmol, 57%); $\boldsymbol{\delta_H}$ (400 MHz, $CDCl_3$) 1.79 (3 H, s, C*H*$_3$), 2.34 (3 H, s, C*H*$_3$), 3.57 (2 H, s, C*H*$_2$), 4.82 (1 H, s, C=C*H*$_2$), 4.87 (1 H, s, C=C*H*$_2$), 7.30 (1 H, t, *J* = 8.5 Hz, ArC*H*), 7.34 - 7.40 (1 H, m, ArC*H*), 7.65 (1 H, d, *J* = 7.8 Hz, ArC*H*), 7.78 (1 H, d, *J* = 8.0 Hz, ArC*H*); $\boldsymbol{\delta_C}$ (101 MHz, $CDCl_3$) 11.5 (*C*H$_3$), 22.1 (*C*H$_3$), 36.9 (*C*H$_2$), 112.2 (C=*C*H$_2$), 121.3 (Ar*C*H), 122.1 (Ar*C*H), 123.6 (Ar*C*H), 123.7 (Ar*C*H), 127.9 (Ar*C*), 136.5 (Ar*C*), 138.5 (Ar*C*), 140.9 (Ar*C*), 143.5 (*C*=CH$_2$); $\boldsymbol{\nu_{max}}$ (neat)/cm^{-1} 710, 752, 891, 1018, 1152, 1272, 1373, 1435, 1460, 1651, 1727, 2913, 2971, 3071; **HRMS** (ESI): Calcd. for $C_{13}H_{15}S$ $(M+H)^+$, 203.0889; found 203.0885.

2-(2-Bromoallyl)-3-methylbenzo[b]thiophene 357



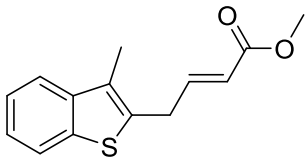
As described in general procedure **T**, 3-methylbenzo[b]thiophene *S*- oxide (32.8 mg, 0.2 mmol), trimethyl(2-bromoallyl)silane (54.0 µl, 0.3 mmol) and trifluoroacetic anhydride (56 µl, 0.4 mmol) in MeCN (2 ml) after purification by flash column chromatography using *n*-hexane gave **357** as a yellow oil (45.5 mg, 0.17 mmol, 85%); δ_H (400 MHz, $CDCl_3$) 2.36 (3 H, s, CH_3), 3.99 (2 H, s, CH_2), 5.56 (1 H, s, C=CH_2), 5.63 (1 H, d, *J* = 1.5, Hz, C=CH_2), 7.30 - 7.42 (2 H, m, 2 x ArC*H*), 7.68 (1 H, d, *J* = 8.0 Hz, ArC*H*), 7.80 (1 H, d, *J* = 7.8 Hz, ArC*H*); δ_C (101 MHz, $CDCl_3$) 11.6 (*C*H_3), 40.3 (*C*H_2), 118.1 (CH=*C*H_2), 121.7 (Ar*C*H), 122.3 (Ar*C*H), 124.0 (Ar*C*H), 124.2 (Ar*C*H), 129.5 (*C*H=CH_2), 130.6 (Ar*C*), 133.5 (Ar*C*), 138.7 (Ar*C*), 140.5 (Ar*C*); ν_{max} (neat)/cm^{-1} 705 726, 905, 1105, 1224, 1435, 1460, 1626, 2915, 3060; **HRMS** (ESI): Calcd. for $C_{12}H_{12}SBr$ $(M)^+$, 266.9835; found 266.9838

2-(2-(Chloromethyl)allyl)-3-methylbenzo[b]thiophene 358



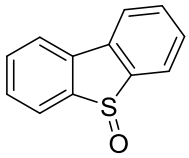
As described in general procedure **T**, 3-methylbenzo[b]thiophene *S*- oxide (32.8 mg, 0.2 mmol), (2-(chloromethyl)allyl)trimethylsilane (54 µl, 0.3 mmol) and trifluoroacetic anhydride (56 µl, 0.4 mmol) in MeCN (2 ml) after purification by flash column chromatography using *n*-hexane gave **358** as a yellow oil (37.1 mg, 0.16 mmol, 79%); δ_H (400 MHz, $CDCl_3$) 2.37 (3 H, s, CH_3), 3.78 (2 H, s, CH_2), 4.06 (2 H, s, CH_2), 5.08 (1 H, s, 1 x C=CH_2), 5.26 (1 H, s, 1 x C=CH_2), 7.32 (1 H, dd, *J* = 8.0, 7.0 Hz, ArC*H*), 7.39 (1 H, dd, *J* = 7.8, 7.0 Hz, ArC*H*), 7.66 (1 H, d, *J* = 8.0 Hz, ArC*H*), 7.78 (1 H, d, *J* = 7.8 Hz, ArC*H*); δ_C (101 MHz, $CDCl_3$) 11.5 (*C*H_3), 32.2 (*C*H_2), 47.4 (*C*H_2), 116.6 (C=*C*H_2), 121.5 (Ar*C*H), 122.2 (Ar*C*H), 123.9 (Ar*C*H), 123.9 (Ar*C*H), 128.8 (Ar*C*), 134.8 (Ar*C*), 138.6 (Ar*C*), 140.8 (Ar*C*), 143.2 (*C*=CH_2); ν_{max} (neat)/cm^{-1} 751, 835, 915, 1017, 1152, 1256, 1435, 1459, 1645, 2914, 3059; **HRMS** (ESI): Calcd. for $C_{13}H_{13}SCl$ $(M)^+$, 236.0421; found 236.0420.

