



Synthesis of a ferrocene-functionalized unsymmetrical benzo[*b*]thienyl-thienylethene photoswitch with a cyclopentene core

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ABSTRACT

A new and potentially general synthetic route toward unsymmetrical benzo[*b*]thienyl-thienylethene compounds is described, with specific focus on conjugation of a ferrocene to the benzo[*b*]thiophene subunit. The route proceeds in an overall yield of 17%.

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The desire to miniaturize electronic components and devices has led to a renewed focus on organic compounds in the development of molecular scale electronics. One such group of compounds is that of diarylethenes,¹ whose photochromic properties are amenable to use in memory applications.^{2–5} The ideal components of the photoswitch scaffold have been well documented over the past 20+ years and include the desirable qualities of: (1) induced reversible ring closure (light, acid, redox), (2) thermal irreversibility, and (3) fatigue resistance. Photochromism in the solid state is also a very desirable characteristic.

Of the large variety of photoswitches developed over the years, symmetric molecules that contain a perfluorinated cyclopentene bridge have remained superior for use in materials applications.⁶ However, if one requires an unsymmetrical perfluorocyclopentene-bridged photoswitch without the tedious separation of a mixture of compounds, there are few synthetic options. Such unsymmetrical compounds are attractive to both materials and biological applications.⁷

Within the last 15 years, there has been an expansion of research regarding the synthesis of perhydrocyclopentene-bridged photoswitches,^{8–10} largely directed toward the more desirable subunits thiophene¹¹ and benzo[*b*]thiophene.¹² Many of these compounds have the key aforementioned requirements of a desirable photoswitch. Additionally, the syntheses of these compounds are generally more amenable to scale up, lower in cost, and use

reagents that are relatively easy to attain and handle in comparison to their fluorinated counterparts.

Our desire in pursuing the unsymmetrical cyclopentene-bridged photoswitch scaffold **1** was driven by our continuing interest in organic monolayer-protected ruthenium nanoparticles.¹³ In recent publications we have demonstrated that ferrocene moieties conjugated to the metal nanoparticle via ruthenium–carbene π bonds display an intervalence transfer at mixed valence. Conversely, a single saturated carbon between the ferrocene and nanoparticle negates any communication between the ferrocenyl metal centers. Within this context, compound **1** provides an interesting test case. Appended to a ruthenium nanoparticle through olefin metathesis of the terminal alkene, photoisomerization of **1** to **2** (Fig. 1) provides for a fully conjugated pathway between the ruthenium core and the ferrocenyl substituent.¹⁴ Reversion to the open form (i.e., **1**) breaks the conjugation and any interaction between metal sites.

However, the synthesis of **1** poses certain challenges. There are few examples of unsymmetrical photoswitch molecules and, to our

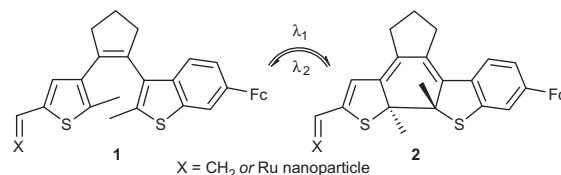


Figure 1. Open (**1**) and closed (**2**) forms of photoswitch; Fc = ferrocene.

