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COMMUNICATION

Mild preparation of functionalized [2.2]paracyclophanes *via* the Pummerer rearrangement†

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[2.2]Paracyclophanes, incorporating functional groups in the aliphatic bridges, suitable for elimination to give [2.2]paracyclophanedienes, are synthesized through a novel approach. It relies on a double Pummerer rearrangement on dithiacyclophane precursors, followed by ring contraction through a photochemical sulfur extrusion, and it is compatible with aryl moieties possessing very different electronic properties.

[2.2]Cyclophanedienes are [2.2]cyclophanes containing two strained carbon–carbon double bonds directly joining the two aromatic rings. Although initially produced to study formally conjugated but orbitally unconjugated compounds, the interest in this class of molecules has recently reemerged, following reports by the groups of Grubbs[1] and Turner,[2] which have successfully explored the ring opening metathesis polymerization (ROMP) of the strained alkene groups embedded in [2.2]cyclophanedienes to afford functionalized *p*-phenylenevinylene (PPV) polymers. These polymers are important components for a series of functional devices, but their conventional syntheses are not controlled.[3] "Living" polymerization procedures, such as ROMP, have demonstrated the possibility to address efficiently the synthesis of block copolymers, useful for controlling film morphology for functional device applications, and to prevent batch-to-batch reproducibility issues. Efficient syntheses of cyclophanediene monomers, allowing structural and electronic variability in the molecular skeleton, are therefore highly desirable.

Although [2.2]paracyclophane-1,9-diene **1** has been known for more than 50 years,[4] less than a handful synthetic procedures for **1** and related aryl substituted derivatives have been reported to date.[5] Boekelheide and coworkers have approached the ring contraction of [3.3]dithiacyclophane skeletons by means of Wittig[6] or Stevens[7] rearrangements, to obtain thioether functionalized [2.2]meta and paracyclophanes, able to undergo oxidation/methylation and subsequent elimination to give the carbon–carbon double bonds (Scheme 1, left). In order to target the synthesis of [2.2]cyclophanedienes bearing electron withdrawing and electron rich aryl moieties, as potential precursors for innovative PPV derivatives to be obtained through ROMP, we have synthesized a variety of [3.3]dithiacyclophanes (Scheme 2). The synthesis followed an established procedure[7a] involving nucleophilic substitution of benzylic dithiols **2–4** (thiolates in the presence of stoichiometric amounts of KOH in the reaction mixture) on benzylic dibromides **5–8**, to give cyclization, under high dilution conditions, affording [3.3]dithiacyclophanes in good to excellent yields after purification by chromatography.

By applying the Boekelheide protocol[7a] (where the Stevens rearrangement is induced by benzyne, generated *in situ* using anthranilic acid and isoamyl nitrite) on [3.3]dithiacyclophane **9**, we were successful in isolating **1** in moderate yields (57% for step *a* in Scheme 1, and 22% for steps *b* and *c*); methylation of phenyl

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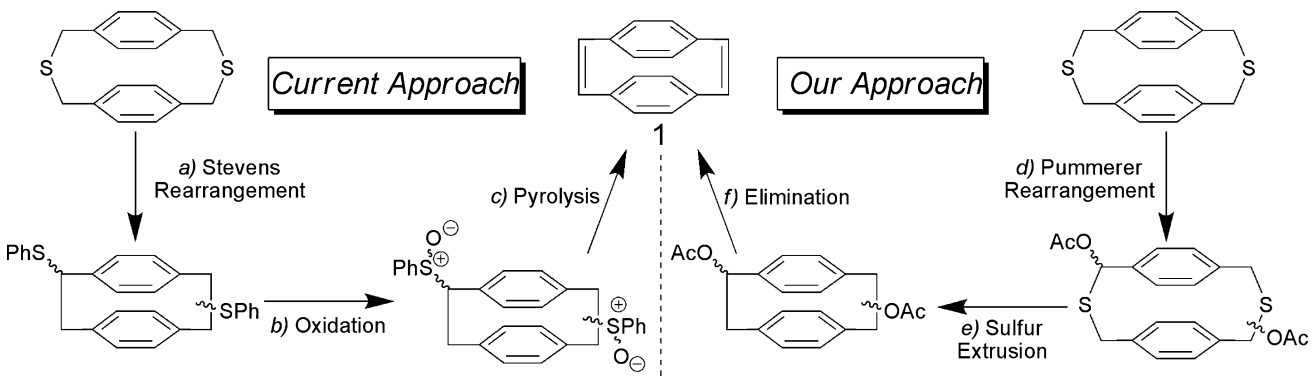
† Electronic supplementary information (ESI) available: detailed experimental procedures, NMR characterization, GC-MS characterization, and stereochemical analysis. See DOI: 10.1039/c1ob05319a



Scheme 1 Comparison between approaches for the ring contraction of [3.3]dithiacyclophanes to [2.2]paracyclophanes and related dienes.

