Chapter 3

Synthesis of Diarylethene Derivatives

3.1 Existing methods to synthesize diarylethenes

Diarylethenes constitute an important class of photochromic molecules, which can undergo a reversible ring-closure reaction upon irradiation with UV and visible light, respectively (see Chapter 2). The photochemical switching process is thermally irreversible and the compounds show high fatigue resistance. These are promising features for application in optical data storage, molecular wires and as molecular switches. The most commonly used diarylethenes are the diarylperfluorocyclopentenes followed by the bisarylmaleic anhydrides, and bisarylmaleimides. Many functionalized derivatives of these diarylethenes have been synthesized. Although the photochromic properties of these compounds are attractive, the synthesis of diarylethenes is not trivial.

The diarylperfluorocyclopentenes are synthesized by a double substitution reaction between a lithiated thiophene derivative and octafluorocyclopentene (Scheme 3.1).

\[
\begin{align*}
    & 3.1 \quad \text{Li} \\
    + & \quad 3.2 \\
    \rightarrow & \quad 3.3 \\
    \text{n-BuLi, -78°C} & \quad \text{THF}
\end{align*}
\]

Scheme 3.1 General synthesis of perfluorocyclopentene-derivatives.

Bisarylethene type switches based on maleic anhydride are also used quite often. Their synthesis starts from thiencycloacetamides, which react with itself to form a stilbene type of molecule (Scheme 3.2). This oxidative coupling involves a nucleophilic substitution followed by elimination of HCl. A disadvantage here is that both the cis and trans isomers of

3.5 are formed (see also addendum), but only the cis isomer can, after hydrolysis, undergo a ring closure to the desired anhydride 3.6. In some cases it has been possible to obtain high yields of the desired product 3.6 by first carrying out a photochemical trans to cis isomerization, followed by hydrolysis to the anhydride.7

![Scheme 3.2 Synthesis of a bisarylmaleic anhydride derivative.](image)

Less frequently used derivatives are the bisarylmaleimides. In Scheme 3.3 an example of such a derivative is depicted. Besides the fact that maleimides can be prepared from anhydrides, also an alternative route has been developed in order to synthesize bisarylmaleimide 3.10.8 Compound 3.8 is prepared by acylation of 3.7 with oxalylchloride in the presence of aminoacetonitrile. Switch 3.10 was then obtained by condensation of the acid chloride of 3.9 and compound 3.8.

![Scheme 3.3 Synthesis of a bisarylmaleimide-derivative.](image)
The physical characterization of photochromic switches by spectroscopic methods and the investigation of the photochromic properties usually requires only a few milligrams of the compound. However, when these photochromic switches are to be incorporated in self-assembling photoactive materials (vide infra), substantially more material is required to study the aggregation behavior and aggregate morphology. For this reason it was considered necessary to develop a new synthetic route to functionalized dithienylcyclopentenes that can be performed on a larger scale and at reasonable costs. Considering these three synthetic methods versus these requirements, it was decided to start with the synthesis of a bisarylmaleic anhydride photochromic switch. The starting-point for the development of this synthesis was based on the synthesis described before (Scheme 3.2), and the results are summarized in the addendum to this chapter. Unfortunately this straightforward synthetic procedure did not work out in our case, due to the formation of chiefly the undesired trans form in the penultimate step. The photochemical conversion of the trans form to the cis form was not successful and also the final step, the hydrolysis to the anhydride, failed miserably.

3.2 Synthesis of diarylcyclopentene-derivatives

An alternative synthetic approach to diaryl cyclopentene switches is shown in Scheme 3.4. In this route, the central cyclopentene ring is formed in the last step by a ring closure reaction of a 1,5-diketone via a McMurry reaction, or by a ring closure metathesis employing a 2,6-diaryl-1,6-heptadiene. The latter compound can be obtained from the 1,5-diketone by a Wittig reaction. The generation of substituted cyclopentenes either via a McMurry reaction or a ring closure metathasis are well established reactions that can be carried out on multigram scale. Moreover, by following this approach the undesired and often troubling formation of the trans isomer of the 1,2-diarylethene is avoided. The McMurry reaction was preferred, because it has one reaction step less. McMurry reactions are performed in two consecutive steps in a one pot procedure. First, the active titanium (Ti(0)) is formed by reduction of TiCl\textsubscript{x} (x = 3,4) in an ethereal solvent with strong reducing agents (i.e. K, Mg, Li, Na, LiAlH\textsubscript{4}, C8K, Zn) under an inert atmosphere. Secondly the substrate is added to the black slurry thus obtained. As an alternative an “instant” method can be used, in which the active titanium is prepared in the same way as described above, but in the presence of the substrate.

The key intermediate in the synthetic route shown in Scheme 3.4 is the 1,5-diaryl-1,5-diketone. Many procedures for the preparation of aryl ketones are known, the most straightforward of which is via a Friedel-Crafts acylation of the corresponding aryl compound by using a 1,5-dicarboxylic acid chloride, or by the addition of a metallated aryl (thienyl) group to a 1,5-dinitrile or 1,5-diester. Again, these acylation methods are well-established and can be conducted on larger scales, but the main advantage is that the dicarboxylic acids needed are readily available cheap chemicals. Even the perfluorinated glutaric acid is cheap (25g for $112,-) compared to octafluorcyclopentene.
Chapter 3

Scheme 3.4 *Retroynthetic scheme of a new route to diarylcyclopentenes.*

The thiophene derivative to be used in this synthesis requires some considerations. The most reactive positions in the thiophene molecule are the 2- and 5-positions, but in this route the acylation should take place at the 3-position. This implies that the 2- and 5-positions have to be substituted for example by an alkyl group and, if possible, a functional group to allow further derivatization of the photochromic switch. This functional group has to be compatible with the reaction conditions, and should have the right directing effect to achieve acylation at the desired position. An ortho-para directing group at the 2-position would direct to the 3- and 5-position, and in combination with the tendency of sulphur to orient to the 5-position this will result in a directing factor of at least 100 to 1 in favor of the 5-position. Electrophilic substitution reactions with thiophenes bearing meta directing groups at the 2-position have been reported to give a mixture of substitution at the 4- (minor) and 5-position (major).

Scheme 3.5 *Synthesis of 1,2-bis(2,5-dimethyl-3-thienyl)cyclopentene.*

First, the synthesis of a simple bis-thienylcyclopentene 3.14 lacking further functional groups was carried out in order to test the viability of the proposed route (Scheme 3.5). Starting compounds for 3.14 are 2,5-dimethylthiophene 3.11 and glutaryl chloride, which are both commercially available. The Friedel-Crafts acylation of 3.11 with glutaryl chloride in

50
CS₂ using AlCl₃ as a Lewis acid gave a tarry reaction product, from which the desired 1,5-diketone 3.13 could be isolated by column chromatography in 40% yield. Ring closure of 3.13 by a McMurry reaction with Mg and TiCl₃(THF)₃ in THF at 40°C gave the desired 1,2-bis-(2′-methyl-5′-methylthien-3′-yl)cyclopentene 3.14 in 58% yield after purification using column chromatography with hexane. Later it was found that unpurified 3.13 could be subjected to the McMurry ring closure reaction without significant decrease of yield. This synthesis can be performed on larger scale and the starting materials are easily accessible, but the drawback of this particular switch is the lack of functionality. Some attempts were made to brominate the 5-methyl groups of 3.14 using NBS, but no discrimination could be achieved between the two different methyl groups present. Later it turned out that the photochemical reactions of these simple bis(2,5-dialkyl-thienyl)cyclopentenes are in fact irreversible, which implies that these compounds are not suitable as photochromic switches (vide infra).

In our group there has been good experience with the bisaldehyde-substituted-perfluorocyclopentene 3.32. It was shown that this compound could easily be transformed to a bis-imine-derivative. These imine-derivatives showed excellent switching behavior. This prompted us to introduce the aldehyde as functional group. Various attempts have been carried out to acylate 3.15 with glutaryl chloride in a Friedel-Crafts reaction using AlCl₃ or SnCl₄ in CS₂ as Lewis acids, but the corresponding diketone was not formed and starting compound 3.15 was recovered from the reaction mixture. Also the acetal derivative 3.16, synthesized from 3.15 and ethylene glycol under Dean-Stark conditions, appeared to withstand acylation under these conditions, and gave only the unprotected aldehyde 3.15 after the reaction, which is not really surprising.

![Scheme 3.6 Attempted synthesis of a functionalized diketone.](image)

An alternative route to the 1,5-diketone (3.13R) is via a Stille cross-coupling reaction between 3.12 and tributyl[5-(1,3-dioxolan-2-yl)-2-methyl-3-thienyl]stannane 3.19 using a Pd- or Ni-catalyst (Scheme 3.8). An important feature of the Stille procedure is that various organic residues (alkyl, aryl, vinyl, alkynyl, etc.) can be transferred from tin to carbon in a cross-coupling reaction, which tolerates a wide variety of functional groups (nitro, nitrile, aryl halide, methoxy, ester, and even aldehyde substituents). Reactions with acid chlorides and substrates in the Stille reaction where a tin-derivative is attached to a thiophene are not widespread, but successful reactions under neutral conditions have been reported for pyrroles and furans. The most important drawback of the Stille coupling are the tin salts that are formed during the reaction, which are very toxic and often hard to remove.
The synthesis of the functionalized thiophene stannane **3.19** is straightforward (Scheme 3.7). First **3.15** was brominated with Br₂ in the presence of AlCl₃ to provide **3.17** regioselectively. The aldehyde was then protected with ethylene glycol and subsequently the bromine atom was substituted for a Bu₃Sn moiety via the corresponding lithium derivative to give **3.19** in a good yield.

Stannane thiophene **3.19** was then subjected to a coupling with glutaryl chloride in HMPA with PhCH₂Pd(PPh₃)₂Cl₂ as palladium source. This approach did not give the desired product but only starting material. Many variations on the Stille coupling have been carried out (Table 3.1), but the desired compound, 1,5-diketone **3.20** was not formed. The isolated products were **3.15**, **3.16** and starting material **3.19**.