Methyl-(E)-4-(3-methylbenzo[b]thiophen-2-yl)but-2-enoate 359



As described in general procedure **T**, 3-methylbenzo[b]thiophene *S*- oxide (32.8 mg, 0.2 mmol), methyl (*E*)-4-(trimethylsilyl)but-2-enoate (51.3 mg, 0.3 mmol) and trifluoroacetic anhydride (56 µl, 0.4 mmol) in MeCN (2 ml) after purification by flash column chromatography using *n*-hexane gave **359** as a yellow oil (11.3 mg, 0.009 mmol, 23%); $\boldsymbol{\delta_H}$ (400 MHz, $CDCl_3$) 2.32 (3 H, s, CH_3), 3.73 (3 H, s, OCH_3), 3.75 (2 H, dd, *J* = 6.2, 1.6 Hz, CH_2), 5.85 (1 H, dt, *J* = 15.6, 1.7 Hz, CH=C*H*CO_2Me), 7.10 (1 H, dt, *J* = 15.6, 6.2 Hz, C*H*=CHCO_2Me), 7.29 - 7.34 (1 H, m, ArC*H*), 7.38 (1 H, td, *J* = 7.5, 1.1 Hz, ArC*H*), 7.65 (1 H, d, *J* = 7.8 Hz, ArC*H*), 7.78 (1 H, d, *J* = 7.8 Hz, ArC*H*); $\boldsymbol{\delta_C}$ (101 MHz, $CDCl_3$) 11.5 (*C*H_3), 30.9 (*C*H_3), 51.5 (*C*H_2), 121.5 (Ar*C*H), 122.2 (CH=*C*HC(O)$_2$$CH_3$), 122.3 (Ar*C*H), 124.0 (Ar*C*H), 124.1 (Ar*C*H), 128.5 (Ar*C*), 133.4 (Ar*C*), 138.6 (Ar*C*), 140.6 (Ar*C*), 145.4 (*C*H=CHC(O)$_2$$CH_3$), 166.5 (*C*$O_2$$CH_3$); $\boldsymbol{\nu_{max}}$ (neat)/cm^{-1} 728, 971, 1020, 1079, 1162, 1219, 1271, 1331, 1435, 1460, 1654, 1720, 2339, 2362, 2949; **HRMS** (ESI): Calcd. for $C_{14}H_{15}O_2S$ $(M)^+$, 247.0785; found 247.0787.

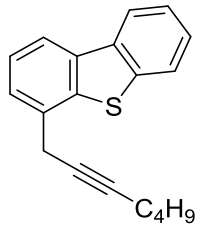
Dibenzo[b,d]thiophene *S*-oxide 360



To dibenzothiophene (0.92 g, 5.0 mmol) in dichloromethane (10 ml) was added *m*CPBA (1.11 g, 5.0 mmol) and the reaction was allowed to stir at room temperature for 2 hour before cooling to 0 ^oC. A saturated aqueous solution of $NaHCO_3$ (10 ml) was then added and the mixture was allowed to warm to room temperature. The organic phase was separated and the aqueous layer was washed with dichloromethane (3 x 10 ml) before the combined organic layers were dried filtered and concentrated *in vacuo*. The crude mixture was purified by flash column chromatography to give **360** as a white solid (0.66 g, 3.32 mmol 66%); **m.p**: 191-193 ^oC; $\boldsymbol{\delta_H}$ (400 MHz, $CDCl_3$) 7.51 (2 H, t, *J* = 7.6 Hz, ArC*H*), 7.60 (2 H, t, *J* = 7.6 Hz, ArC*H*), 7.81 (2 H, d, *J* = 7.9 Hz, ArC*H*), 8.00 (2 H, d, *J* = 7.6 Hz, ArC*H*); $\boldsymbol{\delta_C}$ (101 MHz, $CDCl_3$) 121.9 (Ar*C*H), 127.5 (Ar*C*H), 129.5 (Ar*C*H), 132.5 (Ar*C*H), 137.1 (Ar*C*), 145.1 (Ar*C*); $\boldsymbol{\nu_{max}}$ (neat)/cm^{-1} 691, 752, 871, 940, 978, 987, 1016, 1022,

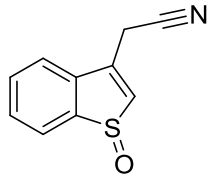
1065, 1124, 1271, 1443, 1478, 1592, 3055; **HRMS** (ESI): Calcd. for $C_{12}H_9SO$ $(M+H)^+$, 201.0369; found 201.0355.

4-(Hept-2-yn-1-yl)dibenzo[b,d]thiophene 361



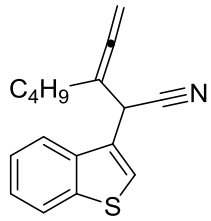
To an oven dried tube under nitrogen atmosphere at 0 ^oC dibenzothiophen S-oxide (40.0 mg 0.2 mmol), and hept-2-yn-1-yltrimethylsilane (50.4 mg, 0.3 mmol) in MeCN (5 ml) was added. Trifluoroacetic anhydride (56 µl, 0.4 mmol) was added to the mixture and the reaction was heated to 80 ^oC for 18 hours. The reaction was then cooled to room temperature and a saturated aqueous solution of $NaHCO_3$ was added (2 ml) along with EtOAc (2 ml). The organic phase was separated and the aqueous phase washed with EtOAc (3 x 5 ml). The combined organic phases were dried ($MgSO_4$), filtered and concentrated *in vacuo* and the resulting crude mixture was purified by flash column chromatography using *n*-hexane: EtOAc (95:5) to give **361** as a yellow oil (43.3 mg, 0.15 mmol, 78%); $\boldsymbol{\delta_H}$ (400 MHz, $CDCl_3$) 0.95 (3 H, t, *J* = 7.3 Hz, C*H*$_3$), 1.43 - 1.61 (4 H, m, 2 × C*H*$_2$), 2.29 (2 H, tt, *J* = 7.0, 2.3 Hz, C*H*$_2$), 3.82 (2 H, s, C*H*$_2$), 7.45 - 7.51 (3 H, m, 3 × ArC*H*), 7.62 (1 H, d, *J* = 7.6 Hz, ArC*H*), 7.87 - 7.92 (1 H, m, ArC*H*), 8.08 (1 H, d, *J* = 7.9 Hz, ArC*H*), 8.14 - 8.20 (1 H, m, ArC*H*); $\boldsymbol{\delta_C}$ (101 MHz, $CDCl_3$) 13.6 (*C*H_3), 18.6 (*C*H_2), 22.0 (*C*H_2), 24.5 (*C*H_2), 31.0 (*C*H_2), 75.6 (*C*C), 83.9 (C*C*), 119.9 (Ar*C*H), 121.7 (Ar*C*H), 122.8 (Ar*C*H), 124.4 (Ar*C*H), 124.8 (Ar*C*H), 125.7 (Ar*C*H), 126.7 (Ar*C*H), 131.9 (Ar*C*), 135.7 (Ar*C*), 135.9 (Ar*C*), 139.2 (Ar*C*); $\boldsymbol{\nu_{max}}$ (neat)/cm^{-1} 768, 879, 931, 958, 987, 1012, 1019, 1065, 1124, 1259, 1262, 1300, 1421, 1556, 1705, 2849, 3055; **HRMS** (ESI): Calcd. for $C_{19}H_{19}S$ $(M+H)^+$, 279.1202; found 279.1199.

