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# Synthesis and Properties of 2,3-Diethynyl-1,3-Butadienes

Madison J. Sowden, Jas S. Ward and Michael S. Sherburn\*

Dedicated to Professor Henning Hopf

Abstract: The first general preparative access to compounds of the 2,3-diethynyl-1,3-butadiene (DEBD) class is reported. The successful synthesis involves a one pot, twofold Sonogashira-type, Pd(0)-catalyzed union of two terminal alkynes and a carbonate derivative of a 2-butyne-1.4-diol. The synthesis is broad in scope, as evidenced by the preparation of 30 diversely-substituted DEBDs. Members of this structural family are sufficiently kinetically stable to be handled using standard laboratory techniques at ambient temperature. They decompose primarily through heat-promoted cyclodimerizations. Alkyl substitution is shown to slow the rate of decomposition whereas extended conjugation through aryl or alkenyl substitution accelerates it. An iterative sequence of these unprecedented Sonogashira-type couplings generates a new type of expanded dendralene. A suitably-substituted DEBD carrying two terminal alkyne groups undergoes Glaser-Eglinton cyclooligomerization to produce a new class of expanded radialenes. These unprecedented cyclic hydrocarbons are chiral, by virtue of restricted rotation about the C2-C3 bond of their constituent 1,3butadiene residues. The structural features giving rise to atropisomerism in these expanded radialenes are distinct from those reported previously.

#### Introduction

In recent times, preparative syntheses of  $sp^{2}$ - and sp-C based acyclic architectures have challenged the widely-held, yet false perception that such compounds are unmanageable.<sup>[1,2],</sup> These studies are opening up regions of poorly chartered structural space, which is revitalizing the field. Applications of acyclic  $sp^{2}$ - and sp-C rich molecules include their use as building blocks in carbon-rich materials<sup>[3]</sup> and transform-driven step economic total synthesis of natural products.<sup>[4]</sup> In order to underpin these downstream developments, broad-spectrum and operationally simple synthetic methods for acyclic  $sp^{2}$ - and sp-C rich molecule of substitution upon their reactivity/stability.

This work focusses on the  $\pi$ -bond rich acyclic branched hydrocarbon 2,3-diethynyl-1,3-butadiene (DEBD) **1** (Scheme 1), a structure comprising only four *sp*<sup>2</sup>-carbons and four *sp*-carbons. It contains two terminal 1,3-enyne units and a central 1,3-butadiene, hence two branch points of cross-conjugation. Relatively little is known about this compound or its substituted

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analogues since no general method for the synthesis of 2,3diethynyl-1,3-butadienes has been reported and no structurereactivity/stability reports have appeared.

DEBDs are by no means unprecedented. Substituted DEBDs are scattered through the literature, with single examples from the groups of Larock,<sup>[5]</sup> Gleiter,<sup>[6]</sup> Grigg,<sup>[7]</sup> and Suzuki,<sup>[8]</sup> three compounds from Faust<sup>[9]</sup> and three from Hopf,<sup>[10]</sup> including the parent hydrocarbon **1**. Ru, Fe, and W complexes containing DEBDs, which display interesting electronic properties, have been studied by Bruce<sup>[11]</sup> and others.<sup>[12]</sup>



**Scheme 1.** 2,3-Diethynyl-1,3-butadiene, DEBD, **1**, reported substituted analogues, and a summary of the approach reported herein.

The contribution from the Hopf group uncovered almost everything that is known about the reactivity of DEBDs, and identified interesting applications. Thus, Hopf and co-workers reported the Diels-Alder reaction of their compounds with dienophiles to prepare cyclic *Z*-endiynes,<sup>[10]</sup> which found application in both Bergman cycloaromatizations<sup>[13]</sup> and in the synthesis of substituted phthalocyanines with potential in photodynamic therapy.<sup>[9]</sup> Hopf also reported the formation of 1,4cyclooctadienes through the thermal [4+4]cycloadditiondimerization of DEBDs. This remarkable transformation represents a formally disallowed process according to Woodward-Hoffman rules.<sup>[14]</sup> Finally, the Hopf group proposed, but did not investigate, the use of DEBDs as precursors to expanded radialenes.<sup>[10]</sup>