<table>
<thead>
<tr>
<th>Acid chloride</th>
<th>Pd-cat</th>
<th>Mol %</th>
<th>Solvent</th>
<th>T (°C)</th>
<th>Yield (%)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glutaryl chloride</td>
<td>BnPd(PPh₃)₂Cl</td>
<td>1</td>
<td>HMPA</td>
<td>68</td>
<td>-</td>
<td>24</td>
</tr>
<tr>
<td></td>
<td>Pd(PPh₃)₂Cl₂</td>
<td>1</td>
<td>DMF</td>
<td>80</td>
<td>-</td>
<td>25</td>
</tr>
<tr>
<td></td>
<td>CuO</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>22</td>
</tr>
<tr>
<td></td>
<td>Pd(PPh₃)₂Cl₂</td>
<td>1/10</td>
<td>DMF</td>
<td>80</td>
<td>-</td>
<td>22</td>
</tr>
<tr>
<td></td>
<td>BnPd(PPh₃)₂Cl</td>
<td>1</td>
<td>THF</td>
<td>66</td>
<td>-</td>
<td>26</td>
</tr>
<tr>
<td></td>
<td>Pd(PPh₃)₂Cl₂</td>
<td>4</td>
<td>Toluene</td>
<td>95</td>
<td>-</td>
<td>27</td>
</tr>
<tr>
<td></td>
<td>CuCN 8 mol%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pd(PPh₃)₂Cl₂</td>
<td>5</td>
<td>Toluene</td>
<td>60</td>
<td>-</td>
<td>28</td>
</tr>
<tr>
<td>Acetylchloride</td>
<td>Pd(PPh₃)₄</td>
<td>5</td>
<td>Toluene</td>
<td>60</td>
<td>-</td>
<td>29</td>
</tr>
</tbody>
</table>

**Table 3.1 Attempted Stille Couplings.**
The catalytic cycle involved in the Stille coupling reaction using acid chlorides is generally accepted to involve the following steps (Scheme 3.9): (1) Formation of an active palladium species generated by reaction between the palladium compound and \( R'SnR''_3 \) bearing two ligands ("PdL_2"); (2) Oxidative addition of the organic moiety \( RCOCl \) to give "RCOPdL_2Cl"; (3) reaction with \( R'SnR''_3 \) to form a species with an \( R-Pd-R' \) linkage and \( R''_3SnCl \); (4) Reductive elimination to give \( RCO-R' \) and regenerate the active palladium species. What most likely happened in this case, is that the active palladium species in step (1) is not formed. Support for this conclusion comes from the observation that the reaction mixture does not turn black, which is normally observed. If there is no active palladium, the Stille coupling will obviously not succeed.

![Scheme 3.9 Catalytic cycle involved in the Stille coupling between an acid chloride and an arylbutyltin derivative](image)

Recently a palladium cross-coupling reaction using an acid chloride and trialkylborane derivatives.\(^{30}\) Also a system using an acid chloride and arylboronic acid derivatives was recently reported.\(^{31}\) These procedures might give better results in case of our system.

![Scheme 3.10 Synthesis of the diketone derivative via an organolithium intermediate.](image)
Ketones can also be prepared by addition of Grignard reagents or organolithium\(^{32}\) compounds to nitriles and subsequent hydrolysis. Here a reaction with an organolithium compound with a nitrile was chosen, because of the availability. Halogen atoms at the 3 or 4-position of thiophene derivatives can easily be exchanged by lithium at \(-70^\circ\text{C}\), and the resulting lithiated thiophene can subsequently undergo a reaction with a nitrile to form a ketone after hydrolysis. Commercially available glutaronitrile \(3.21\) was used as the dinitrile in this reaction. Unfortunately, the reaction of lithiated \(3.18\) with glutaronitrile did not give the desired 1,5-diketone derivative. Instead, only the dehalogenated and hydrolysed thiophene derivatives \(3.15\) and \(3.16\) could be isolated. When the same reaction was performed with propionitrile, no acylated thiophene was obtained either. When benzonitrile was used as a substrate, acylation of thiophene \(3.18\) took place, although the yield of this product was not more than 30\%. It is known that the addition of organolithium compounds to nitriles is subject to various side reactions, and especially \(\alpha\)-deprotonation is often a problem.\(^{32}\) With benzonitrile as substrate \(\alpha\)-deprotonation cannot take place, but with glutaronitrile it will lead to the formation of \(3.15\). Apparently, acylation of \(3.15\) and \(3.16\) at the 3,4-position is very difficult to achieve by conventional synthetic methods. It occurred to us that this might be due to the strong deactivating aldehyde functionality at the 5-position of the thiophene ring.

Other functional groups that provide a handle for further functionalization, but which are much less deactivating than an aldehyde, are the halogens. Moreover, by using halogens the straightforward reaction sequence described in Scheme 3.5 could again be applied. The use of 2-bromo-5-methyl-thiophene as a substrate for the Friedel-Crafts acylation was, however, not successful because it was found that during the Friedel-Crafts acylation the bromine was shifted to the 3-position, followed by acylation at the more reactive 2-position. This rearrangement has been observed before for bromothiophenes,\(^{33}\) and iodines are known to behave similarly. However, chlorines are less reactive and compared to the aldehyde also less deactivating substituents.

Scheme 3.11 Successful synthesis of 1,2-bis(5-chloro-2-methyl-thien-3-yl)cyclopentene.
The starting compound 3.23 for the synthesis of chlorinated switch 1 was easily prepared by chlorination of 2-methylthiophene (3.22) at the 5-position with NCS in a mixture of glacial acid and benzene. An alternative route to synthesize 3.23 is by reaction with sulfuryl chloride. After that, 2-chloro-5-methyl-thiophene 3.23 was subjected to a Friedel-Crafts reaction with AlCl₃ and glutaryl chloride in CS₂ at 0°C, and in this way 1,5-diketone 3.24 was obtained in 98% yield. Apparently, the only mildly deactivating chlorine does not prevent acylation of the thiophene in a Friedel-Craft reaction. It was also found that acylation of the thiophene occurs exclusively at the ortho position relative to the methyl group, whereby the often difficult separation of isomers is not required. The resulting 1,5-bis-(5'-chloro-2'-methylthien-3'-yl)pentadione 3.24 was then used in a McMurry reaction with TiCl₃(THF)₃ and Mg in THF at 40°C. Spectroscopic analysis revealed that instead of the expected product 1, the dechlorinated ring-closed product 3.25 was formed. Apparently, under these conditions the chlorines were reductively removed. Catalytic dechlorination of aromatic chlorides using Grignard reagents in the presence of (C₂H₅)₂TiCl₂ was reported by Takahashi et al. They also reported that the use of THF as a solvent dramatically improves the reactivity in this dehalogenation reaction. This was also observed in the present case as the dehalogenation was complete. Compound 3.25 is not very stable, and deteriorates even at 4°C within a week. McMurry reactions can, however, also be carried out with milder reduction agents like zinc to prepare the Ti(0) species in situ. Fortunately, when this reaction was carried out with TiCl₃(THF)₃ and Zn in THF at 40°C, the desired switch 1 could finally be obtained. Later it was found that instead of TiCl₃, which was suddenly removed from the commercial market, also TiCl₄ could be used, which has the advantage that it is easier to handle. The synthesis of compound 1 can be performed on a large scale (largest scale used to date was 1 mole) and requires only cheap starting materials. Furthermore the photochromic switch can easily be functionalized in many different ways as will be discussed in section 3.3.

It was of course tempting to investigate whether dithienylperfluorocyclopentene switches could also be synthesized following the same route as has been developed for 1. A Friedel-Crafts acylation with hexafluoroglutarlylchloride (3.26), AlCl₃ and benzene or toluene has been described in literature.

Unfortunately this reaction did not work for the combination of 3.23 and hexafluoroglutarlyl chloride, only an undefined black tar was obtained (Scheme 3.12). Also the use of SnCl₄ as a...
Lewis acid did not lead to any improvement. Most likely, the acylation does not occur as the acid chloride is destabilized by the strongly electron withdrawing fluorines.

In the literature the diethyl ester of hexafluoroglutaric acid (3.28) was also used in a reaction with phenyllithium to obtain the corresponding diketone.\(^{39}\) That same approach was used here. Hexafluoroglutareryl ethyl ester 3.29 was synthesized\(^{40}\) by a standard acid-catalysed esterification of hexafluoroglutaric acid in quantitative yield.

![Scheme 3.13](image)

**Scheme 3.13** Synthesis of 1,2-bis(5-chloro-2-methyl-thien-3-yl)perfluorocyclopentene.\(^{41}\)

In this alternative approach 2-chloro-5-methylthiophene (3.23) was used as the starting material. Treatment of this compound with a lithiation reagent would result in lithium-halogen exchange of the chlorine at the 2-position instead of deprotonation at the 4-position. Therefore this compound was first brominated at the 4-position using Br\(_2\) in chloroform to give 3-bromo-5-chloro-2-methylthiophene 3.30. This allows the regioselective lithiation at the 4-position. Compound 3.30 was then lithiated at -78°C in anhydrous diethyl ether using n-butyl lithium. Under these conditions compound 3.30 undergoes exclusive lithium-halogen exchange with the bromine at the 3-position, whereas the chlorine substituent is not affected. Lithiated 3.30 was then treated with a solution of 3.29 in ether at the same temperature. After acidic work-up the 1,5-diketone 3.27 was obtained in good yield, and other regioisomers were not formed. Finally, ring closure was achieved by the McMurry-coupling with TiCl\(_3\)(THF)\(_3\) and Zn in THF at 40°C to provide 2, which was purified by column chromatography. It is, of course, in principle possible to use thiophene derivatives other than 3.30 in this route, provided that they can be lithiated exclusively at the 3-position. However, it was found that 3-bromo-5-chloro-2-methylthiophene is an extremely versatile intermediate for the introduction of functional groups at a later stage at the 5,5\(^{'}\)-positions of the diarylperfluorocyclopentenes.

### 3.3 Derivatization of 1 and 2

Compounds 1 and 2 can easily undergo a lithium-chlorine exchange at *ambient temperature* (Scheme 3.14) thus providing a versatile handle to introduce functionality.
Quenching of the doubly lithiated dithienylcyclopentene switch with, for instance, DMF gave the bis-aldehydes 3.31 and 3.32\textsuperscript{42} in 52% and 66% yield, respectively (Scheme 3.14). The diacid 3.35 (Scheme 3.14) can be obtained via oxidation of 3.31,\textsuperscript{43} or directly by bubbling CO\(_2\)(g) through a solution of lithiated 1 (see chapter 6).\textsuperscript{44} This compound can be used to synthesize amides, which will be discussed in chapter 6 and 7. The bis-aldehyde is also a precursor for imines, for instance, the bis-phenylethylimine derivative (3.33), which has already been synthesized starting from 3.32.\textsuperscript{17} Furthermore a condensation reaction with malonitrile has been carried out to yield 3.34.\textsuperscript{42} Lithiated 1 or 2 can also be quenched with a Brønsted acid to give 3.25. Although this compound is not very stable (\textit{vide supra}), it is a reactive substrate for electrophilic substitutions like, for instance, a Friedel-Crafts reactions (see Chapter 8), and halogenation with the more reactive bromide or iodine. It has been found that in all of these examples substitution exclusively occurs at the most reactive 5-position.