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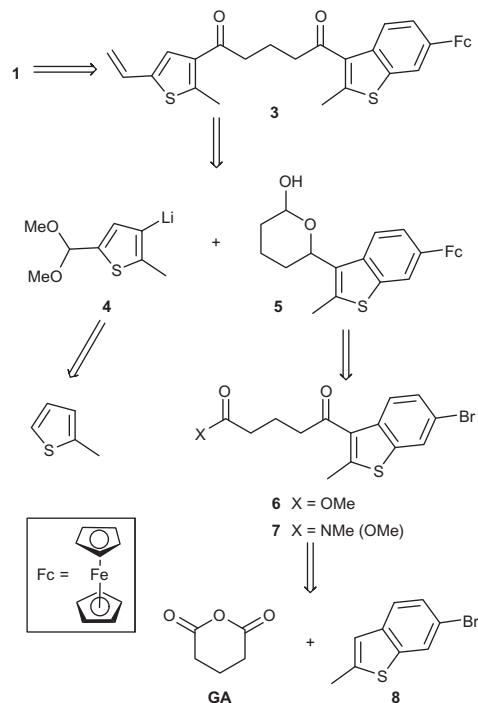
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knowledge, none contain a ferrocene moiety directly bonded to the aromatic ring. During the course of our research, a patent¹⁵ and publication¹⁶ appeared that implicated molecules containing a cyclopentene core and mixed thiophene/benzo[*b*]thiophene subunits as viable photoswitches, and thus provided validation of the proposed target. Unfortunately, the published yields are quite poor and too low for our purposes. Herein, we report the synthesis of **1** via a route that offers considerable flexibility.

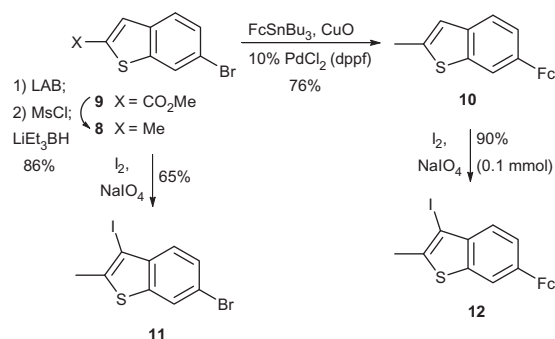
As depicted in [Scheme 1](#), the convergent synthesis of **1** relies heavily on the well precedented intramolecular McMurry reaction of diketones. In our case, the appended functional groups on the thienyl and benzothieryl moieties of **3** were to be introduced prior to the McMurry reaction. The decision to functionalize the thiophene with the vinyl group and the benzo[*b*]thiophene with the ferrocene (and not vice versa) was driven by the anticipated reaction conditions needed for coupling of compounds **4** and **5**. Readily available anion **4**,¹⁷ derived in four steps from 2-methylthiophene, was expected to be used in excess as compared with lactol **5**.¹⁸ In order to furnish lactol **5** via DIBALH reduction, **6** and **7** would undergo ferrocenylation via a microwave Stille reaction under CuO mediated Gronowitz conditions.¹⁹ Friedel–Crafts acylation between glutaric anhydride (**GA**) and **8**, followed by ester or Weinreb amide formation, would provide **6** and **7**.

Reduction of **9** with LiAlH₄ led to some dehalogenation product (Scheme 2). However, in only 5 min, 2.5 equiv of lithium dimethylammonium borohydride reduced **9** to the corresponding primary alcohol on a 25 mmol scale without the unwanted side reaction. Mesylation of the alcohol product followed by subsequent reduction with 2 equiv of lithium triethylborohydride yielded **8** in 91% yield over two steps (86% for all three steps).

Ferrocene cross-coupling reactions have been reviewed,²⁰ and particular success for ferrocene/heteroaryl coupling has been seen in the work of Ma and co-workers.^{21,22} The Stille coupling between heteroaryl halides and tributylstannyl ferrocene²³ was shown to be enhanced by an equivalent of CuO in addition to the Pd(PPh₃)₄ catalyst. This is very similar to the original work of Gronowitz and co-workers which first showed this effect of CuO and other additives



Scheme 1. Retrosynthesis of **1**.