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We supplement this already sizeable list of both proven and predicted uses of DEBDs by noting their untapped potential as building blocks for polymers, and as ligands for organometallic  $\pi$ -complexes (those mentioned above are exclusively  $\sigma$ complexes). We suspect that a contributing factor to the lack of use of DEBDs relates to the aforementioned poor reputation of highly unsaturated acyclic hydrocarbons for instability.<sup>[15]</sup> We unequivocally establish here that such concerns about DEBDs are undeserved. By accessing 30 different categories of substituents and patterns of substitution, we show that the majority of these compounds can be handled neat for short periods at ambient temperature without decomposition. In addition to reporting the first general synthesis of DEBDs (Scheme 1), we elucidate the influence of substitution upon reactivity, we show that Hopf's prediction regarding the potential of DEBDs in the synthesis of expanded radialenes is correct, and we identify the specific DEBD substitution pattern required in order to achieve it.

#### **Results and Discussion**

In terms of atom connectivity, the simplest way to visualize the synthesis of a DEBD **4** (or any other 2,3-disubstituted-1,3butadiene) is by twofold cross-couplings of a 2,3-dihalo-1,3butadiene **6**, which can be accessed from a propargylic diol **5** by twofold substitution with 1,3-transposition (**Scheme 2**). The reaction proceeds by way of mono-coupled intermediate **7**. This is the approach taken by Hopf for the preparation of DEBDs, and one that we have used for dendralene<sup>[16]</sup> and radialene<sup>[17]</sup> synthesis, and others have used for substituted 1,3-butadiene synthesis.<sup>[18]</sup> Two challenges with this approach are: (a) 2,3dihalo-1,3-butadienes **6** are prone to polymerization, and (b) if mono-coupled intermediate **7** is *less* reactive towards crosscoupling than its precursor, then non-productive pathways (i.e. decomposition) might ensue.



Scheme 2. The unprecedented twofold Sonogashira coupling approach to substituted DEBDs  $(2\rightarrow [8]\rightarrow 4)$  and the known pathway involving polymerization-prone dihalides  $(6\rightarrow [7]\rightarrow 4)$ .

We recently reported<sup>[19]</sup> that tetrasubstituted 2-butyn-1,4diols (**5**, R<sub>1</sub>-R<sub>4</sub>  $\neq$  H) undergo twofold Pd(0)-catalyzed couplings with aryl (and some alkenyl) boronic acids, without the need to pre-activate the hydroxyl functionality<sup>[20]</sup> through covalent derivatization, to form densely-substituted 1,3-butadienes. The twofold cross-coupling proceeds with 1,3-transposition at each (C–O to C–C) bond change (cf. **2** $\rightarrow$ [**8**] $\rightarrow$ **4**, Scheme 2). We wanted to devise a synthesis of DEBDs **4** that would permit any substitution pattern, hence the restriction of this earlier method to highly substituted products precluded its application in this case.

Table1. TwofoldSonogashira-typecross-couplingof2-butyn-1,4-dioldicarbonate10with terminal alkynes furnishes2,3-ethynyl-1,3-butadienes thatare symmetrically substituted at the alkyne termini11a-m.



 $^{\rm a}$  Isolated and characterized as its  $\it N$ -methylmaleimide Diels-Alder cycloadduct. See the SI for details.

While there are several examples of twofold, 1,3transpositive couplings involving *activated derivatives* of 2butyn-1,4-diols **5** in the literature<sup>[7,21,22]</sup> none involve Sonogashira-type couplings. We were attracted to this process since, unlike dihalides **6**, carbonate precursors **2** are not prone to polymerization. Moreover, mono-coupled intermediates **8** were anticipated to be more prone to oxidative insertion of Pd(0) than precursor **7**, which would facilitate the desired twofold coupling. Table 1 documents the successful synthesis of thirteen substituted DEBDs using this method. The DEBDs in this Table differ in their substitution at the alkyne termini.