\section*{Scheme 3.14 Derivatization of 1 and 2.}

\subsection*{3.3.1 Cross-coupling reactions}

Photochromic switches with an extended aromatic system are currently the focus of much attention because of their possible application in data storage, display technology, and molecular electronics. It would therefore be of great value if an approach to diarylcyclopentene based switches were available, in which an aromatic moiety could easily
be coupled with a dithienylcyclopentene building block. The bis(chlorothienyl)cyclopentene switches 1 and 2 are in principle such building blocks. The most straightforward method to extend the aromatic system of 1 and 2 is by a cross-coupling reaction using organometallic reagents with organic halides and related electrophiles. The different cross-coupling methods available for synthesis of bisaryls are: (1) Kumada-coupling; a reaction between a Grignard-reagent and an aryl halide catalyzed by Ni-phosphine complexes. (2) Suzuki-coupling; a reaction between a boronic acid derivative and an aryl halide catalyzed by Ni(0), Pd(0) or Fe(I). (3) Stille-coupling; a reaction between an organostannane aryl derivative and an aryl halide catalyzed by Pd(0) or Ni(0). (4) aryl C-C bond formation reactions mediated by organozinc reagents and aryl halides catalyzed by Pd(II), Cu(I), Ni(II), Co(II), Co(III), Fe(III) or Mn(II). In order to attach an aryl group to switch 1 or 2, the switch can be regarded as the aryl halide that can be allowed to react with an organometallic reagent or a boronic acid derivative. Alternatively, the switch can be transformed into the organometallic compound or a boronic acid. Because many arylboronic acids and organometallic compounds are commercially available nowadays, it is easier to use the switch as aryl halide.

### 3.3.2 The Kumada cross-coupling reaction

The first approach to synthesize the oligoaryl switch was via the Kumada cross-coupling reaction, because of the good experience in our group with this reaction for the synthesis of oligothiophenes.

![Scheme 3.15 Kumada cross-coupling reactions.](image)

First the coupling between 3.23 and 3.38 in diethyl ether with Ni(dppp)Cl₂ as catalyst was performed. 5-Methyl-2,2'-bithiophene 3.39 was successfully obtained in 69% yield. Switch 1 was then subjected to analogous reaction conditions, but unfortunately only a mono cross-coupling had taken place to give 3.41 in 40% yield together with a small amount of starting material. Increasing the amount of catalyst to even stoichiometric quantities did not improve this result and only the monoadduct could be obtained. Compound 3.41 is of course very versatile in the synthesis of non-symmetric switches.
Another Ni-phosphine complex often used in the Kumada cross-coupling is Ni(PPh₃)₂Cl₂. When using 1 equivalent of this catalyst under the same conditions as described above, the starting material, mono and the bis-product were recovered from the reaction mixture in a 1/1/4 ratio. Reduction of the amount of catalyst resulted in a lower yield of the bis-product, and at 10 mol% of catalyst or less no bis-product was formed at all. This route clearly does not work well. Most likely, the lower reactivity of the chloride compared to bromides or iodides is the main problem in this Kumada cross-coupling reaction. Usually aryl bromides or aryl iodides are used in the Kumada cross-coupling because of their higher reactivity, although a recent study showed that also chlorobenzene derivatives can be successfully coupled with Grignard-reagents by means of Pd₂(dba)₃ and N-heterocyclic carbenes 3.43 as ligands rather than phosphines. Another successful method is based on the [Pd₂(dba)₃]/PtBu₃ (3.42) system (Scheme 3.17), but the successful application of chlorothiophene derivative in the Kumada cross-coupling have not yet been reported. The Kumada cross-coupling could in principle also be carried out between the Grignard reagent prepared from the chlorinated switch 1 and an aryl bromide, thereby avoiding the two-step conversion of the chlorinated switch 1 to a more reactive brominated switch. In order to investigate the feasibility of this approach, some attempts were made to prepare the Grignard-reagent of 2-chloro-5-methyl-thiophene 3.23 in the following ways: (1) with Mg in diethyl ether or THF, (2) in an exchange reaction with EtMgBr in ether and (3) a lithiation of the chlorine followed by a reaction with MgBrOEt₂. None of the methods mentioned worked. Based on our synthetic experience with the chemistry of these compounds, we can safely say that if it does not work for 3.23, it will not work for 1 either. The most straightforward solution to the successful application of the Kumada cross-coupling seems to be the two-step conversion of the chlorinated switch 1 to a more reactive brominated switch. This modification was, however, not further investigated, because in the meanwhile it also has turned out that it was not possible to prepare Grignard reagents of 5’-bromo-[2,2’-bisthiophene-5-(pyridin-4’-yl)] or 2-bromothiophene-5-(pyridin-4’-yl) (which will be discussed in chapter 5), thereby serious limiting the scope of this approach.

### 3.3.3 The Suzuki cross-coupling reaction

An alternative to the Kumada cross coupling of two aryl fragments is the Suzuki coupling. In the Suzuki cross coupling, an aryl boronic acid is coupled to an aryl halide by using Ni(0), Pd(0) or Fe(0) complexes as a catalysts. These cross-coupling reactions often proceed under mild conditions, provided the organoboron compound is activated with a
suitable base. The key step in this reaction involves the insertion of Pd(0) in the aryl halogen bond. It has proven to be a quite general technique for a wide range of selective C-C bond formation reactions. Organoboronic acids are convenient reagents and are generally thermally stable and inert to water and oxygen, thus allowing their handling without special precautions. Many organoboronic acids are commercially available nowadays or can be prepared from organolithium or magnesium reagents and trialkyl borates. A very wide range of palladium (0) catalysts can be used for this reaction. Pd(PPh₃)₄ is the most commonly used, but PdCl₂(PPh₃)₂ and Pd(OAc)₂ plus PPh₃ or other phospine ligands are also efficient since they are stable to air and readily reduced to the active Pd(0) complexes by the organometallics or phosphines used for the cross-coupling reaction. Aqueous Na₂CO₃ is most frequently used as base and DME as solvent. Recently also the first asymmetric Suzuki-coupling was reported by Buchwald et al.⁵⁰ So far, mostly aryl bromides, iodides, and triflates have been used as starting materials for Suzuki reactions, because of their higher reactivity.

\[
\text{R} \quad \text{S} \quad \text{Cl} \quad + \quad \text{Ar(BOH)₂} \quad \xrightarrow{\text{Pd-cat., L, base, solvent}} \quad \text{R} \quad \text{S} \quad \text{Ar}
\]

**Scheme 3.17 Basic reaction-scheme of the attempted Suzuki cross-coupling reactions.**

Due to the industrial interest in the functionalization of economically attractive aryl chlorides there is currently a great deal of interest in the coupling of aryl chlorides with arylboronic acids.⁵¹ Although nickel catalysts are useful for this reaction as has been demonstrated by Indolese⁵² and Saito et al.,⁵³ most studies have focussed on palladium catalysts. Recently significant breakthroughs in this area have been made by Fu,⁵⁴ Buchwald,⁵⁵ Nolan⁵⁶, Beller⁵⁷ and Trudell.⁵⁸ Suzuki-coupling of chlorothiophene derivatives has not been reported yet, but the recently developed systems (*vide supra*) looked promising for our ends. The following reactions were carried out (Scheme 3.17): (1) 1 with phenylboronic acid in dioxane at 80°C with Cs₂CO₃ as base and [Pd₂(dba)₃]/PtBu₃ as a catalyst;⁵⁴ (2) 1 with 2-thiopheneboronic acid under the same conditions as described for (1); (3) 1 with 2-thienylboronic acid in dioxane at 80°C with Cs₂CO₃ as base and the [Pd₂(dba)₃]/1,3-bis[2,4,6-trimethylphenyl]imidazol-2-ylidene (3.43) as the catalyst;⁵⁶ (4) 1 with phenylboronic acid under the same conditions as described at (3); (5) The same as described at (4) but with 2 times as much of both ligand and Pd-catalyst; (6) The same as described at (4) but with 3 times as much of both ligand and Pd-catalyst. Unfortunately none of these attempts led to cross-coupled product, and starting compound 1 was recovered in all cases. Apparently, also in the Suzuki cross coupling the low reactivity of the chlorothienyl bond prevents the coupling reaction from taking place. The
The most obvious solution to this problem is to convert the chloride switch 1 into the more reactive bromide derivative or to the boronic ester derivative. This latter approach has been applied before in the synthesis of diarylperfluorocyclopentene derivatives by Lehn et al., \(^5^9\) starting from 1,2-bis(5'-bromo-2'-n-hexyl-thien-3'-yl)perfluorocyclopentene. It was found that also 1 could also be converted to a boronic acid by means of an organolithium reagent, which was then allowed to react with an aryl halide in a Suzuki cross coupling reaction.

First, 1 was lithiated with BuLi in THF at room temperature, and then treated with B(OBu)\(_3\) to provide the bis-boronic ester 3.41. This unpurified material was used directly in the Suzuki reaction without any work-up because it was found that the bis boronic ester 3.41 easily hydrolyses to the dehalogenated switch 3.25 during isolation. This has also been observed by Lehn et al.\(^5^9\) for the corresponding bis-2'-n-hexylthiophen-3'-yl-perfluorocyclopentene. For the Suzuki cross coupling reaction, Pd(PPh\(_3\))\(_4\) was added as palladium source, Na\(_2\)CO\(_3\) as base, THF as solvent and several drops of ethylene glycol were added as cosolvent. This system worked excellent, and after column chromatography, yields of up to 70% were reached. Switch 1 gave much higher yields then switch 2 in the Suzuki reaction, even when Lehn’s conditions\(^5^9\) were applied. In chapter 4 the synthesis of various phenyl derivatives of 1 and 2 are described using this method and their photochromic properties compared. The synthesis of oligothiophene derivatives of 1 using this method are described in chapter 5.