3-Carbonitrilebenzo[b]thiophene *S*-oxide 362



As described in general procedure **N**, 3-acetonitrilebenzo[b]thiophene (519 mg, 3.0 mmol) and H_2O_2 (0.31 ml, 3.0 mmol) in dichloromethane and trifluoroacetic acid (1:1), gave **362** (266 mg, 1.40 mmol, 47%) as a white solid; **m.p**: 175-177 ^oC; δ_H (400 MHz, $CDCl_3$) 3.95 (2 H, d, *J* = 1.3 Hz, CH_2CN), 7.30 - 7.35 (2 H, m, 2 × ArC*H*), 7.45 - 7.52 (1 H, m, ArC*H*), 7.73 (1 H, d, *J* = 8.5 Hz, ArC*H*), 7.99 (1 H, d, *J* = 1.8 Hz, ArC*H*); δ_C (101 MHz, $CDCl_3$) 19.2 (*C*H_2), 108.4 (Ar*C*H), 116.3 (*C*N), 126.4 (Ar*C*H), 127.5 (Ar*C*), 127.9 (Ar*C*H), 128.6 (Ar*C*H), 130.2 (Ar*C*H), 135.2 (Ar*C*), 149.9 (Ar*C*); ν_{max} (neat)/cm^{-1} 758, 861, 1027, 1058, 1204, 1404, 1447, 1620, 2222, 2886, 3020; **HRMS** (ESI): Calcd. for $C_{10}H_8SON$ $(M+H)^+$, 190.0321; found 190.0318.

2-(Benzo[b]thiophen-3-yl)-3-(5-allenyl)heptanenitrile 363



To an oven dried tube under nitrogen atmosphere at 0 ^oC 3-acetonitrilebenzo[b]thiophene *S*-oxide (37.8 mg 0.2 mmol), and hept-2-yn-1-yltrimethylsilane (50.4 mg, 0.3 mmol) in MeCN (2 ml), trifluoroacetic anhydride (56 µl, 0.4 mmol) was added and the reaction was heated to 80 ^oC for 18 hours. The reaction was then cooled to room temperature and a saturated aqueous solution of $NaHCO_3$ was added (2 ml) along with EtOAc (2 ml). The organic phase was separated and the aqueous phase washed with EtOAc (3 x 5 ml). The combined organic phases were dried ($MgSO_4$), filtered and concentrated *in vacuo* and the resulting crude mixture was purified by flash column chromatography using *n*-hexane: EtOAc (95:5) to give **363** as a yellow oil (38.9 mg, 0.15 mmol, 73%); δ_H (400 MHz, $CDCl_3$) 0.85 (3 H, t, *J* = 7.3 Hz, CH_3), 1.27 - 1.44 (4 H, m, 2 × CH_2), 1.86 - 2.13 (2 H, m, CH_2), 4.83 (1 H, s, C*H*), 4.91 - 5.03 (2 H, m, C=CH_2), 7.37 - 7.46 (2 H, m, 2 × ArC*H*), 7.55 (1 H, s, ArC*H*), 7.77 (1 H, d, *J* = 7.3 Hz,

ArC*H*), 7.89 (1 H, d, *J* = 7.5 Hz, ArC*H*); $\boldsymbol{\delta_C}$ (101 MHz, $CDCl_3$) 13.8 (*C*H_3), 22.1 (*C*H_2), 28.6 (*C*H_2), 29.4 (*C*H_2), 36.2 (*C*H), 79.7 (C=*C*H_2), 99.6 (*C*=C=CH_2), 118.3 (*C*N), 121.7 (Ar*C*H), 123.1 (Ar*C*H), 124.5 (Ar*C*H), 124.9 (Ar*C*H), 125.5 (Ar*C*H), 127.7 (Ar*C*), 136.6 (Ar*C*), 140.7 (Ar*C*), 206.3 (C=*C*=CH_2); $\boldsymbol{\nu_{max}}$ (neat)/cm^{-1} 669, 755, 856, 908, 1020, 1043, 1076, 1215, 1358, 1427, 1460, 1959, 2244, 2870, 2928, 2957; **HRMS** (ESI): Calcd. for $C_{17}H_{18}SN$ $(M+H)^+$, 268.1154; found 268.1144.

3.3 Appendix: X-Ray Crystal Structures

X-Ray structure and CCDC number. Compound 3a
CCDC 1511568

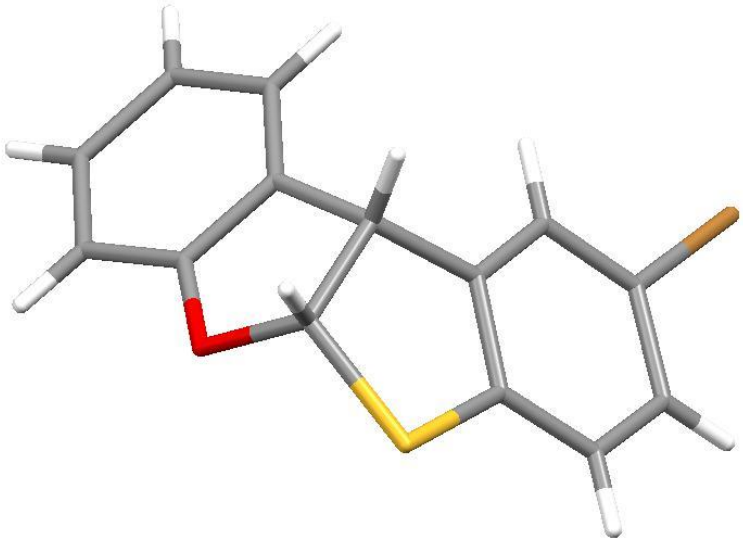


Table 1. Crystal data and structure refinement for s4511ma.