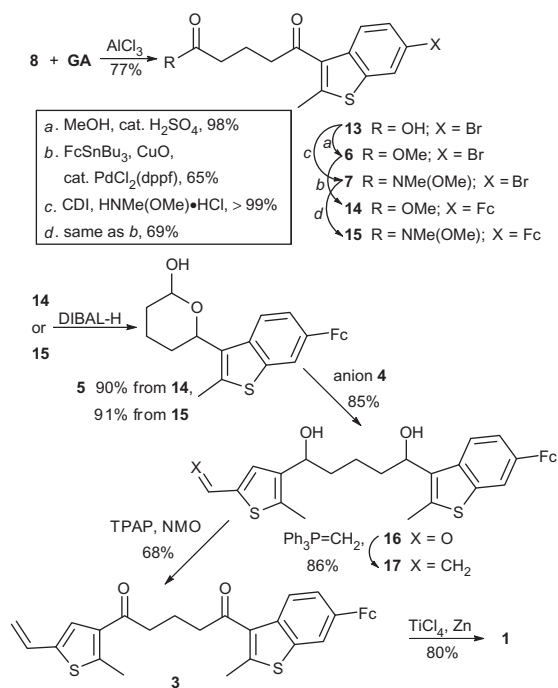


Scheme 2. Synthesis of varied benzo[*b*]thiophene subunits.

On Stille reactions. Optimization of conditions for the Stille coupling of tributylstannyl ferrocene to **8** was conducted in a microwave reactor. Also, a relatively more stable catalyst alternative to $\text{Pd}(\text{PPh}_3)_4$ was sought, which led to the choice of $\text{PdCl}_2(\text{dppf})$ based on a procedure given by Guillaneux and Kagan.²³ In only 20 min at 140 °C, compound **10** was furnished in 76% yield.

Although **8** was anticipated to undergo Friedel–Crafts acylation, the expected competition between the benzothiophene ring and the ferrocene moiety precluded the use of **10**. However, halogenation at the 3-position of **10** or **8** would provide two compounds that could be easily converted into the appropriate lithium anion via lithium–halogen exchange for future synthetic targets. The oxidative conditions to iodinate **8**²⁴ to give dihalide **11** were successfully used on **10** on a 0.1 mmol scale to give **12** in 90% yield. However, any scale-up led to much lower yields and a black insoluble precipitate. Alternative halogenation methods, either with NBS or NCS, returned only decomposed material in a matter of minutes.

Friedel–Crafts acylation between **8** and glutaric anhydride (**GA**) gave carboxylic acid **13** in 77% yield, and methanol esterification or CDI coupling with *N*-methoxy-*N*-methylamine hydrochloride provided **6** and **7**, respectively, in quantitative yield (Scheme 3).



Scheme 3. Synthesis of **1**.

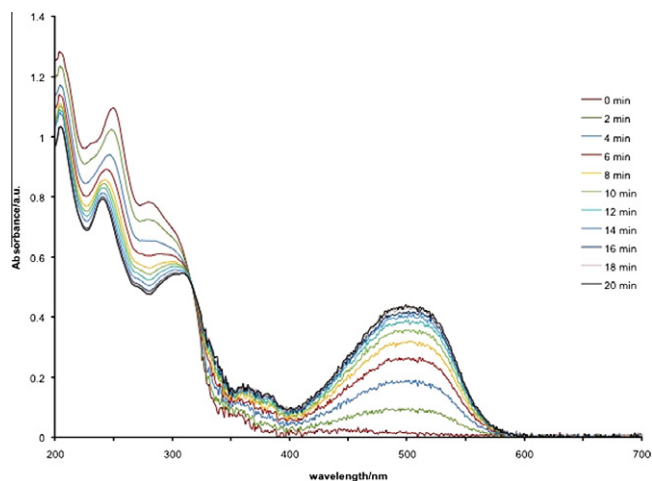


Figure 2. Open to closed. UV-vis spectra of interval irradiation of **1** in heptane (4.5×10^{-5} M) with 306 nm light.