### 3.4 Photochromic behavior of the various derivatives of compounds 1 and 2

The photochromic behaviour of 1, derivatives thereof, and 2 was studied by irradiation with a high pressure mercury lamp at selected wavelengths, and monitored by UV-Vis spectroscopy. Table 3.2 shows the absorption maxima for the open and closed forms of the synthesized derivatives and their corresponding extinction coefficients. During this reaction a photostationary state (PSS) will always be reached. Due to non-zero absorption of the closed form in the UV spectral region, both ring-closure and ring-opening take place after
Chapter 3

photoexcitation, leading to an equilibrium situation (PSS) determined by the quantum yields of ring-closing and ring-opening. However, quantum yields obtained for diarylethenes showed that the cyclization is more efficient than the ring-opening\(^{1,60}\). Therefore it can be assumed that the PSS represents the closed form of the switch. Because we did not have the absorption spectra of the closed form, the extinction coefficients reported in Table 3.2 are those of the PSS. Several attempts were undertaken to separate the open and closed form by column chromatography and HPLC, but they were unsuccessful. Visible light was used in order to switch the closed form back to the open form, which lead to full recovery of the open form. Compared to the known corresponding perfluorocyclopentene derivatives, the wavelengths at the absorption maxima of the closed forms of the cyclopentene switches showed a blue shift. Only 3.34 measured in benzene showed the same absorption maximum in the closed form as was reported earlier for the perfluorocyclopentene analog.\(^{42}\)

![UV/Vis spectrum of an open and closed form](image)

<table>
<thead>
<tr>
<th>Compound</th>
<th>R / R'</th>
<th>Solvent</th>
<th>(\lambda_{\text{max}}) open and ((\varepsilon))</th>
<th>(\lambda_{\text{max}}) PSS and ((\varepsilon))</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>H / Cl</td>
<td>n-hexane</td>
<td>240 (1901)</td>
<td>276, 444 (116)</td>
</tr>
<tr>
<td>2</td>
<td>F / Cl</td>
<td>n-hexane</td>
<td>242 (2486), 300 (483)</td>
<td>334 (1932), 331 (571), 501 (390)</td>
</tr>
<tr>
<td>3.14</td>
<td>H / Me</td>
<td>n-hexane</td>
<td>196 (2077), 233 (2395), 275(^a)</td>
<td>201 (1280)</td>
</tr>
<tr>
<td>3.25</td>
<td>H / H</td>
<td>n-hexane</td>
<td>229 (2100), 270(^a) (924)</td>
<td>231(^a) (997)</td>
</tr>
<tr>
<td>3.31</td>
<td>H / CHO</td>
<td>benzene</td>
<td>280 (4097), 318 (1486)</td>
<td>383 (1661), 379 (1758), 580 (1473)</td>
</tr>
<tr>
<td>3.33</td>
<td>H / CH=NCH(Me)Ph</td>
<td>n-hexane</td>
<td>271 (5396), 308(^a) (2362)</td>
<td>366 (1272), 555 (1240)</td>
</tr>
<tr>
<td>3.34</td>
<td>H / CH=C(CN)$_2$</td>
<td>benzene</td>
<td>334 (2742), 392 (3029)</td>
<td>358 (1829), 448 (1787), 732 (2177)</td>
</tr>
<tr>
<td>3.35</td>
<td>H / COOH</td>
<td>methanol</td>
<td>252 (2972), 290(^a) (991)</td>
<td>253 (1500), 347 (865), 531 (684)</td>
</tr>
<tr>
<td>3.36</td>
<td>H / CONH[C$_2$H$_5$]</td>
<td>methanol</td>
<td>264 (2872), 298(^a) (987)</td>
<td>269 (1290), 347 (800), 522 (885)</td>
</tr>
<tr>
<td>3.46</td>
<td>H / Ph</td>
<td>benzene</td>
<td>277 (5259), 303(^a) (3936)</td>
<td>290 (3669), 358 (1828), 531 (2562)</td>
</tr>
</tbody>
</table>

\(^a\) Shoulder

**Table 3.2** UV-Vis data \(\lambda_{\text{max}}\) (nm) and \(\varepsilon\) (10\(^4\) cm\(^-1\)M\(^{-1}\)), in parenthesis) values of the open and PSS of several compounds. Concentration of the solutions is about 1 x 10\(^{-5}\)M.
First a solution of \( \mathbf{1} \) in n-hexane was studied (Figure 3.1a). The open form showed a distinct absorption in the UV region, after irradiation using the whole spectrum of the mercury lamp, a clear absorption appeared in the visible region with \( \lambda_{\text{max}} = 444 \text{ nm} \) (\( \varepsilon_{\text{PSS}} = 1.16 \times 10^3 \text{ cm}^{-1} \text{ M}^{-1} \)) due to formation of the closed form, which has an extended conjugated structure. After longer irradiation times (\( t > 10\text{ min} \)), \( \mathbf{1} \) started to degrade (Figure 3.1a), probably to the compound proposed by Branda \textit{et al.} (Scheme 2.22).\(^6\) Irradiation of the closed form of \( \mathbf{1} \) at \( \lambda = 435 \text{ nm} \), \textit{i.e} nearby its absorption maximum, the closed form did not fully return to the open form, because of degradation. Apparently the photochemical switching of \( \mathbf{1} \) can take place, but the process is not fully reversible due to degradation processes, which makes \( \mathbf{1} \) unsuitable as a photochromic switch. For compound \( \mathbf{2} \) different behavior was observed. After irradiation at \( \lambda = 313 \text{ nm} \) switch \( \mathbf{2} \) also showed a distinct absorption in the visible region at \( \lambda_{\text{max}} = 501 \text{ nm} \) (\( \varepsilon_{\text{PSS}} = 3.9 \times 10^3 \text{ cm}^{-1} \text{ M}^{-1} \)) due to formation of the closed form. Irradiation of the closed form with \( \lambda > 460 \text{ nm} \) caused a complete conversion to the open form. For this compound it is possible to switch selectively between the open and the closed form for at least five times without any noticeable degradation.

It would be very interesting to see how the derivatives of \( \mathbf{1} \) are behaving upon irradiation with light. After irradiation of compound \( \mathbf{3.31} \) in benzene at \( \lambda = 313 \text{ nm} \) a new absorption band appeared at 583 nm due to formation of the closed form. Visible light was used in order to switch the closed form back to the open form, which lead to full conversion of the closed form. Diarylethenes \( \mathbf{3.14} \) and \( \mathbf{3.25} \) turn yellow upon UV-irradiation next to compounds \( \mathbf{1} \) and \( \mathbf{2} \), which is quite unusual. Most derivatives of \( \mathbf{1} \) that are described in this thesis turned purple upon irradiation, whereas derivatives of \( \mathbf{2} \) mostly turned blue upon irradiation. Diarylethene compounds that turn yellow after irradiation are rare,\(^6\) but are indispensable for covering the whole color spectrum.

\( \mathbf{3.14} \) and \( \mathbf{3.25} \) do not show maxima in the visible region after irradiation with UV-light. The absorption spectra can be compared with the absorption spectrum of \( \mathbf{1} \) after prolonged irradiation (Figure 3.1a). These switches are not suitable for

\textbf{Figure 3.1} (a) UV-Vis spectra of \( \mathbf{1} \) (1.09 \( \times \) 10\(^{-5} \) M in n-hexane) before (---), after (----) irradiation for 5 min, and after irradiation for 40 min (----) and (b) \( \mathbf{3.31} \) (2.05 \( \times \) 10\(^{-5} \) M in benzene) before (---) and after (----) irradiation at 313 nm.
application, because it is too difficult to distinguish between the open and closed form. The switching behavior of the compounds 3.33, 3.35, 3.36 and 3.46 is excellent. The coloring-bleaching cycles can be performed several times without degradation. Dialdehyde 3.31 showed an ± 8% decrease in absorption (UV-Vis) after one cycle, and the perfluorinated bis-aldehyde 3.32 showed the same degradation behavior.42 On the other hand, the bis-imine derivative 3.33 performed very well and after ten cycles no degradation was detected. Five coloring-bleaching cycles were performed with compounds 3.33, 3.36 and 3.46, and they also showed no degradation and the cycles were still fully reversible. Switch 3.34 also showed good switching behavior, but is thermally unstable at elevated temperatures. The half-life of the thermal ring opening in benzene at 60°C of compound 3.34 is 4.27 min. Compared to the perfluorocyclopentene analog42 it shows slower thermal ring opening. It appears that if the conjugation of switch 1 is increased, the switch shows good switching behavior and little fatigue, whereas if the electron withdrawing properties of the substituents attached to 1 become too strong, the thermal stability decreases. This latter decrease in thermal stability was also observed for perfluorocyclopentene-derivatives.

The photochemical ring closure of 3.31 (λ = 313 nm), 3.33 (λ = 313 nm) and 3.34 (λ = 405 nm) in CDCl₃ was observed by ¹H NMR. Both the chemical shift of the methyl group and the thiophene proton before and after irradiation were investigated. The results are displayed in Table 3.3.

<table>
<thead>
<tr>
<th>Compound</th>
<th>δCH₃ open</th>
<th>δCH₃ closed</th>
<th>δCH open</th>
<th>δCH closed</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.31</td>
<td>2.04</td>
<td>2.17</td>
<td>7.42</td>
<td>6.72</td>
</tr>
<tr>
<td>3.33</td>
<td>1.97</td>
<td>1.94</td>
<td>6.95</td>
<td>7.37</td>
</tr>
<tr>
<td>3.33</td>
<td>2.14</td>
<td>2.05</td>
<td>7.40</td>
<td>6.56</td>
</tr>
</tbody>
</table>

Table 3.3 ¹H NMR chemical shift data before and after irradiation (δ in ppm).

The photochemical reaction has proven to be a clean process. After irradiation only a new set of signals appeared corresponding to the closed form. Other products were not observed.

### 3.5 Conclusions

In this chapter the successful syntheses of diarylethene-switches 1 and 2 have been described. The reactions can be performed on large scale (the largest scale at which we performed this reaction was one mole) and cheap(er) starting materials can be used compared to the commonly employed syntheses. These developed chloride switches can be easily derivatized by lithiation and quenching with different electrophiles. Another versatile reaction for successful modification of 1 is the Friedel-Crafts reaction. The scope could even be expanded to the formation of bisaryl carbon-carbon bond formation by means of the Suzuki-reaction. It appears that these bis(thien-3-yl)cyclopentenes, which are now readily accessible, show photochromic behaviour similar to known diarylethenes. Provided the
proper substituents are present thermal irreversibility and fatigue resistance are observed. These synthesis methods will be applied to the synthesis of various different diarylethenes, the synthesis and properties of which will be discussed in this thesis. Also the difference in switching behavior between the cyclopentene- and perfluorocyclopentene will be discussed in chapter 4.