Identification code	s4511ma
Empirical formula	C14 H9 Br O S
Formula weight	305.18
Temperature	150(2) K
Wavelength	1.54178 A
Crystal system, space group	Monoclinic, P2(1)
Unit cell dimensions	a = 5.9996(3) A alpha = 90 deg. b = 4.9812(3) A beta = 91.680(4) deg. c = 18.7925(10) A gamma = 90 deg.
Volume	561.38(5) A^3
Z, Calculated density	2, 1.805 Mg/m^3
Absorption coefficient	6.533 mm^-1
F(000)	304
Crystal size	0.190 x 0.150 x 0.030 mm
Theta range for data collection	2.352 to 71.995 deg.

Limiting indices	-7<=h<=7, -6<=k<=4, -23<=l<=23
Reflections collected / unique	3042 / 1605 [R(int) = 0.0529]
Completeness to theta = 67.679	97.8 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.828 and 0.586829
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	1605 / 1 / 154
Goodnes *S*-of-fit on F^2	1.065
Final R indices [I>2sigma(I)]	R1 = 0.0411, wR2 = 0.1100
R indices (all data)	R1 = 0.0432, wR2 = 0.1114
Absolute structure parameter	0.03(4)
Extinction coefficient	n/a
Largest diff. peak and hole	1.800 and -0.524 e.A^-3

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) for s4511ma.
U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x	y	z	U(eq)
Br(1)	4115(1)	12489(2)	622(1)	27(1)
C(1)	2418(13)	9832(18)	1120(4)	25(2)
C(2)	322(13)	9219(17)	835(4)	26(2)
C(3)	-908(12)	7280(20)	1196(4)	26(2)
C(4)	-87(12)	6181(18)	1823(4)	24(2)
C(5)	655(12)	3977(17)	3050(4)	25(2)
C(6)	1557(11)	7260(20)	3838(4)	25(2)
C(7)	1548(14)	8947(19)	4435(4)	27(2)
C(8)	3332(14)	10680(19)	4549(4)	31(2)
C(9)	5118(13)	10761(18)	4081(4)	28(2)
C(10)	5111(12)	9022(19)	3496(4)	27(2)
C(11)	3307(11)	7330(20)	3375(3)	24(1)

C(12)	2734(12)	5445(17)	2771(4)	24(2)
C(13)	2041(11)	6862(14)	2086(4)	21(2)
C(14)	3295(11)	8760(17)	1735(4)	22(2)
O(1)	-104(9)	5554(12)	3650(3)	27(1)
S(1)	-1418(3)	3765(4)	2340(1)	27(1)

Table 3. Bond lengths [A] and angles [deg] for s4511ma.

Br(1)-C(1)	1.929(8)
C(1)-C(14)	1.363(11)
C(1)-C(2)	1.386(11)
C(2)-C(3)	1.404(13)
C(2)-H(2)	0.9500
C(3)-C(4)	1.376(11)
C(3)-H(3)	0.9500
C(4)-C(13)	1.397(10)
C(4)-S(1)	1.754(8)
C(5)-O(1)	1.458(9)
C(5)-C(12)	1.550(10)
C(5)-S(1)	1.799(8)
C(5)-H(5)	1.0000
C(6)-O(1)	1.348(10)
C(6)-C(11)	1.384(9)
C(6)-C(7)	1.402(12)
C(7)-C(8)	1.387(12)
C(7)-H(7)	0.9500
C(8)-C(9)	1.406(11)
C(8)-H(8)	0.9500
C(9)-C(10)	1.401(12)
C(9)-H(9)	0.9500
C(10)-C(11)	1.384(12)
C(10)-H(10)	0.9500
C(11)-C(12)	1.505(12)
C(12)-C(13)	1.516(10)
C(12)-H(12)	1.0000
C(13)-C(14)	1.387(10)
C(14)-H(14)	0.9500
C(14)-C(1)-C(2)	124.3(8)
C(14)-C(1)-Br(1)	118.9(6)
C(2)-C(1)-Br(1)	116.7(6)
C(1)-C(2)-C(3)	116.7(7)
C(1)-C(2)-H(2)	121.7
C(3)-C(2)-H(2)	121.7
C(4)-C(3)-C(2)	120.5(7)
C(4)-C(3)-H(3)	119.8

C(2)-C(3)-H(3)	119.8
C(3)-C(4)-C(13)	120.4(7)
C(3)-C(4)-S(1)	126.1(6)
C(13)-C(4)-S(1)	113.4(6)
O(1)-C(5)-C(12)	106.3(6)
O(1)-C(5)-S(1)	112.3(5)
C(12)-C(5)-S(1)	108.8(5)
O(1)-C(5)-H(5)	109.8
C(12)-C(5)-H(5)	109.8
S(1)-C(5)-H(5)	109.8
O(1)-C(6)-C(11)	114.9(8)
O(1)-C(6)-C(7)	124.5(6)
C(11)-C(6)-C(7)	120.5(9)
C(8)-C(7)-C(6)	118.5(7)
C(8)-C(7)-H(7)	120.8
C(6)-C(7)-H(7)	120.8
C(7)-C(8)-C(9)	121.3(8)
C(7)-C(8)-H(8)	119.3
C(9)-C(8)-H(8)	119.3
C(10)-C(9)-C(8)	119.2(8)
C(10)-C(9)-H(9)	120.4
C(8)-C(9)-H(9)	120.4
C(11)-C(10)-C(9)	119.3(7)
C(11)-C(10)-H(10)	120.3
C(9)-C(10)-H(10)	120.3
C(10)-C(11)-C(6)	121.1(8)
C(10)-C(11)-C(12)	131.6(6)
C(6)-C(11)-C(12)	107.2(7)
C(11)-C(12)-C(13)	113.6(7)
C(11)-C(12)-C(5)	102.0(6)
C(13)-C(12)-C(5)	107.6(6)
C(11)-C(12)-H(12)	111.1
C(13)-C(12)-H(12)	111.1
C(5)-C(12)-H(12)	111.1
C(14)-C(13)-C(4)	120.0(7)
C(14)-C(13)-C(12)	125.6(7)
C(4)-C(13)-C(12)	114.4(7)
C(1)-C(14)-C(13)	117.9(7)
C(1)-C(14)-H(14)	121.0
C(13)-C(14)-H(14)	121.0
C(6)-O(1)-C(5)	107.2(6)
C(4)-S(1)-C(5)	93.1(4)

