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ARTICLE TYPE

Immobilisation of Photoswitchable Diarylcyclohexenes Synthesised via Cobalt-Mediated Diels-Alder Reaction

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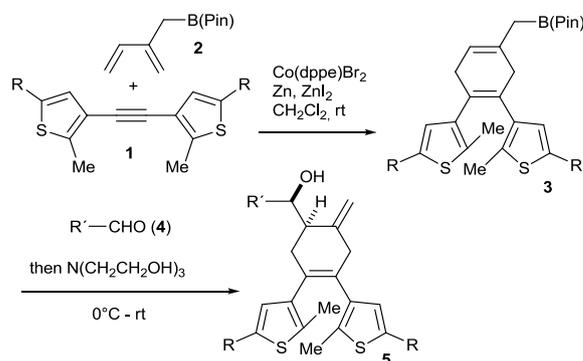
Functionalised photoswitches in two steps: Photochromic dithienylcyclohexenes were prepared by a cobalt-mediated Diels-Alder reaction of internal alkynes with isoprenyl-pinacolboronic ester. The three-component - one-pot reaction sequence provides the photochromic dithienylcyclohexenes in up to 67% overall yield.

Photochromic compounds find increasing interest in material science¹ or as tools in molecular biology.² Recent applications are optical data storage,³ materials with photoswitchable refractive indices⁴ or conformation⁵ and photochromic agonists or inhibitors that affect the physiological activity of ion channels,⁶ enzymes⁷ and proteins.⁸ Widely used are photochromic diarylethenes, which show in many cases high fatigue resistance, complete photoisomerisation and slow thermal interconversion of the photoisomers.⁹ Two main routes for the synthesis of diarylethenes were reported by Irie¹⁰ and Feringa¹¹ utilizing either non-volatile 1,2-dichlorohexafluorocyclopentene or unsymmetrical diarylketones as starting materials.

Recently, we explored cycloaddition routes¹² for the synthesis of photochromic diarylethenes and described a cobalt-catalysed [2+2] reaction of diarylalkynes with cyclopentene or norbornene derivatives.¹³ However, the photophysical properties of the obtained dithienylcyclobutenes were not satisfactory and the scope of possible functionalisation limited. Therefore, we turned our attention to the cobalt-mediated Diels-Alder cycloaddition of a dithienylacetylene **1** with boroprene **2** [= isoprenyl-pinacolboronic ester (Pin = pinacole)]¹⁴ giving the dihydroaromatic intermediate **3** (Scheme 1). The allylboronic ester reacts *in situ* with aldehydes (**4**) affording photochromic diarylcyclohexene **5**. This last step of the synthesis allows the facile introduction of a variety of functional groups modifying the backbone of the photoswitch without altering its photophysical properties. The modification can be used to introduce specific labels, probes, binding sites or anchoring groups for immobilisation.¹⁵ In order to investigate the immobilisation of dithienylcyclohexenes different aldehydes (**4**) with additional functional groups were selected to establish a range of potential anchors.

For the Diels-Alder-type [4+2] cycloaddition, an established catalyst system consisting of Co(dppe)Br₂, zinc iodide and zinc powder in dichloromethane was used.¹⁶ The catalyst converts a

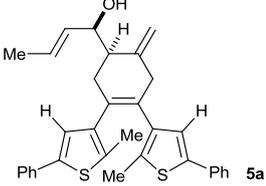
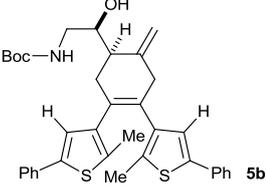
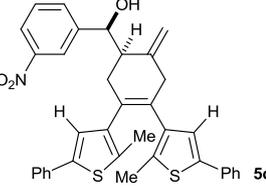
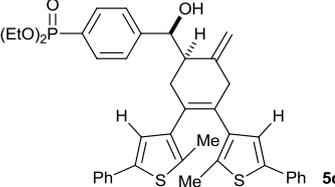
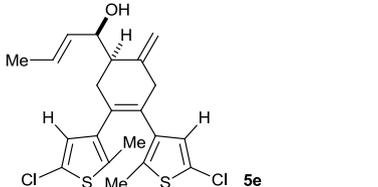
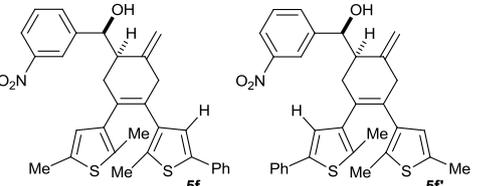
range of dithienylalkynes **1** and boroprene **2** under mild reaction conditions into the dihydroaromatic dithienylethenes **3**. The products of the cycloaddition reaction are subsequently reacted without isolation with different aldehydes **4** yielding the desired diarylcyclohexenes **5a-f** in moderate to good overall yield as single diastereomers. The results of this three-component one-pot reaction sequence are summarised in Table 1.