3.6 Experimental section

General information:
Starting materials were commercially available and were used without further purification. Diethyl ether and THF were distilled from Na. Melting points were determined on a Büchi melting point apparatus and are uncorrected. $^1$H NMR were recorded on a Varian Gemini-200 spectrometer (at 200 MHz), a Varian VXR-300 spectrometer (at 300 MHz) or a Varian 500 spectrometer (at 500 MHz) at ambient temperature. The splitting patterns are designated as follows: s (singlet); d (doublet); dd (double doublet); t (triplet); q (quartet); m (multiplet) and br (broad). $^{13}$C NMR were recorded on a varian Gemini-200 (at 50.3 MHz), a varian VXR-300 (at 75.4 MHz), or a Varian Gemini-500 (at 125.7 MHz). $^{19}$F-NMR were recorded on a Varian Gemini-200 spectrometer (at 188.2 MHz) or a Varian 500 (at 470.3 MHz). Chemical shifts are denoted in $\delta$ (ppm) referenced to the residual protic solvent peaks. Coupling constants $J$, are denoted in Hz. Masses were recorded with a MS-Jeol mass spectrometer, with ionisation according to CI$, DEI$ or EI$^+$ procedures by A. Kiewiet. The dithienylethene switches are sometimes hard to sublimate and only by means of DEI (desorption electron ionization) it is then possible to obtain the mass spectrum. However, this ionization technique is so fast that it is impossible to get a exact mass, due to an unfavorable signal/noise ratio. Elemental analyses were performed at the analytical department of the Stratingh Institute by H. Draayer, J. Ebels and J. Hommes. Aldrich silica gel Merck grade 9385 (230-400 mesh) was used for column chromatography. The solvents were distilled and dried before use, if necessary, using standard methods. Reagents and starting materials were used as obtained from Aldrich, Acros Chimica or Fluka. Derivates synthesized starting from compounds 1 or 2 are light sensitive and were therefore exclusively handled in the dark using brown glassware, and column chromatography was performed in yellow light. Irradiations were performed with a high pressure mercury lamp (200W, Oriel) and the appropriate filters (Andover corporation)

1,5-Bis(2'-methyl-5'-methylthien-3'-yl)pentadione (3.13): AlCl$_3$ (7.02 g, 52.7 mmol) and 2,5-dimethylthiophene (5 ml, 43.9 mmol) were added to CS$_2$ (100 ml). The mixture was heated to reflux and glutarylchloride 3.12 (3.71 g, 21.95 mmol) in CS$_2$ (25 ml) was added dropwise. After the addition of glutaryl chloride, the reaction mixture was refluxed for 2 hours. After cooling to r.t. cold H$_2$O (50 ml) was carefully added to the reaction mixture, the water layer was extracted with diethyl ether (3 x 75 ml). The combined organic phases were
washed with sat. NaHCO₃ solution (1 x 50 ml) and water (1 x 50 ml), dried (Na₂SO₄), filtered and the solvent evaporated in vacuo to yield a yellow solid (3.78 g, 54%), which was used in subsequent reactions without further purification. 

\[ ^1H \text{ NMR (200 MHz, CDCl}_3): \delta_{H} 1.85 \text{ (s, CH}_3), 1.95-2.09 \text{ (m, 2H), 2.34 (s, 6H), 2.73 (t, } J = 7.2, \text{ 9.6 Hz, 4H), 6.41 (s, 2H); } ^{13}C \text{ NMR (75.4 MHz, CDCl}_3): \delta_C 14.88 \text{ (q), 15.97 (q), 18.49 (t), 40.61 (t), 125.96 (d), 134.91 (s, 135.33 (s), 147.11 (s), 195.91 (s); MS (EI): 320 [M⁺]; IR (Nujol): 1669 cm}^{-1} (\text{C=O). Anal. calc. for: C}_{17}H_{20}O_2S_2: C 63.72, H 6.29; found: C 64.14, H 6.33.} 

1,2-Bis(2'-methyl-5'-methylthien-3'-yl)cyclopentene (3.14): TiCl₃(THF)₃ (0.42 g, 1.13 mmol) and Mg (0.069 g, 2.83 mmol) were stirred under nitrogen in dry THF (30 ml) at 40°C until the blue colour of TiCl₃(THF)₃ was disappeared and then 3.13 (0.36 g, 1.13 mmol) was added to the black solution. After stirring for 2 h at 40°C, the mixture was poured into hydrochloric acid (6N, 50 ml). This solution was extracted with diethyl ether (2 x 50 ml), and the combined diethyl ether layers were washed with saturated sodium bicarbonate solution (2x 25 ml) and H₂O (1 x 25 ml), dried (Na₂SO₄), filtered and the solvent evaporated in vacuo to yield a brown oil (0.28 g, 86%). Chromatography of the oil over silica gel (hexane/ethyl acetate = 9/1) afforded the compound as a white solid (0.19 g, 58%). 

\[ ^1H \text{ NMR (300MHz, CDCl}_3): \delta_{H} 1.85 \text{ (s, 6H), 1.95-2.09 (m, 2H), 2.34 (s, 6H), 2.73 (t, } J = 7.6 \text{ Hz, 7.2Hz, 4H), 6.41 (s, 2H); } ^{13}C \text{ NMR (75.4 MHz, CDCl}_3): \delta_C 13.77 \text{ (q), 14.91 (q), 22.67 (t), 38.23 (t), 125.94 (d), 131.91 (s), 134.04 (s), 134.78 (s), 150.85 (s); MS (EI): 288 [M⁺]; Anal. calc. for: C}_{17}H_{20}S_2: C 70.78, H 6.99; found: C 70.13, H 6.92.} 

2-Methyl-5-thiophenecarbaldehyde (3.15): A mixture of 2-methylthiophene 3.22 (24.2 ml, 0.25 mol) and DMF (25.6 ml, 0.33 mol) was cooled down to 0°C and then POCl₃ (29.4 ml, 0.32 mol) was added very slowly. After the addition was complete the mixture was heated and at about 70°C a vigorous reaction occurred. Immediately an ice bath was put under the vessel until no HCl gas evolved anymore. The mixture was then heated for an additional hour at 110°C. After cooling to r.t the mixture was poured into icedwater (200 ml) and neutralised with sodium bicarbonate. The resulting slurry was extracted with diethyl ether (3 x 100ml), drying (NaSO₄) and after evaporation of the solvent under vacuo 3.15 (27.3 g, 87%) was obtained. 

\[ ^1H \text{ NMR (300MHz, CDCl}_3): \delta_{H} 2.49 \text{ (s, 3H), 6.83 (d, } J = 3.6, \text{ 1H), 7.53 (d, } J = 3.6, \text{ 1H), 9.73 (s, 1H); } ^{13}C \text{ NMR (75.4 MHz, CDCl}_3): \delta_C 16.00 (q), 126.93 (d), 137.20 (d), 150.85 (s), 151.43 (s), 182.41 (d); MS (EI): 126 [M⁺].} 

2-(5-Methyl-2-thienyl)-1,3-dioxolane (3.16): Under Dean-Stark conditions a mixture of 3.15 (4 g, 22.6 mmol), ethyleneglycol (2.5 ml, 45.2 mmol) and p-TsOH (catalytic amount) was refluxed in benzene (200 ml). After 18 h the solution was cooled down to r.t. and poured into NaOH (3M, 150 ml). The organic layer was subsequently washed with NaOH (3M, 2 x 50 ml) and H₂O (100 ml) and then dried (NaSO₄). After evaporation of the solvent 3.16 (7.08 g, 38.0 mmol) was obtained. 

\[ ^1H \text{ NMR (300 MHz, CDCl}_3): \delta_{H} 2.46 (s, 3H), 3.95-4.14 (m, 4H), 6.01 (s, 1H), 6.62 (d, } J = 3.3 \text{ Hz, 1H), 6.94 (d, } J = 3.3 \text{ Hz, 1H); } ^{13}C \text{ NMR (75.4 MHz,}
Synthesis of Diarylethene Derivatives

CDCl₃: δC 15.32 (q), 65.06 (t), 100.35 (d), 124.60 (d), 126.30 (d), 138.92 (s), 141.10 (s); MS (EI): 170 [M+].

4-Bromo-5-methyl-2-thiophenecarbaldehyde (3.17): AlCl₃ (26.40 g, 198 mmol) was placed in a three-necked flask equipped with a powerful stirrer, and 3.15 (10.0 g, 79.3 mmol) was added under vigorous stirring, while keeping the temperature below 60°C. To the resulting brown liquid Br₂ (4.70 ml, 91.2 mmol) was added at once and this mixture was left for 1h. Then it was poured into HCl conc. (50 ml) and enough ice to allow hydrolysis at 0°C. The water phase was extracted with diethyl ether (3 x 50 ml). The combined organic layers were washed with saturated bicarbonate solution (2 x 50 ml) and H₂O (50 ml). After drying (Na₂SO₄) and evaporation of the solvent, the resulting tar was subjected to a bulb to bulb distillation, which yielded a off white solid (11.4 g, 70%), b.p. 85-87°C/ 9mm Hg. ¹H NMR (300MHz, CDCl₃): δH 2.45 (s, 3H), 7.56 (s, 1H), 9.74 (s, 1H); ¹³C NMR (75.4 MHz, CDCl₃): δC 15.81 (q), 111.13 (s), 138.60 (d), 140.04 (s), 145.70 (s), 181.48 (d); MS (EI): 206 [M+].