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters (A^2 x 10^3) for s4511ma.
The anisotropic displacement factor exponent takes the form:
-2 pi^2 [h^2 a*^2 U11 + ... + 2 h k a* b* U12]

	U11	U22	U33	U23	U13	U12
Br(1)	25(1)	26(1)	30(1)	1(1)	5(1)	-4(1)
C(1)	21(4)	27(4)	26(3)	-1(3)	5(3)	4(3)
C(2)	23(4)	24(4)	30(4)	-1(3)	1(3)	5(3)
C(3)	21(3)	25(4)	32(3)	-4(4)	1(3)	-3(4)
C(4)	11(3)	24(4)	36(4)	-8(3)	5(3)	-2(3)
C(5)	22(4)	26(4)	29(3)	1(3)	9(3)	2(3)
C(6)	22(3)	19(4)	34(3)	7(4)	5(3)	3(4)
C(7)	25(4)	29(5)	27(3)	0(3)	6(3)	1(3)
C(8)	25(4)	38(5)	29(4)	-1(4)	-3(3)	5(4)
C(9)	19(4)	29(5)	35(4)	2(3)	-3(3)	0(3)
C(10)	15(4)	34(5)	31(4)	4(3)	-1(3)	2(3)
C(11)	17(3)	27(4)	27(3)	8(4)	0(2)	0(4)
C(12)	15(3)	26(4)	30(4)	0(3)	2(3)	2(3)
C(13)	14(3)	22(5)	29(3)	-5(3)	4(3)	-2(2)
C(14)	12(3)	20(4)	33(4)	-8(3)	6(3)	-3(3)
O(1)	20(3)	30(3)	31(3)	-2(2)	5(2)	-4(2)
S(1)	18(1)	29(1)	35(1)	1(1)	4(1)	-5(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (A^2 x 10^3) for s4511ma.

	x	y	z	U(eq)
H(2)	-252	10070	416	31
H(3)	-2318	6717	1007	31
H(5)	1078	2132	3214	31
H(7)	349	8905	4753	33
H(8)	3347	11836	4951	37
H(9)	6316	11982	4162	34
H(10)	6331	9000	3185	32
H(12)	3979	4155	2692	29
H(14)	4720	9296	1917	26

Table 6. Torsion angles [deg] for s4511ma.

C(14)-C(1)-C(2)-C(3)	-2.8(13)
Br(1)-C(1)-C(2)-C(3)	179.8(6)
C(1)-C(2)-C(3)-C(4)	3.5(13)
C(2)-C(3)-C(4)-C(13)	-3.9(13)
C(2)-C(3)-C(4)-S(1)	179.5(7)
O(1)-C(6)-C(7)-C(8)	-177.4(8)
C(11)-C(6)-C(7)-C(8)	-0.2(13)
C(6)-C(7)-C(8)-C(9)	0.0(13)
C(7)-C(8)-C(9)-C(10)	-1.1(13)
C(8)-C(9)-C(10)-C(11)	2.5(12)
C(9)-C(10)-C(11)-C(6)	-2.7(13)
C(9)-C(10)-C(11)-C(12)	174.3(9)
O(1)-C(6)-C(11)-C(10)	179.1(8)
C(7)-C(6)-C(11)-C(10)	1.6(14)
O(1)-C(6)-C(11)-C(12)	1.4(11)
C(7)-C(6)-C(11)-C(12)	-176.1(8)
C(10)-C(11)-C(12)-C(13)	-71.8(12)
C(6)-C(11)-C(12)-C(13)	105.5(8)
C(10)-C(11)-C(12)-C(5)	172.7(10)
C(6)-C(11)-C(12)-C(5)	-10.0(9)
O(1)-C(5)-C(12)-C(11)	14.7(8)
S(1)-C(5)-C(12)-C(11)	135.9(6)
O(1)-C(5)-C(12)-C(13)	-105.1(7)
S(1)-C(5)-C(12)-C(13)	16.1(8)
C(3)-C(4)-C(13)-C(14)	3.4(12)
S(1)-C(4)-C(13)-C(14)	-179.7(6)
C(3)-C(4)-C(13)-C(12)	-178.6(8)
S(1)-C(4)-C(13)-C(12)	-1.7(8)
C(11)-C(12)-C(13)-C(14)	56.1(9)
C(5)-C(12)-C(13)-C(14)	168.3(7)
C(11)-C(12)-C(13)-C(4)	-121.7(7)
C(5)-C(12)-C(13)-C(4)	-9.6(9)
C(2)-C(1)-C(14)-C(13)	2.3(12)
Br(1)-C(1)-C(14)-C(13)	179.7(6)
C(4)-C(13)-C(14)-C(1)	-2.5(11)
C(12)-C(13)-C(14)-C(1)	179.8(7)
C(11)-C(6)-O(1)-C(5)	8.6(10)
C(7)-C(6)-O(1)-C(5)	-174.0(8)
C(12)-C(5)-O(1)-C(6)	-14.6(8)
S(1)-C(5)-O(1)-C(6)	-133.5(6)
C(3)-C(4)-S(1)-C(5)	-173.1(8)
C(13)-C(4)-S(1)-C(5)	10.1(6)
O(1)-C(5)-S(1)-C(4)	102.3(6)
C(12)-C(5)-S(1)-C(4)	-15.1(6)

Symmetry transformations used to generate equivalent atoms:

Table 7. Hydrogen bonds for s4511ma [A and deg.].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
C(12)-H(12)...S(1)#1	1.00	2.86	3.719(8)	143.8
C(3)-H(3)...Br(1)#2	0.95	3.07	3.948(9)	153.6

Symmetry transformations used to generate equivalent atoms:
#1 x+1,y,z #2 x-1,y-1,z