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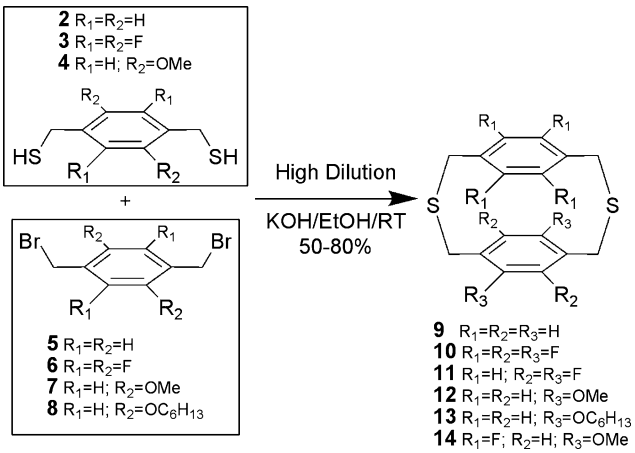


Scheme 2 Synthesis of [3.3]dithiacyclophanes used in this study.

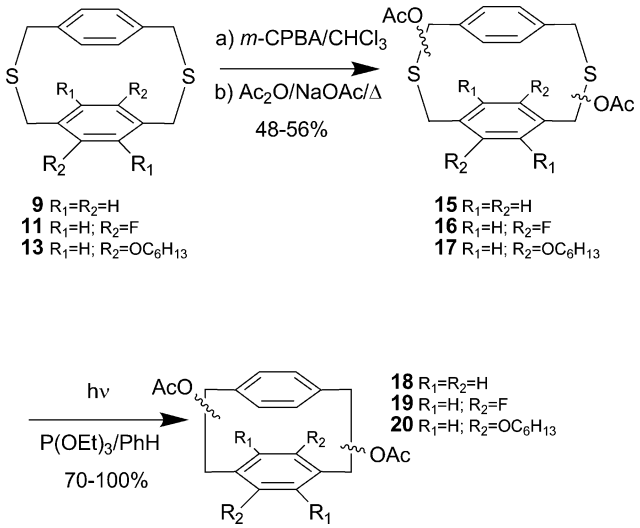
sulfide intermediate after step *a* and base-induced elimination (tBuOK), as an alternative to steps *b* and *c*, did not improve the yield of **1** (21%). Furthermore, using either of the two methods with dithiacyclophane **12**, the corresponding cyclophanediene was obtained in low yield, it was detected by GC-MS but could not be separated from byproducts. Using fluorinated dithiacyclophanes **10**, **11** and **14**, instead, the products of the Stevens rearrangement after step *a* could not be obtained.

As there is reported evidence that this rearrangement proceeds through a radical pathway,[8] its effectiveness could be greatly influenced by the reactivity of the benzylic positions towards radical species, and therefore on the nature of the aryl substituents.

The Stevens rearrangement effectively does two things: it effects the ring contraction in [3.3]dithiacyclophanes, and at the same time it installs into the resulting ethane bridges two functionalities amenable to be transformed into leaving groups for subsequent elimination and double bond formation. In focusing on alternative synthetic pathways, we realized that the Pummerer rearrangement,[9] in its classical form, is a mild, efficient way to install an acetate ester functionality (a good leaving group) in the α-position of an aliphatic thioether moiety. Furthermore, single and multilayered [2.2]cyclophanes are readily prepared *via* an efficient photochemical ring contraction, through sulfur extrusion from [3.3]dithiacyclophanes, to afford the two carbon atom saturated bridge between the two aromatic rings.[10] The combined use of these two methodologies could overcome the use of the Stevens rearrangement (Scheme 1, right, steps *d*, *e* and *f*). [3.3]Dithiacyclophanes **9**, **11** and **13**, containing aryl moieties with differing electronic character, were subjected to the protocol described in Scheme 3. They were oxidized to sulfoxides with *m*-CPBA (2.2 eq), and then treated with an excess of Ac_2O at reflux in the presence of a catalytic amount of NaOAc.

The products **15–17** were purified by collecting the chromatographically homogeneous materials, and obtained in good, unoptimized yields, as a mixture of regio and stereoisomers, as the double Pummerer rearrangement can occur on both sides of each of the thioether bridges.

The mixtures were analyzed by NMR spectroscopy. Although complex sets of signals were observed in the ^{1}H NMR spectra of **15–17**, their relative ratios were consistent with the proposed structures, confirming that a double Pummerer rearrangement had occurred in all cases.‡ The compounds were then subjected



Scheme 3 Synthesis of functionalized [2.2]paracyclophanes.