Standard Sonogashira coupling conditions<sup>[23]</sup> were effective for the reaction between known 2-butyn-1,4-diol dicarbonate **10**<sup>[24]</sup> and terminal alkynes **9** throughout, with [Pd(PPh<sub>3</sub>)<sub>4</sub>] and Cul as co-catalysts and diisopropylamine as base. Alkyne substituents that are tolerated include alkyl, alkenyl, trialkylsilyl, aryl, heteroaryl, and hydroxyalkyl groups. Isolated yields are generally good, the exceptions stemming from difficulties faced during separation of the DEBD product from the alkyne oxidative homocoupling product. While there are several reported methods to address this issue, none were completely effective in our hands.<sup>[25]</sup> The anomalously low yield of bis-cyclohexyl DEBD **11d** is due to its heightened sensitivity to autoxidation.

The twelve new DEBD structures listed in Table 2 show that all conceivable substitution patterns (mono-, 2 × di-, tri-, and tetra-) at the two alkene termini are accessible through the new twofold Sonogashira method. The propargylic substituents of the 2-butyne-1,4-diol precursor **5** are parlayed into alkene substituents in DEBD product **4**. A number of propargylsubstituted 2-butyn-1,4-diol precursors are commercially available, but their preparation from acetylene and ketones/aldehydes is trivial.<sup>[26,27]</sup> Interestingly, the twofold Sonogashira coupling is poorly *E/Z*-stereoselective with methyl substituents (**12a**, **12h** and **12i**) but gives exclusive *E*stereoselectivity with a phenyl group (**12b**, **12c**, **12d** and **12j**).

So far, the method has been shown to grant access to DEBDs with a wide variety of terminal alkyne substituents, and variation in the number and type of alkene substituents. The preparation of DEBDs with a different substituent on each alkyne terminus would require a sequence of couplings between a 2butyn-1,4-diol dicarbonate and two different alkynes, which would be challenging since the second cross-coupling  $(8 \rightarrow 4,$ Scheme 2) is invariably faster than the first  $(2 \rightarrow 8$ , Scheme 2). We considered a stepwise synthesis, in which the second crosscoupling could not proceed, for example by using a monocarbonate derivative of the 2-butyne-1,4-diol, but we were discouraged by the necessity of several additional steps to perform this synthesis, and instead opted for a one flask method in which two alkynes and the di-carbonate were simultaneously present. Thus, slow addition of the faster reacting acetylene, namely TMS-acetylene 13 to a mixture of the other reaction components delivered the best outcome, with a product ratio approximating to the best-case statistical ratio of the three products (i.e. 50:25:25) being obtained (Scheme 3). While the yields are modest, it is challenging to come up with a better approach, due to the very short step count (only 2 steps from inexpensive, commercial precursors) and operational simplicity.

 

 Table 2. Twofold Sonogashira-type cross-coupling of variously-substituted 2butyn-1,4-diol dicarbonates 2a-j with terminal acetylenes furnishes 2,3diethynyl-1,3-butadienes 12a-I carrying one, two, three or four substituents at the 1,3-butadiene termini.









Scheme 3. One flask synthesis of DEBDs 14 and 15 carrying two different alkyne substituents.

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Figure 1. Approximate first half-lives of substituted DEBDs at 70 °C, from an initial 1M concentration benzene solution, and empirical substituent effects.

With many new DEBDs in hand, representing a very wide diversity of structural possibilities, we were in a position to examine the influence of substitution upon kinetic stability. In general, substituted DEBDs are robust compounds. While we advocate long term storage of pure materials under Ar in a – 80 °C freezer, representative neat samples exposed to typical laboratory conditions (ambient fluorescent laboratory light, ambient temperature, in air) for an hour showed no sign of decomposition.

Figure 1 depicts the results of induced thermal decompositions of variously-substituted DEBDs, performed at the same temperature with the same starting concentration solution. As mentioned in the introduction, the Hopf laboratory reported the [4+4] cyclodimerization of DEBD **11h** in 34% yield from an initial 1.0 M concentration solution, with no sign of the [4+2] cyclodimer.<sup>[10b]</sup> In our hands, heating concentrated solutions of DEBDs **11j** and **11h** led to substantial polymerization and low yields of dimers, both in the presence or absence of acid scavengers and radical traps. Moreover, we observe the formation of a ca. 2:3 mixture of the [4+2] cyclodimer (**18, 19**) and the [4+4] cyclodimer (**16, 17**) in both cases (Scheme 4).