Chapter 4: References

1. Pummerer, R., *Chem. Ber.* **1910,** *43* (2), 1401-1412.
2. Bur, S. K.; Padwa, A., *Chem. Rev.* **2004,** *104* (5), 2401-2432.
3. Feldman, K. S., *Tetrahedron* **2006,** *62* (21), 5003-5034.
4. Smith, L. H. S.; Coote, S. C.; Sneddon, H. F.; Procter, D. J., *Angew. Chem., Int. Ed.* **2010,** *49*, 5832-5844.
5. Akai, S.; Kita, Y., *Top. Curr. Chem.* **2007,** *274*, 35-76.
6. Tamura, Y.; Yakura, T.; Shirouchi, Y.; Haruta, J. I., *Chem. Pharm. Bull.* **1986,** *34* (3), 1061-1066.
7. Feldman, K. S.; Vidulova, D. B., *Tetrahedron Lett.* **2004,** *45* (26), 5035-5037.
8. Haimowitz, T.; Fitzgerald, M. E.; Winkler, J. D., *Tetrahedron Lett.* **2011,** *52* (17), 2162-2164.
9. Marino, J. P.; Kim, M. W.; Lawrence, R., *J. Org. Chem.* **1989,** *54* (8), 1782-1784.
10. Marino, J. P.; Rubio, M. B.; Cao, G.; de Dios, A., *J. Am. Chem. Soc.* **2002,** *124* (45), 13398-13399.
11. Haraguchi, K.; Matsui, H.; Takami, S.; Tanaka, H., *J. Org. Chem.* **2009,** *74* (6), 2616-2619.
12. García Ruano, J. L.; Alemán, J.; Aranda, M. T.; Arévalo, M. J.; Padwa, A., *Org. Lett.* **2004,** *7* (1), 19-22.
13. Halder, S.; Satyam, A., *Tetrahedron Lett.* **2011,** *52* (11), 1179-1182.
14. King, R. R., *J. Org. Chem.* **1978,** *43* (19), 3784-3785.
15. Jung, M. E.; Kim, C.; von dem Bussche, L., *J. Org. Chem.* **1994,** *59* (12), 3248-3249.
16. Jung, M. E.; Jachiet, D.; Khan, S. I.; Kim, C., *Tetrahedron Lett.* **1995,** *36* (3), 361-364.
17. Akai, S.; Takeda, Y.; Iio, K.; Takahashi, K.; Fukuda, N.; Kita, Y., *J. Org. Chem.* **1997,** *62* (16), 5526-5536.
18. Akai, S.; Takeda, Y.; Iio, K.; Yoshida, Y.; Kita, Y., *J. Chem. Soc., Chem. Commun.* **1995,** *0* (10), 1013-1014.
19. Kita, Y.; Takeda, Y.; Iio, K.; Yokogawa, K.; Takahashi, K.; Akai, S., *Tetrahedron Lett.* **1996,** *37* (42), 7545-7548.
20. Kita, Y.; Takeda, Y.; Matsugi, M.; Iio, K.; Gotanda, K.; Murata, K.; Akai, S., *Angew. Chem., Int. Ed.* **1997,** *36* (13-14), 1529-1531.
21. Akai, S.; Iio, K.; Takeda, Y.; Ueno, H.; Yokogawa, K.; Kita, Y., *J. Chem. Soc., Chem. Commun.* **1995,** *0* (22), 2319-2320.
22. Kita, Y.; Iio, K.; Kawaguchi, K.-i.; Fukuda, N.; Takeda, Y.; Ueno, H.; Okunaka, R.; Higuchi, K.; Tsujino, T.; Fujioka, H.; Akai, S., *Chem. Eur. J.* **2000,** *6* (21), 3897-3905.
23. Akai, S.; Kawashita, N.; Morita, N.; Nakamura, Y.; Iio, K.; Kita, Y., *Heterocycles* **2002,** *58*, 75-78.
24. Feldman, K. S.; Vidulova, D. B.; Karatjas, A. G., *J. Org. Chem.* **2005,** *70* (16), 6429-6440.
25. Feldman, K. S.; Karatjas, A. G., *Org. Lett.* **2006,** *8*, 4137-4140.
26. Akai, S.; Kakiguchi, K.; Nakamura, Y.; Kuriwaki, I.; Dohi, T.; Harada, S.; Kubo, O.; Morita, N.; Kita, Y., *Angew. Chem., Int. Ed.* **2007,** *46*, 7458-7461.
27. Feldman, K. S.; Fodor, M. D.; Skoumbourdis, A. P., *Synthesis* **2009,** (18), 3162-3173.
28. Feldman, K. S.; Skoumbourdis, A. P., *Org. Lett.* **2005,** *7* (5), 929-931.

