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Synthesis and reactivity of anthracenyl-substituted arenediynes

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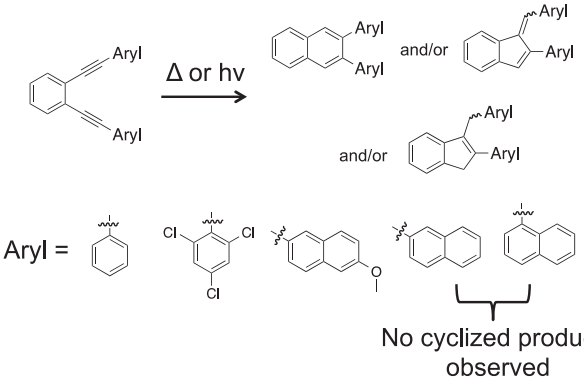
ABSTRACT

Cyclization reaction pathways of aryl-substituted arenediynes depend on the interplay between the steric interactions and electronic properties of the aryl substituents. Herein, to further probe the impact of bulky and electron rich aryl substituents on the cyclization of arenediynes, anthracenyl-substituted arenediynes (**1**–**3**) with different *ortho* substituents were synthesized and their thermal, photo, and radical initiated cyclization reactions were studied.

Cyclization reactions of enediynes with aliphatic groups at the alkyne terminus are well studied compared to their aryl substituted counterparts.[1–4] Cyclization of aryl-substituted arenediynes yields a 5-membered ring (via C^1–C^5 cyclization) or a 6-membered ring (via C^1–C^6 Bergman cyclization), hence the reaction is a useful synthetic method to generate polycyclic aromatic hydrocarbons and fulvenes.[3,5–14] Polycyclic aromatic hydrocarbons with extended π-conjugation exhibit useful optical and charge transport properties for applications in photovoltaics and organic transistors.[12,14–16] Moreover, the photophysical properties of polycyclic aromatic hydrocarbons containing the 5-membered ring are unusual compared to the analogous molecules with 6-membered rings.[3,5–13,15] It is thus of interest to develop a better understanding of the structure–property relationships of the 5-membered ring containing polycyclic aromatic hydrocarbons. Cyclization of aryl-substituted arenediynes proceeds via C^1–C^5 cyclization (5-membered cyclic product) or C^1–C^6 Bergman cyclization (6-membered cyclic product) pathway that can be modulated by the sterics and electronics of aryl substituents. For example, phenyl-substituted arenediyne generates both Bergman and C^1–C^5 cyclized product whereas the bulky trichlorophenyl-susbstituted arenediyne yields only C^1–C^5 cyclized products upon thermal induced cyclization (Scheme 1).[7,17] Electronic effects on the cyclization pathway are more apparent in the case of naphthalenyl-substituted arenediynes.[9] Photoreaction of electron rich naphthalenyl-substituted arenediyne (6-methoxy naphthalen-2-yl derivative) yields a Bergman cyclized product whereas the naphthalenyl-substituted arenediynes (naphthalen-1-yl and naphthalen-2-yl derivatives) do not generate the expected cyclized products.[9] Photoreaction of dianthracene-*homo*-enediyne in which only one of the anthracenylacetylene is in π-conjugation with aryl moiety generates a cyclized product with benzene which is used as a solvent for the reaction.[18]



Scheme 1. Previously reported products from cyclization of aryl-substituted arenediynes.

In this work, to further probe the interplay between steric and electronic effects of the aryl substituents on arenediyne cyclization reactions, 9-anthracenylethynyl arenediynes **1**–**3** (Fig. 1) in which both the anthracenylacetylenes are in π-conjugation with the aryl moiety were synthesized and their thermal, photo, and radical initiated cyclization reactions are studied. We expect the