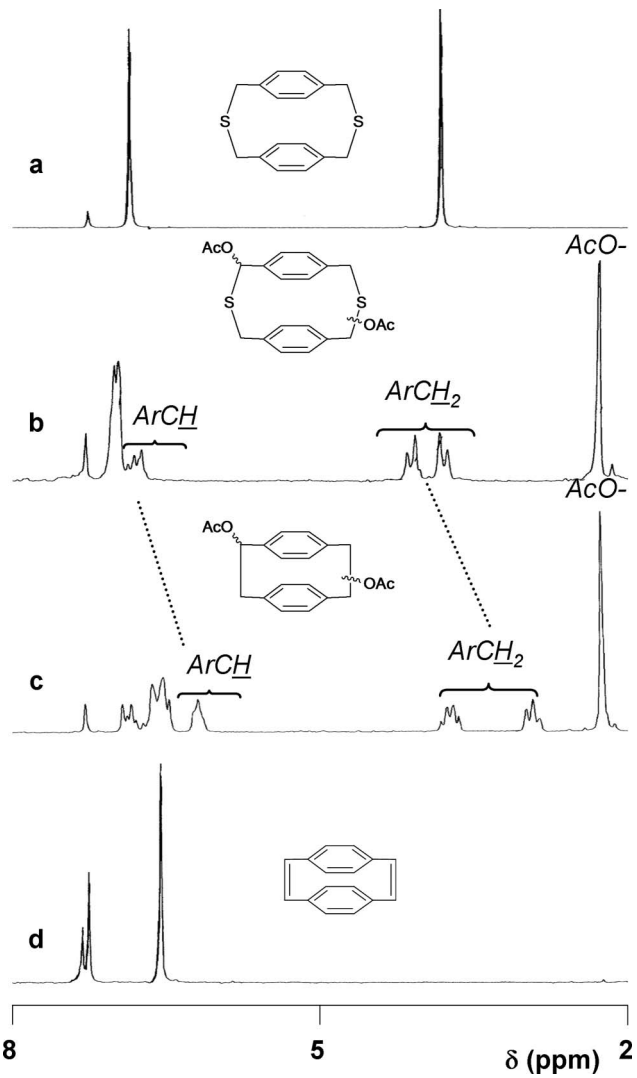


Fig. 1 ^{1}H NMR (200 MHz, $CDCl_3$) of compounds: a) **9**; b) **15**; c) **18**; d) **1**, obtained from **18**.

to a photochemical sulfur extrusion method previously used for bridge unsubstituted [3.3]thiacyclophanes;[10c] essentially quantitative conversions for **15–17** could be observed. The relative ratios of the different sets of signals were consistent with the proposed structures, and the diagnostic resonances for the benzylic protons in **15–17** were shifted, as expected, to higher fields in **18–20** as a consequence of the removal of the sulfur atoms from the molecular skeleton, efficiently occurring on both sides of the modified thiacyclophanes (Fig. 1b *vs.* 1c, and Fig S1 and S2). The purity and identity of the mixtures of regio and stereoisomers **18–20** were confirmed by GC-MS.

The elimination of the acetate groups to generate the strained carbon–carbon double bonds has been attempted using acid catalysis (PTSA, refluxing toluene), affording essentially starting material; base-induced elimination, instead, required a strong, non nucleophilic base (LDA, THF, room temperature) and afforded **1** in 58% yield.§

In conclusion, we have disclosed a new, mild and high-yielding strategy for the synthesis of bridge-functionalized [2.2]paracyclophanes; this strategy relies on a combination of a Pummerer rearrangement on the precursor [3.3]dithiacyclophanes and a photochemical ring contraction through sulfur extrusion, which is here reported for the first time for bridge functionalized [3.3]dithiacyclophanes. The synthetic methodology is compatible with aryl functionalities with either an electron-rich or electron-withdrawing nature. This strategy could lead to a milder, more general and more efficient pathway for the synthesis of [2.2]paracyclophanedienes, as successfully demonstrated in the case of **1**. Together with the before mentioned applications in materials science, uses of this methodology for the synthesis of [2.2]paracyclophanes with substituents at specific positions, to be used in the field of catalysis,[11] can be foreseen.

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Notes and references

‡ In the case of **15**, two spots could be separated, showing essentially superimposable ^{1}H NMR spectra. In the case of **17**, ^{1}H NMR spectra were further complicated as the 2,5-dialkoxy substituted aryl ring is a stereogenic element of planar chirality, thus effectively multiplying the number of stereoisomers which in principle can be obtained. See Supporting Information.

§ In the case of **19** and **20**, the mentioned conditions did not afford cleanly the corresponding cyclophanedienes. It is likely that conditions will have to be tuned for each of **19** and **20**, and related structurally and electronically variable paracyclophanes to be prepared. It is also possible that optimal conditions will have to take into account the substitution of the acetate functionalities with a better leaving group. It is our aim to address these themes in the near future.

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