2-(4-Bromo-5-methyl-2-thienyl)-1,3-dioxolane (3.18): Under the same conditions as described for 3.16, 3.17 (5.95 g, 28.9 mmol) was reacted with ethylene glycol (4.0 ml, 69.3 mmol) and p-TsOH (catalytic amount) in benzene (200 ml) to afford 3.18 (6.43 g, 89%). ¹H NMR (300MHz, CDCl₃): δH 2.36 (s, 3H), 3.94-4.10 (m, 4H), 5.98 (s, 1H), 6.95 (s, 1H); ¹³C NMR (75.4 MHz, CDCl₃): δC 14.76 (q), 65.09 (t), 99.58 (t), 108.35 (s), 128.68 (d), 135.23 (s), 138.64 (s); MS (EI): 249 [M+]

Tributyl[5-(1,3-dioxolan-2-yl)-2-methyl-3-thienyl]stannane (3.19): Under nitrogen 3.18 (0.5 g, 2 mmol) in THF (25 ml) was cooled to -80°C and n-BuLi (1.56 ml of 1.6M solution in hexane, 2.5 mmol) was added slowly. After addition the temperature was allowed to rise to -50°C during 30 min. The temperature was lowered to -70°C and SnBu₃Cl (0.57 ml, 2.1 mmol) was added at once. The cooling bath was removed, when the temperature had reached r.t., the reaction mixture was poured into an aqueous NaOH solution (50ml, 0.01M) and extracted with diethyl ether (3 x 25 ml). After drying (Na₂SO₄) and evaporation of the solvent yellow oil was obtained (0.73 g, 80%). ¹H NMR (300MHz, CDCl₃) δH 0.87 (t, J = 6.9 Hz, 7.5 Hz, 9H), 1.04 (t, J = 8.4 Hz, 8.1 Hz, 6H), 1.25-1.34 (m, 6H), 1.43-1.53 (m, 6H), 2.47 (s, 3H), 3.93-4.12 (m, 4H), 6.02 (s, 1H), 6.94 (s, 1H); ¹³C NMR (75.4 MHz, CDCl₃): δC 8.58 (q), 9.90 (t), 13.48 (q), 27.19 (t), 29.00 (t), 64.98 (t), 100.53 (d), 132.82 (d), 135.28 (s), 138.79 (s), 146.57 (s); MS (CI): 461 [M+H⁺]

2-Chloro-5-methylthiophene (3.23): 2-Methylthiophene (100 ml, 1.03 mol) and N-chlorosuccinimide (152 g, 1.13 mol) were added to a stirring solution of benzene (400 ml) and acetic acid (400 ml). The suspension was stirred for half an hour at room temperature, then after one hour of heating at reflux, the cooled mixture was poured into an 3M aq NaOH solution (300 ml). The organic phase was washed with a 3 M aq NaOH solution (3 x 300 ml), dried (Na₂SO₄), filtered and the solvent evaporated in vacuo to yield a slightly yellow liquid.
Purification of the product by vacuum distillation (19 mm, 55°C) afforded a colourless liquid
(111 g, 84%). $^1$H NMR (300 MHz, CDCl$_3$): δ$_H$ 2.30 (s, 3H), 6.40-6.42 (m, 1H), 6.58 (d, $J = 2.2$ Hz, 1H); $^{13}$C NMR (75.4 MHz, CDCl$_3$): δ$_C$ 15.24 (q), 124.29 (s), 125.68 (s), 126.39 (s),
138.40 (s); MS (EI): 131 [M+]; Anal. calc. for: C$_5$H$_5$ClS: C 45.29, H 3.80; found: C 45.76, H
3.77. b.p. 55°C (19 mm).

1,5-Bis(5′-chloro-2′-methylthien-3′-yl)pentadione (3.24): Under vigorous stirring AlCl$_3$
(48 g, 0.36 mol) was added in portions to an ice cooled solution of 3.23 (32.3 ml, 0.3 mol)
and glutarylchloride (25 g, 0.15 mmol) in CS$_2$ (300 ml). After addition of AlCl$_3$, the reaction
mixture was stirred for 2 h at room temperature. Then ice-water (100 ml) was carefully added
to the reaction mixture, the water layer was extracted with ether (3 x 150 ml). The combined
organic phases were washed with water (1 x 100 ml), dried (Na$_2$SO$_4$), filtered and evaporated
in vacuo to yield a brown tar (53 g, 98 %). This tar can be purified by flash chromatography
(hexane/ethyl acetate = 9/1), a white solid is then obtained (25.9 g, 48%). For further
reactions it is not necessary to purify this tar. $^1$H NMR (200 MHz, CDCl$_3$): δ$_H$ 1.98-2.12 (m,
2H), 2.66 (s, 6H), 2.86 (t, $J = 6.8$ Hz, 2H), 7.19 (s, 2H); $^{13}$C NMR (125.7 MHz, CDCl$_3$):
δ$_C$ 15.97 (q), 18.06 (t), 40.42 (t), 125.19 (d), 126.68 (s), 134.73 (s), 147.62 (s), 194.74 (s); MS
(EI): 360 [M+]; IR (Nujoll): 1675 cm$^{-1}$ (C=O). Anal. calc. for: C$_{15}$H$_{14}$Cl$_2$O$_2$S$_2$: C 49.87, H
3.91; found: C 49.46, H 3.94.

1,2-Bis(2′-methylthien-3′-yl)cyclopentene (3.25) TiCl$_3$(THF)$_3$ (1.57 g, 4.23 mmol) and Mg
(0.26 g, 10.6 mmol) were stirred under nitrogen in dry THF (30 ml) at 40°C until the blue
colour of TiCl$_3$(THF)$_3$ was disappeared, whereup 3.24 (1.53 g, 4.23 mmol) was added to the
black solution. After stirring for 30 min at 40°C, the mixture was cooled down to r.t. and
poured into hydrochloric acid (6N, 50 ml). The resulting mixture was extracted with diethyl
ether (2 x 50 ml). The combined organic layers were washed with saturated sodium
bicarbonate solution (2x 25 ml) and H$_2$O (1 x 25 ml), dried (Na$_2$SO$_4$), filtered and the solvent
evaporated in vacuo to yield a brown oil (0.79 g, 72%). Chromatography of the oil over silica
gel (pet. ether 40/60) afforded the compound as a yellow oil (0.22 g, 20%). $^1$H NMR (200
MHz, CDCl$_3$): δ$_H$ 1.92 (s, 6H), 1.97-2.14 (m, 2H), 2.79 (t, $J = 7.6$ Hz, 7.4Hz, 4H), 6.74 (d, $J$
= 5.0Hz, 2H), 6.95 (d, $J = 5.0$Hz, 2H); $^{13}$C NMR (125.7 MHz, CDCl$_3$): δ$_C$
13.88 (q), 22.86 (t), 38.31 (t), 120.99 (d), 128.04 (s), 134.31 (d), 136.51 (s), 143.15 (s); MS
(EI): 260 [M+].

1,2-Bis(5′-chloro-2′-methylthien-3′-yl)cyclopentene (1): “Instant method”; A mixture of
3.24 (1.13 g, 3.13 mmol), TiCl$_3$(THF)$_3$ (2.32 g, 6.26 mmol), Zn dust (0.82 g, 7.83 mmol) and
THF (30 ml) was stirred under nitrogen at 40°C for 1 h. The mixture was cooled to r.t. and
poured over a glass filter containing with silica gel that was pretreated with PE ether. The
silica was rinsed with PE ether 40/60. After evaporation of the solvent a yellow solid (0.97 g,
94%) was obtained. Pure 1 was obtained as a white solid (0.45 g, 44%) was obtained after
purification by chromatography over silica gel (PE ether 40/60). $^1$H NMR (200 MHz,
CDCl$_3$): δ$_H$ 1.98 (s, 6H), 1.94-2.09 (m, 2H), 2.71 (t, $J = 7.6$, 7.4Hz, 4H), 6.58 (s, 2H); $^{13}$C
NMR (75.4 MHz, CDCl₃): δC 14.90 (q), 23.55 (t), 39.05 (t), 125.87 (d), 127.37 (s), 133.97 (s), 135.10 (s), 135.50 (s); MS (EI): 328 [M+]; Anal. calc. for: C₁₅H₁₄Cl₂S₂; C 54.71, H 4.29; found: C 54.54, H 4.24.

1,2-Bis(5’-chloro-2’-methylthien-3’-yl)cyclopentene (1): Due to lack of TiCl₃ the reaction was later on carried out with TiCl₄. THF (50 ml) and Zn-dust (2.5 g) were put in a three-neck flask under nitrogen. TiCl₄ (6.2 ml, 28.8 mmol) was added very cautiously by a glass syringe. The solution turned yellow and was refluxed for 45 min. After that it was cooled in an icebath and 3.24 (6.9 g, 19.2 mmol) was added in portions. This mixture was refluxed for 2 h, subsequently quenched with 10% K₂CO₃ (50 ml), extracted with diethyl ether (4 x 20 ml). The combined organic layers were washed with H₂O (1 x 25 ml), dried (Na₂SO₄) and the solvent removed in vacuo. The compound was purified with column chromatography in the same way as described before (3.16 g, 50%).

Hexafluoroglutaral chloride (3.26): Hexafluoroglutaric acid 3.28 (1.0 g, 4.2 mmol) and thionylchloride (0.61 ml, 8.4 mmol) were heated at 60°C for 30 min, then a few drops of POCl₃ were added and the mixture was heated for another 15 min. After cooling to r.t. thionylchloride was removed in vacuo to yield hexafluoroglutaral chloride 3.26 (1.1 g, 95%). bp 112-113°C, ¹⁹F NMR (188.2 MHz, CDCl₃): δF -113.94 (s, 4F), -122.18 (s, 2F); ¹³C NMR (75.4 MHz, CDCl₃): δC 108.20 (t), 113.70 (t), 162.76 (s); MS (CI): 295 [M+NH₄⁺].

Hexafluoroglutaral ethyl ester (3.29): hexafluoroglutaric acid 3.28 (10.0 g, 41.7 mmol) was dissolved in ethanol (100 ml), subsequently HCl (30%, 0.5 ml) was added and the reaction mixture was refluxed overnight. After cooling to r.t., the ethanol was evaporated and diethyl ether (50 ml) was added. The organic layer was washed with a NaOH solution (2M, 2x) and a HCl solution (2M, 2x), dried (Na₂SO₄). After removal of the solvent the residual oil was subjected to a bulb to bulb distillation to afford the corresponding ester (3.8 mm, 70°C) (12.3 g, 100%). ¹H NMR (300 MHz, CDCl₃): δH 1.35 (t, J = 7.5 Hz, 6H), 4.40 (q, J = 7.2 Hz, 7.5 Hz, 4H); ¹³C NMR (75.4 MHz, CDCl₃): δC 13.54 (q), 64.56 (t), 108.04 (t), 110.57 (t), 151.24 (s); ¹⁹F NMR (470.3 MHz, CDCl₃): δF -119.93 (t, 4F), -125.44 (t, 2F). MS (CI): 314 [M+NH₄⁺].