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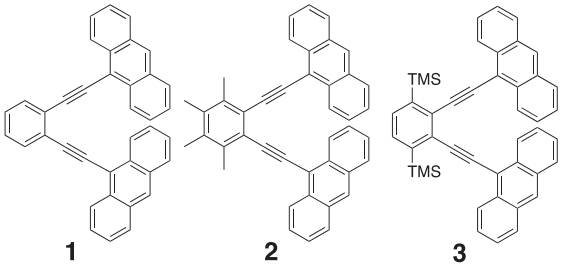
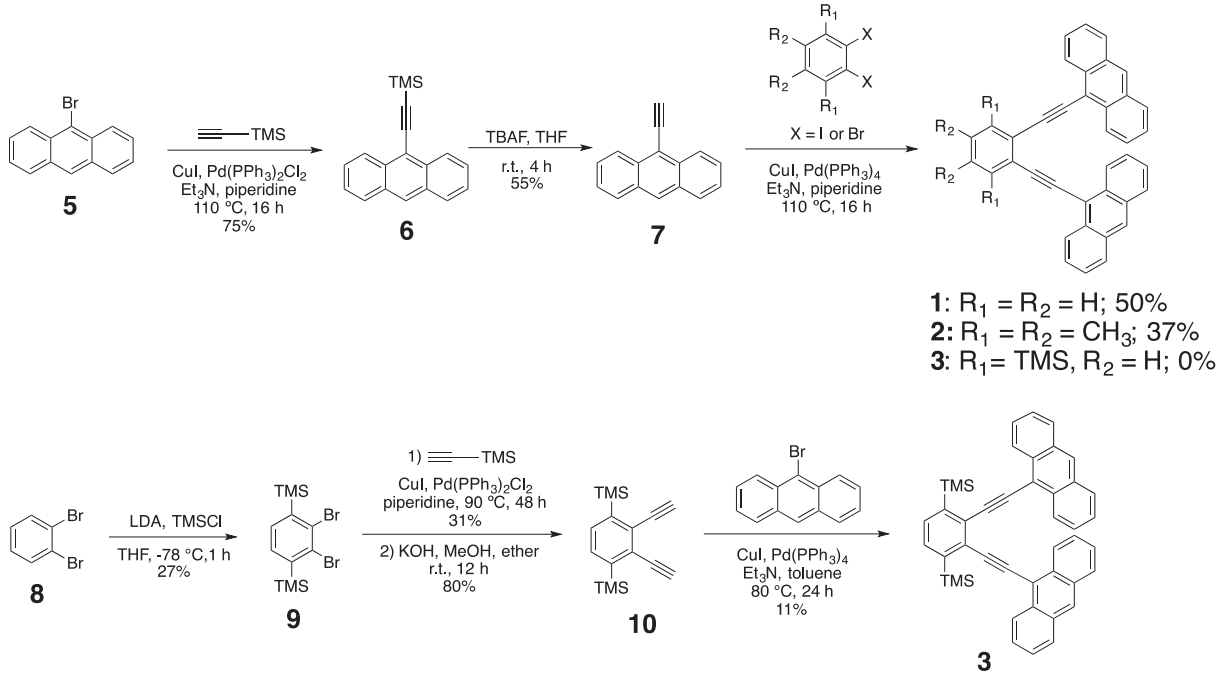


Figure 1. Chemical structures of anthracenyl-substituted arenediynes synthesized and studied in this work.

cyclization of compounds **1**–**3** to proceed via C^1–C^5 cyclization pathway given that anthracene is more sterically demanding than naphthalene. In addition, anthracene is also electron rich compared to naphthalene due to extended π-conjugation. In arenediynes, it is also known that the *ortho* substituents on the phenyl ring impact the kinetics of the cyclization reaction.[19,20] Thus, we have also varied the size of the *ortho* substituents (–H, $–CH_3$, and –TMS) on the phenyl ring and studied its impact on the conformation of anthracenyl groups and the cyclization reaction.

9-Anthracenylethynyl arenediyne derivatives **1**–**3**, possessing *ortho* substituents of increasing steric demand –H (**1**), $–CH_3$ (**2**), and –TMS (**3**) were synthesized (Scheme 2). Compounds **1** and **2** were prepared starting from 9-bromoanthracene (**5**). Sonogashira coupling of **5** with TMS acetylene followed by TMS deprotection yielded anthracenylacetylene (**7**). Sonogashira coupling of **7** with 1,2-diiodobenzene or 3,4,5,6-tetramethyl-1,2-diiodobenzene yielded **1** and **2**, respectively.[9] Unfortunately, in the case of **3**, Sonogashira coupling of **7** with (2,3-dibromo-1,4-phenylene)bis(trimethylsilane) afforded only the mono-substituted product due to the influence of the bulky –TMS groups. Thus, **3** was synthesized following an alternative route via Sonogashira coupling of 9-bromoanthracene with **10** ((2,3-diethynyl-1,4-phenylene)bis(trimethylsilane)).[21] Compound **10** was prepared in three steps from dibromobenzene (**8**).

Cyclization reactions of arenediynes depend on the distance between the alkyne groups and the nature of the aryl substituents.[1–4] Single crystals of molecules **1**–**3** were grown to determine the distance between alkyne groups and the preferred intramolecular orientation of anthracenyl moieties (Fig. 2). From the crystal structures, it is evident that the intramolecular distance between the alkynes and anthracene groups as well as their orientation with



Scheme 2. Synthesis of anthracenyl arenediynes **1**–**3**.

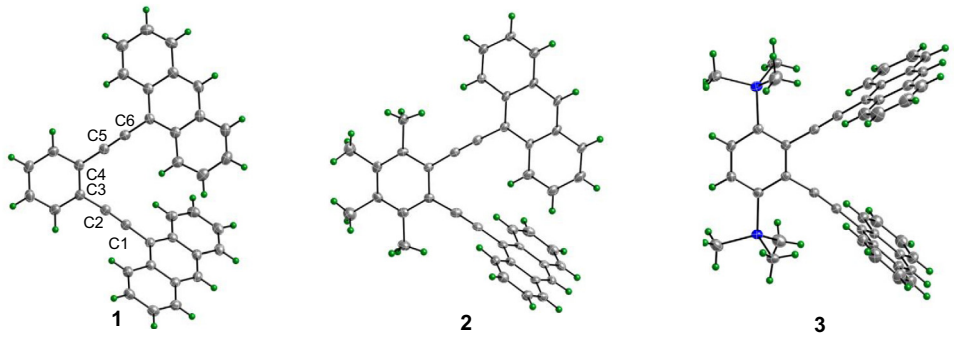


Figure 2. ORTEP view of crystal structures of **1**–**3**.