Whereas *catalyzed* [4+4] cyclodimerizations of 1,3butadienes are well established,<sup>[28]</sup> heat-promoted processes are much rarer events,<sup>[29]</sup> and heat promoted, concerted pericyclic [4+4] cycloadditions are disallowed by Woodward-Hoffman rules.<sup>[14]</sup> We suspect that [4+4] cyclodimers of DEBDs are either the products of a stepwise biradical mechanism,<sup>[10b,17]</sup> or the result of [2+2] cyclodimerization/Cope rearrangement.<sup>[29b]</sup> Diels-Alder dimers **18** and **19** were found to decompose on prolonged heating, which explains the absence of the [4+2] cycloadduct from the product mixtures analyzed by the Hopf group.

It is clear from the results summarized in Figure 1 that both the location and nature of substituents decorating a DEBD core have a pronounced influence upon its kinetic stability. The most reactive DEBDs are those carrying a conjugating substituent on either the alkyne or alkene termini. Thus, diphenyl-DEBD **11j** and di-cyclohexenyl-DEBD **11e** are even more prone to react on heating than the parent DEBD **1** (prepared by desilylation of **11h**). Alkyl and trialkylsilyl substitution slows down thermal selfreaction, such that hexa-substituted DEBD **12k**, for example, is inert at 70 °C as a 1M solution.

Combinations of stabilizing and destabilizing substituents appear to be additive, as can be seen from the group **11a**, **11j**, **12c** and **12d**. Further evidence for this comes in the form of the most reactive compound prepared, namely di-(4-cyanophenyl)-DEBD **20** (Figure 2). This compound underwent cyclodimerization at ambient temperature so rapidly that the monomer could not be isolated. Nonetheless, inclusion of four methyl groups at the 1,3-butadiene termini furnished a compound (**21**) that was readily isolable.



Figure 2. DEBD 20 is extremely prone to cyclodimerization but its tetramethyl congener 21 is kinetically stable.

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Expanded radialenes and expanded dendralenes are designed molecules in which (oligo)alkyne "spacers" are inserted between a pair of sp<sup>2</sup>-carbons.<sup>[30]</sup> Work on expanded dendralenes has been headed by the Tykwinski laboratory, who reported elegant, systematic studies have on isopolydiacetylenes (iso-PDAs), iso-polytriacetylenes (iso-PTAs) and unsymmetrical analogues.<sup>[31]</sup> These expanded dendralenes contain a repeating unit comprising a single 1,1-disubstituted C=C bond, connected by either a -C=C- or a -C=C-C=Cspacer (Figure 3). Dendralenes have recently been shown to exhibit UV-vis absorption maxima that are consistent with strans-1,3-butadiene units, and have been shown to react as multi-dienes in sequences of Diels-Alder cycloadditions.[2c] With DEBDs in hand, we wondered if they could be elaborated into expanded dendralenes that are structurally distinct to those previously accessed, which comprise dendralene behaviordefining 1.3-butadiene units, connected through acetylenic spacers (Figure 3).



**Figure 3.** The known *iso*-polydiacetylenes (*iso*-PDAs) and *iso*-polytriacetylenes (*iso*-PTAs) "expand" a dendralene by separating individual C=C units. Here, we report the first expanded dendralene comprising 1,3-butadiene units. The repeating unit is shaded in each structure.

The synthesis of the first such molecule, an expanded [6]dendralene comprising three 1,3-butadienes spaced by -C=C- units, is depicted in Scheme 5, in a process that is an iterative application of the methodology described earlier (Tables 1 and 2).



Scheme 5. Synthesis of the first expanded dendralene comprising 1,3-butadiene units, 23.

On first inspection, the successful outcome of this reaction is surprising, in light of the fact that both precursors, **22** (generated

by desilylation of  $12k^{[27]}$  and 10, are symmetric bifunctional building blocks. That a polymer is not the product of this reaction is the result of a substantially faster rate for the second C–C cross-coupling ( $8\rightarrow 4$ , Scheme 2) relative to the first ( $2\rightarrow 8$ , Scheme 2). Evidently, the 38% yield for this reaction is an indication that some of the product 23 reacts with biselectrophile 10, leading to higher oligomers. Triple DEBD product 23 lacks stabilizing alkyl substitution at the central 1,3butadiene and carries conjugating groups at its alkyne termini, hence it is amongst the least kinetically stable of the isolable compounds reported herein, and higher oligomers with the same repeating unit are anticipated to be less kinetically stable still, which explains why they are not isolated from this reaction.