Scheme 1 Synthesis of functionalised dithienylethenes **5** by [4+2] cycloaddition.

The reaction of alkynes with phenyl substituted thiophenes (entries 1-4) gave acceptable overall yields for both steps. The results obtained in entries 1-4 also show that the allylboration reaction with α,β -unsaturated and aromatic aldehydes works well whereas the allylboration with the protected amino aldehyde (entry 2) was much more problematic. The reaction with the chloro-substituted thiophene (entry 5) gave incomplete conversion of the alkyne, which we attribute to electronic and steric effects limiting the scope of the method for such substrates. Most importantly, functional groups in a remote position of the aldehyde do not affect the chromophore and can be easily introduced in the last step of the sequence by applying the appropriate aldehyde. An interesting example was realised in the phosphonate ester functionality in **5d**.

Table 1 Diarylethenes of type **5** generated via a cobalt-mediated Diels-Alder and allylboration reaction sequence.

Entry	Product	Yield
1		64%
2		25%
3		58%
4		67%
5		32% ^a
6		30% ^a

^a Compound **5f** was obtained as regioisomeric mixture and the ratio was determined by NMR spectroscopy (**5f**:**5f'** = 59:41).

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Next, the photochromic properties of compounds **5a-f** upon irradiation with light of 312 nm wavelength were determined. This is exemplarily shown for compound **5d** (Fig. 1). The closed isomers are stable for days in the dark and isomerise quantitatively to the open forms upon irradiation with a 200 W tungsten light source that was passed through a 420 nm cut-off filter to eliminate shorter wavelengths. The photo stationary state (PSS) was determined exemplarily for compound **5b** to be 80%. Unfortunately, the diarylethenes **5a-f** photodegrade and after 10 photoisomerisation cycles the absorption of the chromophore at 530 nm is reduced to about 60% of the original value (see SI).

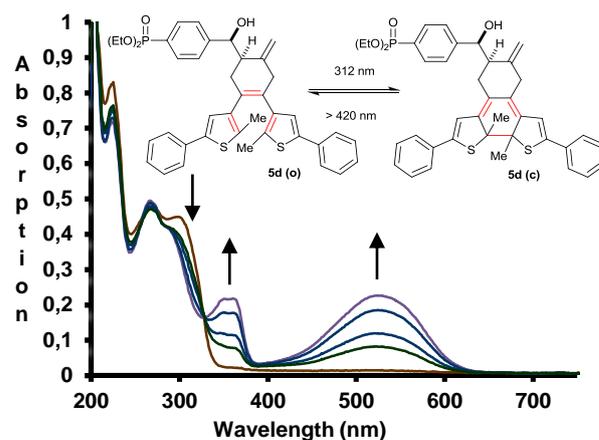
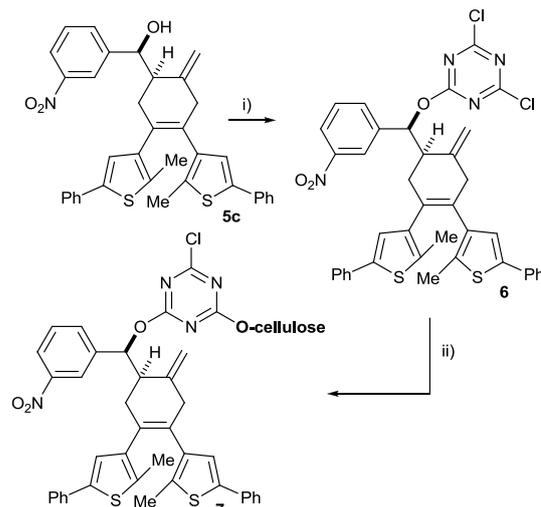


Fig. 1 UV/vis absorption spectrum of compound **5d** ($c = 3.0 \cdot 10^{-5} \text{ mmol} \cdot \text{L}^{-1}$ in MeOH). Irradiation of diarylcyclohexene **5d** with UV-light (312 nm) in MeOH. Irradiation times were 15, 30, 45 and 60 s.