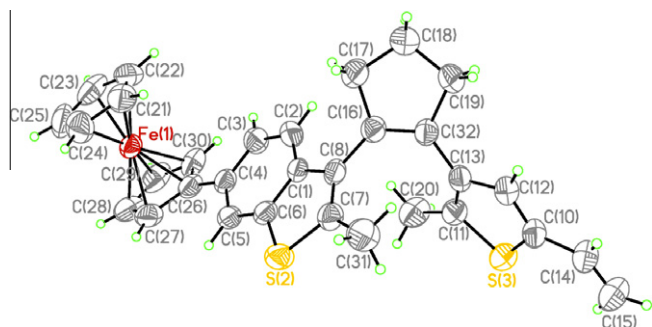


Figure 3. X-ray crystal structure of **1**.

Additionally, the previously described microwave Stille conditions gave **14** and **15** in 65% and 69% yield, respectively.

One of the main goals of our synthesis of an unsymmetrical photoswitch was to avoid the possibility of mixtures and the corresponding decreased overall yield. Methyl ester **14** or Weinreb amide **15** would allow us to pursue this goal without the need to directly protect the ketone portion of the molecule. Reduction of both carbonyl functionalities of **14** or **15** with DIBAL-H provided lactol **5**, which bore the desired masked aldehyde functionality that is revealed in the presence of excess lithium anion **4** (Scheme 3). Precedence for this type of reaction with complex anions is seen in the work toward the total synthesis of (+)-macbecin I by Martin and co-workers.²⁵ Multiple equivalents of nucleophile were necessary to give a good yield of diol **16** as a noticeable color change from red to brown above -40°C signified possible anion decomposition. It should be noted that the dimethyl acetal was readily hydrolyzed during acidic workup to give diol **16**. The utility of this particular nucleophilic addition should be highly advantageous to the creation of a variety of mixed photoswitches.

Aldehyde **16** was treated with excess methylenetriphenylphosphorane to give alkene **17** in 85% yield. Oxidation of diol **17** did not proceed well under PCC, Swern, or Dess–Martin conditions, providing mostly decomposed product. However, Ley conditions provided a 68% yield of diketone **3**. The McMurry reaction proceeded smoothly to furnish **1** in 80% yield as orange crystals.^{12,16} The yield of **1** from commercially available **9** over nine steps, through Weinreb amide **15**, is 17%.

To investigate the degree of photocyclization, solutions of **1** were irradiated with monochromatic light from a xenon source

(306 nm). The molecule displays distinct maxima typical to dithienylethene compounds in the UV at 206 and 252 nm, as well as shoulders at 284 and 360 nm (Fig. 2). There is also a weaker intensity peak that extends from the UV into the visible region (maximum 450 nm), which can be attributed to ferrocene. Irradiation of a dilute solution of **1** with UV light turns the solution from colorless to red and gives rise to a new peak at 505 nm. Over irradiation time the intensity of the peaks below 350 nm decrease and there is a noticeable hypsochromic shift from 252 to 242 nm. Also, the shoulder at 284 nm is replaced with a more defined peak at 310 nm.

X-ray quality single crystals of **1** were formed upon slow evaporation from a mixture of hexanes and dichloromethane.²⁶ The ORTEP diagram of the structure is given in Figure 3. The distance between the reactive carbon atoms, labeled C7 and C11 in Fig. 1, is 3.67 Å, well below the determined necessary distance for solid-state cyclization (~ 4.2 Å)²⁷ upon irradiation with UV light at a suitable wavelength. However, under UV irradiation, the yellow crystals of **1** do not appear to photocyclize in the solid state. As discussed above, in the solution phase a colorless or pale yellow solution of **1** becomes pink to dark red upon irradiation with 306 nm light. The yellow crystals of **1** do not change color following irradiation with UV light.

Conclusions

A new synthetic route toward unsymmetrical benzo[*b*]thienylthienylethene photoswitches, which allows the potential for an extensive variation of subunits, is described. Each aryl subunit is functionalized prior to the McMurry cyclization, which reduced the handling of the photoactive compound. Further study of the photoswitch properties of **1**, together with experiments to attach **1** to ruthenium nanoparticles, is underway and will be reported in due course.

Acknowledgments

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.tetlet.2013.01.033>.

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