Finally, we return to test Hopf's proposal<sup>[10b]</sup> that the cyclooligomerization of DEBDs could generate expanded radialenes (see Introduction). When this proposal was published in 1996,<sup>[10b]</sup> the first examples of expanded radialenes had recently been published by the Diederich laboratory.[32a] The field has since experienced significant growth, with many expanded radialenes now known, comprising, as a repeating unit, a single 1,1-disubstituted C=C bond, connected by one or more -C=Cspacers. Such structures are the cyclic analogues of iso-PDAs, iso-PTAs and their unsymmetrical congeners (Figure 3). Nonetheless, there are no DEBD-based cyclo-oligomers known: in fact, until now there have been no expanded radialenes comprising cross-conjugated 1,3-butadiene units.[33] The synthesis and single crystal X-ray analyses of the first such compounds are depicted in Scheme 6, which were prepared by Glaser-Eglinton oxidative cyclo-oligomerization of tetramethyl-DEDB monomer 22.



Scheme 6. Glaser-Eglinton cyclo-oligomerization of tetramethyl-DEBD 22 gives chiral, carbon-rich cyclodimer 24 and cyclotrimer 25. H atoms are omitted from the X-ray crystal structures for clarity.

These compounds were prepared under high dilution conditions. Specifically, slow addition of DEBD precursor 22 to the reagent mixture gave cyclotrimer 25 (an expanded [6]radialene) as major product, with even slower addition giving rise to mixtures richer in the cyclodimer 24 (an expanded [4]radialene).<sup>[27,34]</sup> The ideal shape<sup>[35]</sup> of molecules of cyclodimer 24 identified by crystallography have  $D_2$  symmetry, whereas those of cyclotrimer 25 have C1 symmetry.<sup>[36]</sup> Perhaps the most striking feature, on first inspection, is the significant distortion from linearity that is visible around the 1,3-butadiyne portions of cyclodimer 24. Related 12-membered carbocyclic structures containing a pair of 1,3-butadiyne groups have been previously reported,<sup>[37]</sup> and the bending around the 1,3-butadiynes in our structure is similar to those published. 18-Membered carbocycles related to cyclotrimer 25 have also been reported.[38] Nonetheless, the new structures depicted in Scheme 6 have unique structural and conformational features that warrant a more detailed discussion.

In stark contrast to the successful cyclo-oligomerization of tetramethyl-DEBD 22, the parent DEBD 1, and its E,E-dimethyl analogue 26 (generated by desilylation of 11h and 12h, respectively<sup>[27]</sup>) did not furnish isolable monodisperse products. We ascribe this lack of success to the lower kinetic stability of DEBD precursors 1 and 26 and their cyclo-oligomeric products relative to DEBD 22 and its products (cf. Figure 1). An additional contributing factor is their preferred conformations. Molecular structures from single crystal X-ray analyses and DFT studies<sup>[27]</sup> (Figure 4) reveal that the parent DEBD 1 and its E,E-dimethyl analogue 26 prefer the in-plane, s-trans 1,3-butadiene conformation, in which the two ethynyl termini point in opposite directions (Figure 4, (C≡)C2'-C2-C3-C3'(≡C) dihedral: X-ray, calc:  $\theta$ =180°). In contrast, tetramethyl-DEBD 22 prefers a nonplanar conformation, with the two ethynyl groups in the same hemisphere (Scheme 6, (C≡)C2'-C2-C3-C3'(≡C) dihedral: Xray:  $\theta$ =67°; calc:  $\theta$ =81°).



Figure 4. The parent DEBD 1, and its *E,E*-dimethyl analogue 26 and their molecular structures from calculations and single crystal X-ray analyses. H atoms are omitted from the X-ray crystal structure and calculated structure for clarity.