29. Feldman, K. S.; Skoumbourdis, A. P.; Fodor, M. D., *J. Org. Chem.* **2007,** *72*, 8076-8086.
30. Bates, D. K.; Winters, R. T.; Picard, J. A., *J. Org. Chem.* **1992,** *57* (11), 3094-3097.
31. Fernandez-Salas, J. A.; Pulis, A. P.; Procter, D. J., *Chem. Commun.* **2016,** *52* (83), 12364-12367.
32. Yoshida, S.; Yorimitsu, H.; Oshima, K., *Org. Lett.* **2007,** *9* (26), 5573-5576.
33. Yoshida, S.; Yorimitsu, H.; Oshima, K., *Org. Lett.* **2009,** *11* (10), 2185-2188.
34. Kobatake, T.; Fujino, D.; Yoshida, S.; Yorimitsu, H.; Oshima, K., *J. Am. Chem. Soc.* **2010,** *132*, 11838-11840.
35. Huang, X.; Patil, M.; Farès, C.; Thiel, W.; Maulide, N., *J. Am. Chem. Soc.* **2013,** *135* (19), 7312-7323.
36. Huang, X.; Maulide, N., *J. Am. Chem. Soc.* **2011,** *133* (22), 8510-8513.
37. Peng, B.; Geerdink, D.; Farès, C.; Maulide, N., *Angew. Chem., Int. Ed.* **2014,** *53* (21), 5462-5466.
38. Peng, B.; Huang, X.; Xie, L.-G.; Maulide, N., *Angew. Chem., Int. Ed.* **2014,** *53* (33), 8718-8721.
39. Kaiser, D.; Veiros, L. F.; Maulide, N., *Chem. Eur. J.* **2016,** *22* (14), 4727-4732.
40. Kaldre, D.; Maryasin, B.; Kaiser, D.; Gajsek, O.; González, L.; Maulide, N., *Angew. Chem., Int. Ed.* **2017,** *56* (8), 2212-2215.
41. Shang, L.; Chang, Y.; Luo, F.; He, J.-N.; Huang, X.; Zhang, L.; Kong, L.; Li, K.; Peng, B., *J. Am. Chem. Soc.* **2017**.
42. Magnier, E.; Blazejewski, J.-C.; Tordeux, M.; Wakselman, C., *Angew. Chem., Int. Ed.* **2006,** *45* (8), 1279-1282.
43. Macé, Y.; Blazejewski, J.-C.; Pradet, C.; Magnier, E., *Eur. J. Org. Chem* **2010,** *2010* (30), 5772-5776.
44. Macé, Y.; Urban, C.; Pradet, C.; Blazejewski, J.-C.; Magnier, E., *Eur. J. Org. Chem.* **2009,** *2009* (31), 5313-5316.
45. Macé, Y.; Urban, C.; Pradet, C.; Marrot, J.; Blazejewski, J.-C.; Magnier, E., *Eur. J. Org. Chem.* **2009,** *2009* (19), 3150-3153.
46. Akai, S.; Kawashita, N.; Satoh, H.; Wada, Y.; Kakiguchi, K.; Kuriwaki, I.; Kita, Y., *Org. Lett.* **2004,** *6* (21), 3793-3796.
47. Padwa, A.; Nara, S.; Wang, Q., *Tetrahedron Lett.* **2006,** *47* (4), 595-597.
48. Eberhart, A. J.; Imbriglio, J. E.; Procter, D. J., *Org. Lett.* **2011,** *13* (21), 5882.
49. Eberhart, A. J.; Cicoira, C.; Procter, D. J., *Org. Lett.* **2013,** *15* (15), 3994-3997.
50. Eberhart, A. J.; Procter, D. J., *Angew. Chem., Int. Ed.* **2013,** *52* (14), 4008-4011.
51. Ma, S.; He, Q.; Zhang, X., *J. Org. Chem.* **2005,** *70* (8), 3336-3338.
52. Pérez, I.; Sestelo, J. P.; Sarandeses, L. A., *J. Am. Chem. Soc.* **2001,** *123* (18), 4155-4160.
53. Zhang, W.-W.; Zhang, X.-G.; Li, J.-H., *J. Org. Chem.* **2010,** *75* (15), 5259-5264.
54. Matsuzawa, H.; Miyake, Y.; Nishibayashi, Y., *Angew. Chem., Int. Ed.* **2007,** *46* (34), 6488-6491.
55. Eberhart, A. J.; Procter, D. J., *Angew. Chem., Int. Ed.* **2013,** *52* (14), 4008-4011.
56. Takimiya, K.; Osaka, I., *Chem. Rec.* **2015,** *15* (1), 175-188.
57. Takimiya, K.; Osaka, I.; Mori, T.; Nakano, M., *Acc. Chem. Res.* **2014,** *47* (5), 1493-1502.
58. Takimiya, K.; Shinamura, S.; Osaka, I.; Miyazaki, E., *Adv. Mater.* **2011,** *23* (38), 4347-4370.
59. Osaka, I.; Kakara, T.; Takemura, N.; Koganezawa, T.; Takimiya, K., *J. Am. Chem. Soc.* **2013,** *135* (24), 8834-8837.

60. Mitsui, C.; Okamoto, T.; Yamagishi, M.; Tsurumi, J.; Yoshimoto, K.; Nakahara, K.; Soeda, J.; Hirose, Y.; Sato, H.; Yamano, A.; Uemura, T.; Takeya, J., *Adv. Mater.* **2014,** *26* (26), 4546-4551.
61. Rajagopalan, S.; Zweifel, G., *Synthesis* **1984,** (02), 111-112.
62. Eberhart, A. J.; Shrives, H. J.; Álvarez, E.; Carrër, A.; Zhang, Y.; Procter, D. J., *Chem. Eur. J.* **2015,** *21* (20), 7428-7434.
63. Fleming, I.; M. Mwaniki, J., *J. Chem. Soc., Perkin. Trans. 1.* **1998,** (7), 1237-1248.
64. Fernández-Salas, J. A.; Eberhart, A. J.; Procter, D. J., *J. Am. Chem. Soc.* **2016,** *138* (3), 790-793.
65. Marzano, G.; Ciasca, C. V.; Babudri, F.; Bianchi, G.; Pellegrino, A.; Po, R.; Farinola, G. M., *Eur. J. Org. Chem* **2014,** *2014* (30), 6583-6614.
66. Carsten, B.; He, F.; Son, H. J.; Xu, T.; Yu, L., *Chem. Rev.* **2011,** *111* (3), 1493-1528.
67. Segawa, Y.; Maekawa, T.; Itami, K., *Angew. Chem., Int. Ed.* **2015,** *54* (1), 66-81.
68. Hermann, J. C.; Chen, Y.; Wartchow, C.; Menke, J.; Gao, L.; Gleason, S. K.; Haynes, N.-E.; Scott, N.; Petersen, A.; Gabriel, S.; Vu, B.; George, K. M.; Narayanan, A.; Li, S. H.; Qian, H.; Beatini, N.; Niu, L.; Gan, Q.-F., *ACS. Med. Chem. Lett.* **2013,** *4* (2), 197-200.
69. Osaka, I.; Shinamura, S.; Abe, T.; Takimiya, K., *J. Mater. Chem.* **2013,** *1* (7), 1297-1304.
70. Shinamura, S.; Miyazaki, E.; Takimiya, K., *J. Org. Chem.* **2010,** *75* (4), 1228-1234.
71. Chen, Y.; Chang, H.; Tian, H.; Bao, C.; Li, W.; Yan, D.; Geng, Y.; Wang, F., *Org. Electron.* **2012,** *13* (12), 3268-3275.
72. Parvatkar, P. T.; Parameswaran, P. S.; Tilve, S. G., *Chem. Eur. J.* **2012,** *18* (18), 5460-5489.
73. Godoi, B.; Schumacher, R. F.; Zeni, G., *Chem. Rev.* **2011,** *111* (4), 2937-2980.
74. Nielsen, K. T.; Bechgaard, K.; Krebs, F. C., *Macromolecules* **2005,** *38* (3), 658-659.
75. Cabanetos, C.; El Labban, A.; Bartelt, J. A.; Douglas, J. D.; Mateker, W. R.; Fréchet, J. M. J.; McGehee, M. D.; Beaujuge, P. M., *J. Am. Chem. Soc.* **2013,** *135* (12), 4656-4659.
76. Gao, P.; Beckmann, D.; Tsao, H. N.; Feng, X.; Enkelmann, V.; Pisula, W.; Mullen, K., *Chem. Commun.* **2008,** (13), 1548-1550.
77. Ebata, H.; Miyazaki, E.; Yamamoto, T.; Takimiya, K., *Org. Lett.* **2007,** *9* (22), 4499-4502.
78. Takimiya, K.; Konda, Y.; Ebata, H.; Niihara, N.; Otsubo, T., *J. Org. Chem.* **2005,** *70* (25), 10569-10571.
79. Shinamura, S.; Osaka, I.; Miyazaki, E.; Nakao, A.; Yamagishi, M.; Takeya, J.; Takimiya, K., *J. Am. Chem. Soc.* **2011,** *133* (13), 5024-5035.
80. Croxtall, J. D.; Plosker, G. L., *Drugs* **2009,** *69* (3), 339-359.
81. Muchmore, D. B., *The Oncologist* **2000,** *5* (5), 388-392.
82. Liu, K.; Xu, L.; Szalkowski, D.; Li, Z.; Ding, V.; Kwei, G.; Huskey, S.; Moller, D. E.; Heck, J. V.; Zhang, B. B.; Jones, A. B., *J. Med. Chem.* **2000,** *43* (19), 3487-3494.
83. Crombie, A. L.; Antrilli, T. M.; Campbell, B. A.; Crandall, D. L.; Failli, A. A.; He, Y.; Kern, J. C.; Moore, W. J.; Nogle, L. M.; Trybulski, E. J., *Bioorg. Med. Chem. Lett.* **2010,** *20* (12), 3742-3745.
84. Havaldar, F. H. B., S., Burudkar, *J. Serb. Chem. Soc.* **2004,** (69), 527-532.
85. Sun, C.-L.; Shi, Z.-J., *Chem. Rev.* **2014,** *114* (18), 9219-9280.
86. Venier, C. G.; Squires, T. G.; Chen, Y. Y.; Smith, B. F., *J. Org. Chem.* **1982,** *47* (19), 3773-3774.