3-Bromo-5-chloro-2-chlorothiophene (3.30): A solution of bromine (3.78 ml, 73.3 mmol) in CHCl₃ (20 ml) was added slowly to an ice cooled solution of 3.23 (9.72 g, 73.3 mmol) in CHCl₃ (75 ml). After addition of the bromine, the reaction mixture was stirred for 2 h at room temperature, and subsequently poured into H₂O (150 ml). The water layer was extracted with dichloromethane (3 x 50 ml). The combined organic extracts were dried (Na₂SO₄), filtered and evaporated in vacuo to yield a yellow/brown oil (14.4 g, 93%). ¹H NMR (200 MHz, CDCl₃): δH 2.32 (s, 6H), 6.73 (s,1H); ¹³C NMR (75.4 MHz, CDCl₃): δC 14.49 (q), 107.38 (s), 126.65 (d), 128.29 (s), 133.03 (s); MS (EI): 211 [M+]; Anal. calc. for: C₇H₄BrClS: C 28.39, H 1.91; found: C 28.74, H 1.97.
Chapter 3

1,2-Bis(5'-chloro-2'-methylthien-3'-yl)hexafluoropentadione (3.27): n-Butyllithium (1.6M in hexane, 5.4 ml, 8.64 mmol) was added to a stirred solution of 3.30 (1.75 g, 8.29 mmol) in anhydrous diethyl ether (25 ml) under nitrogen at -78°C. After 15 min of stirring at that temperature, 3.29 (0.91 ml, 4.15 mmol) in anhydrous diethyl ether (2 ml) was added slowly to the mixture in about 30 min. The reaction mixture was quenched by hydrochloric acid (2N, 10 ml), extracted with diethyl ether (3 x 25 ml). The combined organic layers were washed with saturated sodium bicarbonate solution (1 x 25 ml) and H2O (1 x 25 ml), dried (Na2SO4), filtered and the solvent evaporated in vacuo to yield a brown/reddish oil (1.36 g, 70%). 1H NMR (200 MHz, CDCl3): δH 2.70 (s, 6H), 7.31 (s, 2H); 13C NMR (125.7 MHz, CDCl3): δC 17.05 (q), 110.37 (t), 111.08 (t), 125.80 (d), 126.19 (s), 128.92 (s), 155.37 (s), 177.85 (s); 19F NMR (470.3 MHz, CDCl3): δF -116.18 (t, 4F), -122.73 (t, 2F); MS (EI): 467 [M+]; IR (Nujol): 1696 cm⁻¹ (C=O).

1,2-Bis(5'-chloro-2'-methylthien-3'-yl)perfluorocyclopentene (2): “Instant method”: A mixture of 3.27 (0.96 g, 2.06 mmol), TiCl3(THF)₃ (1.5 g, 4.12 mmol), Zn dust (0.53 g, 8.24 mmol) and THF (25 ml) were stirred under nitrogen at 40°C for 1 h. The mixture was cooled and poured over a glass filter containing silica gel that was pretreated with pet. ether (40/60). The silica was rinsed with pet. ether (40/60). A white solid (0.49 g, 55 %) was obtained after purification by chromatography over silica gel (pet. ether 40/60). 1H NMR (200 MHz, CDCl3): δH 1.88 (s, 6H), 6.88 (s, 2H); 13C NMR (500 MHz, CDCl3): δC 14.29 (q), 110.67 (t), 117.73 (t), 123.92 (d), 125.36 (s), 127.88 (s), 140.37 (s); 19F NMR (470.3 MHz, CDCl3): δF -114.78 (t, J = 5.5, 5.0Hz, 4F), -136.37 (t, J = 6.2, 5.0Hz, 2F); MS (EI): 436 [M+], M.p.; 132°C.

1,2-Bis(5'-formyl-2'-methylthien-3'-yl)cyclopentene (3.31): n-Butyllithium (7.85 ml of 1.6M solution in hexane, 12.56 mmol) was added to a stirred solution of 1 (1.97 g, 5.98 mmol) in anhydrous THF (20 ml) under nitrogen at room temperature. One hour after the addition the reaction mixture was quenched with anhydrous dimethylformamide (0.97 ml, 12.56 mmol). The mixture was stirred then for an additional hour at room temperature, before it was poured into HCl (2N, 50 ml). The mixture was extracted with diethyl ether (3 x 25 ml). The combined organic layers were washed with saturated sodium bicarbonate solution (2x 25 ml) and H2O (1 x 25 ml), and dried (Na2SO4), filtered and evaporated in vacuo to yield a brown solid (1.89 g, 90%). Chromatography of the solid over silica gel (hexane/ethyl acetate = 9/1) afforded the compound as a brown/orange solid (0.98 g, 52%). 1H NMR (200 MHz, CDCl3): δH 2.04 (s, 6H), 2.07-2.17 (m, 2H), 2.83 (t, J = 7.5Hz, 4H), 7.42 (s, 2H), 9.74 (s, 2H); 13C NMR (75.4 MHz, CDCl3): δC 15.30 (q), 22.81 (t), 38.33 (t), 134.85 (d), 136.93 (s), 137.26 (s), 140.11 (s), 146.25 (s), 182.22 (s); MS (EI): 316 [M+]; IR: 1662 cm⁻¹ (C=O); Anal. calc. for: C17H16O2S2: C 64.53, H 5.10; found: C 63.32, H 4.98.
1,2-Bis(5′-formyl-2′-methylthien-3′-yl)perfluorocyclopentene (3.32): Under the same conditions as described for 1, n-Butyllithium (1.6M in hexane, 0.13ml, 1.8 mmol) was added to a stirred solution of 2 (30 mg, 0.06 mmol) in anhydrous diethyl ether (5 ml) under nitrogen at room temperature and quenched with anhydrous dimethylformamide (0.05 ml, 0.6 mmol). Trituration from hexane/CH₂Cl₂ afforded the compound as a brown/orange solid (20 mg, 66%). M.p.; 182°C ¹H NMR (200 MHz, CDCl₃): δH 2.02 (s, 6H), 7.73 (s, 2H), 9.85 (s, 2H); ¹⁹F NMR (188.2 MHz, CDCl₃): δF -111.97 (t, J = 0Hz, J = 4.8Hz, 4F), -133.55 (t, J = 4.8Hz, J = 6.0Hz, 2F). ¹³C NMR (50.3 MHz, CDCl₃): δC 15.21 (q), 110.1 (t), 115.7 (t), 125.77 (d), 135.34 (s), 136.5 (t) 142.19 (s), 151.32 (s), 181.49 (s). MS (CI): 424 [M⁺].

1,2-Bis[5′-(2′,2′′-methylphenylimine)-2′-methylthien-3′-yl]cyclopentene (3.33): 3.31 (40.3 mg, 0.13 mmol) was dissolved in R(+)-1-phenylethylamine (3.4 ml of a stock solution of 1 ml amine in 99 ml methanol). After 18 h of stirring at room temperature, the solvent was removed in vacuo. The mixture was diluted with dichloromethane and dried (Na₂SO₄), filtered and evaporated in vacuo to yield a brown oil (0.28 g, 86%). Chromatography over Al₂O₃ (hexane/ethyl acetate/Et₃N = 2:1:0.02) afforded a purple oil (17.6 mg, 33%). IR: 1631 cm⁻¹; ¹H NMR (200 MHz, CDCl₃): δH 1.55 (d, J = 6.6, 6H), 1.97 (s, 6H),1.94-2.10 (m, 2H), 2.76 (t, J = 7.8 Hz, J = 7.6 Hz, 4H), 4.45 (q, J = 6.8 Hz, J = 6.4 Hz, 2H), 6.95 (s, 2H), 7.24-7.36 (m, 10H), 8.25(s, 2H); ¹³C NMR (75.4 MHz, CDCl₃): δC 12.85 (q), 20.85 (t), 22.76 (q), 36.33 (t), 67.08 (d), 124.60(d), 124.73 (d), 126.35(d), 129.60 (s), 132.40 (s), 133.90 (s), 136.36 (s), 135.95 (s), 143.10 (s), 150.65 (d); MS (EI): 522 [M⁺].

1,2-Bis[5′-(2′,2′′-dicyanoethenyl)-2′-methylthien-3′-yl]cyclopentene (3.34): A mixture of malonitrile (15.3 mg, 0.23 mmol), 3.31 (35.0 mg, 0.111 mmol) and a catalytic amount of piperidine (1 drop of a stock solution of 1 drop amine in 2 ml absolute ethanol) in absolute ethanol (1.5 ml) was heated to reflux. After 17 hours the solution was cooled down to r.t. and the solvent was removed in vacuo. Trituration of the crude product in methanol resulted in the formation of a brown/orange solid, which was filtered in the dark and dried in vacuo (33 mg, 72%): m.p. 154-156 °C; IR: 2343 cm⁻¹, 2223 cm⁻¹ (C≡N), 1574 cm⁻¹ (C=C-CN)]]; ¹H NMR (200 MHz, CDCl₃): δH 2.14 (s, 6H), 2.05-2.20 (m, 2H), 2.82 (t, J = 7.2 Hz, 4H), 7.40 (s, 2H), 7.63 (s, 2H); ¹³C NMR (75.4 MHz, CDCl₃): δC 15.30 (q), 22.76 (q), 36.33 (t), 67.08 (d), 124.60(d), 124.73 (d), 126.35(d), 129.60 (s), 132.40 (s), 133.90 (s), 136.36 (s), 135.95 (s), 143.10 (s), 150.65 (d); MS (EI): 412 [M⁺].

1,2-bis(5′-carboxy-2′-methylthien-3′-yl)cyclopentene (3.35): Ag₂O was used to oxidize 3.31 (0.74 g, 2.34 mmol), this was made in situ by adding AgNO₃ (1.64 g, 9.6 mmol) to a solution of NaOH (0.75g, 18.7 mmol) in H₂O (15 ml). Ag₂O immediately precipitated. This suspension was then added to 3.31 and refluxed for 1h, subsequently filtered over a glass filter (G4) and rinsed with hot water. The filtrate was cooled and acidified with 2M HCl in an ice bath. The compound precipitated and was filtered over a glassfilter (G4). The residual water was azeotropically removed with toluene to yield an off-white solid (0.51g, 62%). ¹H
NMR (DMSO, 300MHz): $\delta_H$ 1.91 (s, 6H, CH$_3$), 1.95-2.05 (m, 2H, CH$_2$), 2.77 (t, $J = 7.8$ Hz, 4H, CH$_2$), 7.40 (s, 2H, CH); $^{13}$C NMR (75.4 MHz, CDCl$_3$): $\delta_C$ 14.37 (q), 22.36 (t), 37.93 (t), 130.50 (s), 133.90 (d), 134.34 (s), 136.43 (s), 141.75 (s), 162.68 (s); IR: $\nu$ 1550, 1663, 2578, 2841, 2953 cm$^{-1}$, MS (EI): 348 [M$^+$].