Calculations<sup>[27]</sup> on the parent DEBD **1** and its *E,E*-dimethyl analogue **26** reveal a *skew*-conformation (similar to the preferred conformation of tetramethyl-DEBD **22**, Scheme 6) as a local energy minimum, some 13-14 kJ/mol higher in energy than the lowest energy *s*-trans conformation shown in Figure 4. The rotational barriers about the central  $C(sp^2)-C(sp^2)$  single bond in these molecules correspond to the *s*-*cis* and orthogonal

conformers, both of which lie around 21-24 kJ/mol above the preferred *s-trans* conformation. For cyclo-oligomerization of **1** or **26** to occur, each individual DEBD unit within the acyclic precursor to the cyclo-oligomer would need to simultaneously adopt a conformation conducive to cyclization, which would involve a substantial energetic penalty. Thus, vanishingly low populations of cyclization-ready conformations are present in solution, which results in a cyclization step that cannot compete with intermolecular processes.

Single crystal X-ray analyses of cyclodimer 24 and cyclotrimer 25 were essential in order to identify the two products. These analyses, along with associated VTNMR studies and associated calculations, also reveal a fascinating and, as far as we can ascertain, unprecedented form of atropisomerism in 1,3-butadienes. Restricted rotation about the C2-C3 bond in 1,3-butadienes carrying sterically demanding substituents at C2 and C3 is well established, primarily due to contributions from the Hopf group.[39] Cyclodimer 24 and cyclotrimer 25 exhibit restricted rotation in their 1,3-butadiene units owing to a combination of the inside (Z)-methyl groups at C1 and C4 of each 1,3-butadiene, which disfavor in-plane conformations, and the rather rigid nature of the tether connection between the two ethynyl termini of each DEBD residue, which precludes a through-the-ring rotation of one exocyclic alkene to invert the configuration of a DEBD unit.

Both cyclodimer **24** and cyclotrimer **25** exhibit chiral structures in the solid state, with both enantiomeric forms being present in each crystal. These chiral structures stem from the aforementioned twisted conformations of each 1,3-butadiene unit.

<sup>1</sup>H and <sup>13</sup>C NMR spectra of cyclodimer **24** at 25 °C reveal two proton environments and six carbon environments. At –5 °C, two sets of resonances are present in a ca. 70:30 ratio. Thus, <sup>1</sup>H and <sup>13</sup>C NMR spectra reveal the presence of two diastereomeric forms of **24** undergoing slow conformational interchange on the NMR timescale at cooler temperatures. VTNMR studies with line shape analysis estimate the barrier for interconversion between these two forms at ca. 66 kJ/mol.

Scheme 7 depicts the three conformers of DEBD cyclodimer **24** and the mechanism of interconversion between them, which explains these experimental observations. The two enantiomeric forms, *M*,*M*-24 and *P*,*P*-24, differ in stereogenicity at both 1,3-butadiene groups. Thus, stereochemical inversions at both 1,3-butadiene groups must occur in order for a molecule to enantio-isomerize. We propose that this process takes place in a stepwise manner, by way of meso-diastereomer *M*,*P*-24, which is the second diastereomeric form detected spectroscopically.

A DFT conformer search located only the chiral and meso conformers, and predict a Boltzmann population (gas phase, 298.15K) of 79:21 for *M,M-24/P,P-24* : *M,P-24*, which is in good agreement with the experimentally-measured ratio of 70:30, from integration of <sup>1</sup>H NMR spectra (CDCl<sub>3</sub>) recorded at –5 °C. The DFT calculated barrier for methyl/methyl crossing through the *s-cis* conformation of tetramethyl-DEBD **22** is ca. 100 kJ/mol, which is a little higher than the value of 66 kJ/mol from VTNMR studies performed on cyclodimer **24**. A lower barrier would be

#### 10.1002/anie.201914807

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expected for cyclodimer **24** due to ring strain, which has the effect of splaying the 1,3-butadienes (C1=C2-C3 bond angles from X-ray structures as follows: monomer **22**,  $\theta$ =122.9°; cyclodimer **24**,  $\theta$ =125.3-125.5°), which would be expected to increase the *inside* Me/Me distance at their crossing point.



Scheme 7. Conformational dynamics of DEBD cyclodimer 24. H atoms are omitted from the X-ray crystal structures and calculated structure for clarity.