87. Pouzet, P.; Erdelmeier, I.; Ginderow, D.; Mornon, J.-P.; Dansette, P.; Mansuy, D., *J. Chem. Soc., Chem. Commun.* **1995,** (4), 473-474.
88. Li, Y.; Thiemann, T.; Sawada, T.; Mataka, S.; Tashiro, M., *J. Org. Chem.* **1997,** *62* (23), 7926-7936.
89. Mock, W. L., *J. Am. Chem. Soc.* **1970,** *92* (26), 7610-7612.
90. Li, Y.; Matsuda, M.; Thiemann, T.; Sawada, T.; Matake, S.; Tashiro, M., *Synlett* **1996,** *1996* (05), 461-464.
91. El Amoudi, M. S. E. F.; Geneste, P.; Olivé, J. L., *Tetrahedron Lett.* **1978,** *19* (11), 999-1000.
92. Ueda, K.; Yanagisawa, S.; Yamaguchi, J.; Itami, K., *Angew. Chem., Int. Ed.* **2010,** *49* (47), 8946-8949.
93. Tang, D.-T. D.; Collins, K. D.; Glorius, F., *J. Am. Chem. Soc.* **2013,** *135* (20), 7450-7453.
94. Yuan, K.; Doucet, H., *ChemCatChem* **2013,** *5* (12), 3495-3496.
95. Colletto, C.; Islam, S.; Juliá-Hernández, F.; Larrosa, I., *J. Am. Chem. Soc.* **2016,** *138* (5), 1677-1683.
96. Yamaguchi, K.; Yamaguchi, J.; Studer, A.; Itami, K., *Chem. Sci.* **2012,** *3* (6), 2165-2169.
97. Funaki, K.; Sato, T.; Oi, S., *Org. Lett.* **2012,** *14* (24), 6186-6189.
98. Yuan, K.; Doucet, H., *Chem. Sci.* **2014,** *5* (1), 392-396.
99. Tang, D.-T. D.; Collins, K. D.; Ernst, J. B.; Glorius, F., *Angew. Chem., Int. Ed.* **2014,** *53* (7), 1809-1813.
100. Yanagi, T.; Otsuka, S.; Kasuga, Y.; Fujimoto, K.; Murakami, K.; Nogi, K.; Yorimitsu, H.; Osuka, A., *J. Am. Chem. Soc.* **2016,** *138* (44), 14582-14585.
101. Clark, P. D.; Mesher, S. T., *Phosphorus, Sulfur Silicon Relat. Elem.* **1995,** *105* (1-4), 157-162.
102. Kamila, S.; Mukherjee, C.; Mondal, S. S.; De, A., *Tetrahedron* **2003,** *59* (8), 1339-1348.
103. Wippich, J.; Schnapperelle, I.; Bach, T., *Chem. Commun.* **2015,** *51* (15), 3166-3168.
104. Xia, Y.; Liu, Z.; Feng, S.; Zhang, Y.; Wang, J., *J. Org. Chem.* **2015,** *80* (1), 223-236.
105. Minvielle, M. J.; Bunders, C. A.; Melander, C., *MedChemComm* **2013,** *4* (6), 916-919.
106. Kaur, N., *Cat. Rev.* **2015,** *57* (4), 478-564.
107. Eberhart, A. J.; Cicoira, C.; Procter, D. J., *Org. Lett.* **2013,** *15* (15), 3994-3997.
108. Eberhart, A. J.; Imbriglio, J. E.; Procter, D. J., *Org. Lett.* **2011,** *13* (21), 5882-5885.
109. Lockhart, T. P.; Comita, P. B.; Bergman, R. G., *J. Am. Chem. Soc.* **1981,** *103* (14), 4082-4090.
110. Holland, H. L. T., C. D; Andreana, P. R; Nguyen, D., *Can. J. Chem.* **1999,** *77*, 463-471.
111. Iaroshenko, V. O.; Ali, S.; Mkrtchyan, S.; Gevorgyan, A.; Babar, T. M.; Semeniuchenko, V.; Hassan, Z.; Villinger, A.; Langer, P., *Tetrahedron Lett.* **2012,** *53* (52), 7135-7139.