However, more important than the expected reversible photochromic behaviour was the application of the functional groups introduced via the allylboration with aldehydes (**4**) as anchor groups. The reaction sequence yields a secondary hydroxyl group, which can be used for facile subsequent modifications and surface immobilisation of the chromophores. Reactive dye **6** was obtained from diarylcyclohexene **5c** and cyanuric chloride under basic conditions (Scheme 2).

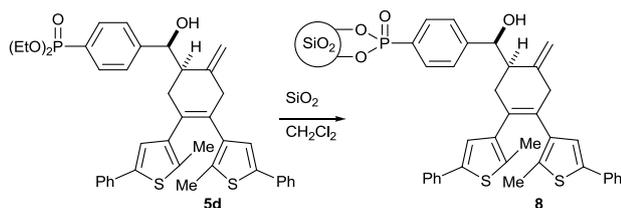


Scheme 2 Immobilisation of diarylethene **5c** on cellulose: i) cyanuric chloride; K_2CO_3 , THF; ii) cellulose, K_2CO_3 , DMF, 60 °C.

The sensitive compound was isolated by flash column chromatography. For the immobilisation of **6** a cellulose sheet was heated for 12 hours at 60 °C with the crude reactive dye and potassium carbonate in DMF (Scheme 2). To remove not immobilised chromophore molecules, the cellulose sheet was washed with dichloromethane, acetone and ethanol until no dye could be detected in the rinsing solution. After drying, the cellulose sheet **7** showed visible photochromic properties upon irradiation with UV-light and visible light for several cycles. The average dye loading of the cellulose was determined gravimetrically to be $3.0 \pm 0.8 \cdot 10^{-4} \text{ mmol}_{\text{dye}}/\text{mg}_{\text{cellulose}}$. This

corresponds to about 5% conversion of the cellulose primary hydroxyl groups.

For the immobilisation of photoswitchable derivatives on silica gel as solid support the phosphonate ester bearing dithienylethene **5d** was used. Accordingly, silica gel powder (0.04–0.063 mm) was incubated with a solution of diarylcyclohexene **5d** in dichloromethane for 12 h to afford **8** (Scheme 3).



Scheme 3 Immobilisation of phosphonate ester **5d** on silica gel.

The reaction mixture was filtered and washed with dichloromethane and ethanol until no coloration of the rinsing solvent was detected after irradiation with UV-light. The dye loading of the SiO₂ **8** was determined by elemental analysis to be 2.2·10⁻⁵ mmol_{dye}/mg_{silicagel}. The functionalised SiO₂ powder is reversible photochromic and showed a broad absorption at 522 nm after UV-irradiation (See SI). Suspending the coated silica gel in water with poly-2-ethylloxazoline polymer (200.000 g/mol) gave a photochromic paint. Unfortunately, the immobilised chromophores did not show an increased reversibility. Actually, after three photocycles the relative absorption of the closed isomer decreased to about 50% (see SI).

Conclusions

In conclusion, we have developed a new cycloaddition route for the synthesis of reversible photochromic dithienylcyclohexenes in a three-component one-pot reaction. The chromophores were generated via a cobalt-mediated Diels-Alder reaction of internal dithienylalkynes with isoprenyl-pinacolboronic ester under mild reaction conditions followed by an allylboration with various aldehydes. The aldehydes allow the facile introduction of different functional groups without affecting the chromophore. Most importantly, we demonstrated immobilising of the functionalised dithienylethenes chromophores retaining their photochromic properties on cellulose via the secondary alcohol functionality and on silica gel via a phosphonate group. The method allows the fast and facile synthesis and immobilisation of photochromic dithienylethenes for a broad range of applications. Attempts to increase their photostability are ongoing.

Notes and references

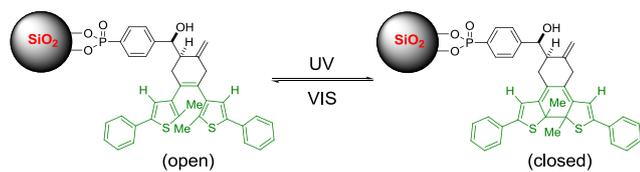
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† Electronic Supplementary Information (ESI) available: [details of any supplementary information available should be included here]. See DOI: 10.1039/b000000x/

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Graphical Abstract and Textual Abstract



5

Functionalised photoswitches in two steps – Photochromic dithienylcyclohexenes were prepared by a cobalt-mediated Diels-Alder reaction of internal alkynes with isoprenylpinacolboronic ester. The primary cycloaddition products were reacted *in situ* with different aldehydes introducing an additional functional group, which allows immobilisation on cellulose or silica gel.