<sup>1</sup>H and <sup>13</sup>C NMR spectra of cyclotrimer **25** show six proton resonances and twenty-three <sup>13</sup>C resonances. Interestingly, no significant change was seen in NMR spectra within the temperature range -60 °C  $\rightarrow$  +70 °C. The  $C_1$  symmetry conformation of cyclotrimer **25** should exhibit twelve <sup>1</sup>H NMR resonances and thirty-six <sup>13</sup>C NMR resonances. A second diastereomeric atropisomeric form with  $D_3$  symmetry is possible for DEBD cyclotrimer **25**, as shown in Scheme 8. This more symmetric structure should give rise to <sup>1</sup>H and <sup>13</sup>C NMR spectra with only two and six resonances, respectively. Evidently, either the  $C_1$  form is populated exclusively, or a mixture of the  $C_1$  and  $D_3$  forms are present throughout.





Scheme 8. Interconversion between the two diastereomeric forms of DEBD cyclotrimer 25. Only one enantiomer of each is depicted. H atoms are omitted from the X-ray crystal structure and calculated structure for clarity.

#### Conclusion

In summary, substituted 2,3-ethynyl-1,3-butadienes (DEBDs) are now readily available, through a short and operationally simple 2-4 step synthesis from commodity chemicals. All possible arrangements of substituents and substitution patterns are accessible from this broad-spectrum approach, which deploys inexpensive and readily available building blocks that are not prone to polymerization.

The vast majority of substituted DEBDs can be stored neat for extended periods of time in a -80 °C freezer, or for short periods at ambient temperature. Heat brings about decomposition, with modest yields of mixtures of [4+2] and [4+4] cyclodimers being isolable, and the majority of material seemingly undergoing polymerization. Both the type and number of substituents determine the rate of decomposition of DEBDs, and systems have been designed to both accelerate and impede this process. In general, conjugating substituents destabilise DEBDs, whereas alkyl and silyl groups stabilize them.

The first steps towards incorporating DEBDs into novel materials have been taken, with unprecedented expanded dendralene and radialene systems being prepared. The novel expanded radialenes **24** and **25** are 12- and 18-membered ring systems comprising a 2:1 ratio of  $sp:sp^2$  carbons.<sup>[40]</sup> They exhibit chiral conformations as a result of atropisomerism about the constituent DEBD cores. While chiral 1,3-butadienes are known, the structural features that give rise to atropisomerism in expanded radialenes **24** and **25** (small C1 and C4 *Z*-substituents on a 1,3-butadiene with a constrained cisoid conformation) are distinct from those reported previously (sterically bulky C2 and C3 substituents). There is significant scope for modification of

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the general design principles described herein to invent compounds that are atropisomerically-stable at ambient temperature. Such systems offer new design possibilities for enantiomer recognition and catalysis.

The preparation of expanded dendralene **23** (Scheme 5) and radialenes **24** and **25** (Scheme 6) represent a proof-of-principle. Evidently, many variations on these themes can be envisaged, including the incorporation of arylene, heteroatom, and metal-based spacers, with potential applications of these new cross-conjugated materials in optics and electronics. Attempts to experimentally verify these predictions are under way.

#### **Experimental Section**

Full experimental details are provided in the Supporting Information.

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**Keywords:** hydrocarbons • 1,3-butadienes • cross-coupling • conformation analysis • atropisomerism

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# **RESEARCH ARTICLE**

### **Entry for the Table of Contents**

## **RESEARCH ARTICLE**



**Just diene to be chiral.** The first general synthesis of 2,3-diethynyl-1,3-butadienes (DEBDs) uses commodity chemical precursors (acetylene, two terminal alkynes, and two aldehydes/ketones) and involves, as a key step, an unprecedented twofold Sonogashira-type cross-coupling of a 2-butyn-1,4-diol derivative. The process is of extremely wide scope, with 30 structurally diverse examples reported. The value of DEBDs as building blocks for novel expanded dendralenes and expanded radialenes is demonstrated. The latter exhibit an unprecedented form of atropisomerism.

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Page No. – Page No.

Synthesis and Properties of 2,3-Diethynyl-1,3-Butadienes.