2-Thienylmagnesium bromide (3.38): A solution of 2-bromothiophene (1 ml, 10.3 mmol) in anhydrous diethyl ether (8 ml) was added dropwise to magnesium turnings (0.30 g, 12.4 mmol) in diethyl ether (2 ml). The mixture spontaneously started to reflux, became turbid and the amount of magnesium diminished in time. After 1 h of reflux the Grignard reagent was ready for use in the Kumada coupling.

5-Methyl-2,2'-bithiophene (3.39): 3.23 (0.89 ml, 8.24 mmol) was dissolved in anhydrous diethyl ether (10 ml) and Ni(dppp)Cl$_2$ (42 mg, 0.08 mmol) was added, to yield a suspension. At 0°C 3.38 in diethyl ether was added dropwise. The mixture turns dark-brown to black, and was refluxed for 8 hr after addition. Then the reaction mixture was quenched with 2N HCl at ambient temperature, extracted with diethyl ether (3 x 50 ml) and dried (Na$_2$SO$_4$). After evaporation of the solvent an oil was obtained (1.28 g, 69%) $^1$H NMR (300MHz, CDCl$_3$) $\delta_H$ 2.47 (s, 3H), 6.66 (dd, $J = 1.2$, 1H), 6.96 (d, $J = 4.2$, 1H), 6.99 (d, $J = 3.6$, 1H), 7.09 (dd, $J = 2.7$, 1H), 7.16 (dd, $J = 0.6$, 1H); $^{13}$C NMR (74.5 MHz, CDCl$_3$) $\delta_C$ 15.24 (q), 122.93 (d), 123.15 (d), 123.64 (d), 125.81 (d), 127.59 (d), 134.99 (s), 137.77 (s), 139.02 (s); MS (EI): 180 [M$^+$].

1-[5'-(Thiophen-2-yl)-2'-methylthien-3'-yl]-2-[5'-chloro-2'-methylthien-3'-yl]cyclopentene (3.41): A Grignard reagent was made of 2-bromothiophene (0.57 ml, 4.84 mmol), Mg (0.12 g, 5.08 mmol) and diethyl ether (5 ml) according to the procedure described for 3.38. At the same time I (0.4 g, 1.2 mmol) was added to a suspension of Ni(dppp)Cl$_2$ (21 mg, 0.04 mmol) in anhydrous diethyl ether (10 ml). The thienylmagnesium bromide solution was added dropwise at 0°C. The mixture turned black immediately. After addition the mixture was refluxed for 20 h. Subsequently the reaction mixture was quenched with 2N HCl at 0°C, extracted with diethyl ether (3 x 50 ml) and dried (Na$_2$SO$_4$). After column chromatography (pet. ether 40/60) 3.41 was obtained as a red oil (0.18 g, 40%). $^1$H NMR (300MHz, CDCl$_3$) $\delta_H$ 1.90 (s, 3H), 1.95 (s, 3H), 2.00-2.09 (m, 2H), 2.72-2.82 (m, 4H), 6.62 (s, 1H), 6.86 (s, 1H), 6.99 (d, $J = 4.2$ Hz, 1H), 7.05 (d, $J = 3.6$ Hz, 1H), 7.15 (d, $J = 5.1$, 1H); $^{13}$C NMR (75.4 MHz, CDCl$_3$) $\delta_C$ 14.18 (q), 14.22 (q), 22.85 (t), 38.32 (t), 38.40 (t), 122.93 (d), 123.71 (d), 124.32 (d), 126.73 (d), 127.64 (d), 133.11 (s), 133.22 (s), 133.92 (s), 134.95 (s), 135.02 (s), 135.99 (s), 137.61 (s); MS (EI): 377 [M$^+$].

1,2-Bis(5'-(thiophen-2-yl)-2'-methylthien-3'-yl)cyclopentene (3.40): A Grignard reagent was made of 2-bromothiophene (4 ml, 0.04 mol), Mg (1.0 g, 0.05 mol) and diethyl ether (50 ml) according to the procedure described for 3.41. At the same time I (199 mg, 0.6 mmol) was added to a suspension of Ni(PPh$_3$)$_2$Cl$_2$ (0.40 g, 0.6 mmol) in anhydrous diethyl ether (10
ml). Then 20 ml of the thienylmagnesium bromide solution was added dropwise at 0°C. The mixture turned black immediately. After addition the mixture was refluxed for 20 hr. subsequently the reaction mixture was quenched with 2N HCl at 0°C, extracted with ether (3 x 50 ml) and dried (Na₂SO₄). After evaporation of the solvent a mixture of 3.40 and 3.41 was obtained in a 4/1 ratio. After column chromatography (pet. ether 40/60) 3.40 was obtained as an oil (51 mg, 20%). ¹H NMR (300 MHz, CDCl₃) δH 1.95 (s, 6H), 2.01-2.11 (m, 2H), 2.80 (t, J = 7.5, 4H), 6.88 (s, 2H), 6.96 (dd, J = 3.9 Hz, 3.3 Hz, 2H), 7.04 (dd, J = 0.6 Hz, 2H), 7.14 (d, J = 5.1 Hz, 2H); ¹³C NMR (75.4 MHz, CDCl₃) δC 14.30 (q), 22.93 (t), 38.47 (t), 122.90 (d), 123.66 (d), 124.48 (d), 127.64 (d), 133.00 (s), 133.98 (s), 134.50 (s), 136.25 (s), 137.74 (s); MS (EI): 424 [M⁺].

Bis-(1,3-(2,4,6-trimethylphenyl))imidazol-2-ylidene (3.43): Paraformaldehyde (1.51 g, 0.05 mol) was suspended in toluene (15 ml), then 2,4,6-trimethylaniline (14 ml, 0.1 mol) in toluene (15 ml) was added dropwise in 15 min at r.t.. The mixture was then heated until complete solution of the compounds occurred. At 40°C aq HCl (6N, 8.3 ml, 0.05 mol) was added very slowly, resulting in the immediate precipitation of copious amounts of white solid. Finally glyoxal in H₂O (40%, 7.26 ml, 0.05 mol) was added. The mixture was heated to reflux for 2hr. Cooling the mixture and removing the volatiles in vacuo left a sticky black tar. The substance was then triturated and washed with acetone (15 ml). Upon filtration, 3.40 was isolated 100% pure as a greyish solid (8.39 g, 49%). m.p. ¹H NMR (300MHz, DMSO) δH 2.13 (s, 12H), 2.34 (s, 6H), 7.20 (s, 4H), 8.35 (s, 2H), 9.94 (s, 1H); ¹³C NMR (74.5 MHz, DMSO) δC 16.97 (q), 20.65 (q), 121.33 (d), 124.84 (d), 129.36 (d), 131.02 (s), 134.29 (s), 140.49 (s); MS (EI): 303 [M-Cl⁻].

1,2-Bis(5'-boronyl-2'-methylthien-3'-yl)cyclopentene (3.44): 1 (1.75g, 5.3 mmol) was dissolved in anhydrous THF (12 ml) and n-BuLi (4.5 ml of 2.5M solution in hexane, 11.2 mmol) was added under nitrogen at r.t. in 5 portions using a syringe. This solution was stirred for 30 min at r.t., then B(n-OBu)₃ (4.3 ml, 15.9 mmol) was added in one portion. This reddish solution was stirred for 1 h at r.t. and was then used in the Suzuki cross-coupling reaction without any workup because boronic acid 3.44 is deboronized during isolation.

1,2-Bis(5'-boronyl-2'-methylthien-3'-yl)perfluorocyclopentene (3.45): This boronic ester was prepared in the same way as described for 3.44.

1,2-Bis(5'-(phenyl-2-yl)-2'-methylthien-3'-yl)cyclopentene (3.46): 2-Bromobenzene (1.12 ml, 9.29 mmol) was dissolved in THF (12 ml) and Pd(PPh₃)₄ (0.37 g, 0.3 mmol) was added, the resulting solution was stirred for 15 min at r.t.. Then aqueous Na₂CO₃ (23 ml, 2M) and 6 drops of ethylene glycol were added. This two phase system was heated in an oilbath just below reflux at a temperature of 60°C and the solution of 3.44 was added dropwise via a syringe in a short time period of approximately 5 min. Subsequently the mixture was refluxed for 2 h and cooled to r.t. and diethyl ether (50 ml) and H₂O (50 ml) were added. The organic layer was separated and dried (Na₂SO₄). After evaporation the compound was purified by
column chromatography on silica (hexane) to yield a brown/yellowish solid (1.03 g, 47%). $^1$H NMR (300MHz, CDCl$_3$) $\delta$H 1.98 (s, 6H), 2.03-2.13 (m, 2H), 2.84 (t, $J$ = 6.9 Hz, 2H), 2.85 (s, 2H), 2.97-3.10 (m, 1H), 3.02 (t, $J$ = 7.2 Hz, 2H), 3.14 (d, $J$ = 7.2, 2H); 13C NMR (75.4 MHz, CDCl$_3$) $\delta$C 14.43 (q), 23.00 (t), 38.48 (t), 123.88 (s), 125.19 (d), 126.82 (d), 128.67 (d), 134.40 (s), 134.51 (s), 135.5 (s), 139.53 (s); anal. calcd. for CH$_{15}$: C, 78.60, H, 5.86. Found: C, 78.65, H, 5.90.

1,2-Bis(5'-phenyl-2'-methylthien-3'-yl)perfluorocyclopentene (3.47): The same procedure as described for 3.46 was followed, except 2 (200 mg, 0.5 mmol) and 2-bromobenzene (0.1 ml, 1.0 mmol) were used to obtain the crude compound. After evaporation it was also purified by column chromatography on silica (hexane) to obtain a greenish solid (16 mg, 7%). $^1$H NMR (300 MHz, CDCl$_3$) $\delta$H 1.96 (s, 6H), 7.28 (s, 2H), 7.29 (d, $J$ = 6.9 Hz, 2H), 7.38 (t, $J$ = 7.5 Hz, 2H), 7.53 (d, $J$ = 7.5 Hz, 2H); 13C NMR (75.4 MHz, CDCl$_3$) $\delta$C 14.53 (q), 120.49 (d), 122.35 (d), 125.57 (d), 127.87 (d), 128.97 (d), 133.27 (s), 141.25 (s), 142.19 (s); 19F NMR (188.2 MHz, CDCl$_3$): $\delta$F –111.26 (s, 4F), -133.03 (s, 2F). HRMS calcd. for C$_{27}$H$_{18}$F$_{6}$S$_{2}$ 520.075, found 520.075.

3.7 References and notes

1 Irie, M. Chem. Rev. 2000, 100, 1685.