respect to each other changes as the *ortho* substituents are varied. The distance between the C^1–C^6 carbons in **1**, **2**, and **3** is 4.27, 4.02, and 4.18 Å, respectively, and the distance between C^1–C^5 carbons in **1**, **2**, and **3** is 3.75, 3.52, and 3.61 Å, respectively. Furthermore, the anthracene moieties in **1** and **2** are interacting in an edge-to-face fashion whereas the anthracene moieties in **3** are interacting in face-to-face fashion.

Absorption and fluorescence spectra (Fig. 3) were recorded to gain further insights into the intramolecular interaction between the anthracene groups in molecules **1**–**3**. Absorption spectra of **1**–**3** are red shifted compared to phenyl and naphthalenyl-substituted arenediynes due to enhanced pi-conjugation.[9] Absorption spectra of **1**–**3** are similar except that the peaks in **1** and **2** are generally broader than those for **3**. This could be because of the restricted rotational freedom of the anthracene moieties in **3** due to the bulky –TMS groups. Emission spectra of **1**–**3** (Fig. 3) are also similar. The absorption and emission spectra of **1**–**3** indicate that there are no significant differences in the intramolecular interactions between the anthracene moieties in all three compounds.

Bulky aryl groups are known to increase the activation energy for the cyclization reaction and favor C^1–C^5 cyclized products over Bergman cyclized products.[9,17] In order to predict the preferred cyclization pathways in **1**–**3**, activation energies ($\Delta G^{\ddagger}$) for the formation of both C^1–C^5 and Bergman cyclized products in **1**–**3** were calculated at the B3LYP/6-31G(d) level of theory (Table 1).[16] The activation energy for both C^1–C^5 and Bergman cyclization decreases as the size of the *ortho* substituents increases in **1**–**3**. The decrease in intramolecular distance between the alkyne carbons in **1**–**3** as a result of the increased steric repulsion between the *ortho* substituents and the alkyne carbons could be the reason for the observed trend. Additionally, the activation energy for C^1–C^5 cyclization is ca. 5–7 kcal/mol lower than that for the Bergman cyclization pathway, indicating that the bulky anthracenyl group should direct the cyclization toward the C^1–C^5 cyclization pathway as expected.

Compounds **1**–**3** were subjected to thermal, photo, and radical induced cyclization reaction conditions. To determine the thermal reactivity of **1**–**3**, differential scanning calorimetry (DSC) of compounds **1**–**3** were recorded. It has been shown that the cyclization reaction in enediynes is associated with an exothermic peak in DSC.[6,22–25] Thermogravimetric analyses (TGA) (Supporting information Fig. S1) and DSC (Fig. 4) of **1**–**3** were recorded to determine the decomposition temperature and the onset temperature for the cyclization reaction. The decomposition temperatures of **1**, **2**, and **3** were found to be 383, 191, and 237 °C, respectively. The DSC of **1** shows both endothermic (maximum: 215 °C) and exothermic peaks (maximum: 265 °C) while **2** and **3** do not show any peaks below their decomposition temperature. The endothermic peak at 215 °C matches with the experimentally determined melting point of **1**, while the exothermic peak at 265 °C might be associated with the cyclization reaction. The absence of exothermic peaks in **2** and **3** below their decomposition temperatures indicates that the cyclization reaction in these compounds in solid state is adversely affected by the geometrically constrained environment created by the bulky *ortho* ($-CH_3$ and –TMS in **2** and **3**) and/or anthracenyl substituents. Since **1** showed an exothermic peak in DSC corresponding to a thermal induced reaction, a cyclization reaction of **1** was carried out in 1,4-cyclohexadiene[17,19] in a sealed tube at 250 °C, which is the onset temperature determined from the DSC analysis. Thermal induced cyclization reaction of **1** resulted in a mixture of products. The ^{1}H NMR spectra of the isolated products were complex and could not be assigned to the expected cyclized product, thus making it difficult to deduce the actual chemical structures. Subsequent reactions that were carried out at a lower temperature (200 °C) in toluene with alternative proton sources such as 1,4-cyclohexadiene and phenol were also unsuccessful. Cyclization reactions of **2** and **3** in a mixture of toluene and 1,4-cyclohexadiene at 150 °C, below their decomposition temperature, were unsuccessful. Although the calculated thermal activation energy barriers for cyclization of the phenyl-, trichlorophenyl-, and anthracenyl-substituted arenediynes are very close, the anthracenyl derivative does not result in the expected cyclized products. Failure to observe the expected cyclized products in the case of anthracenyl-substituted arenediynes could be due to the

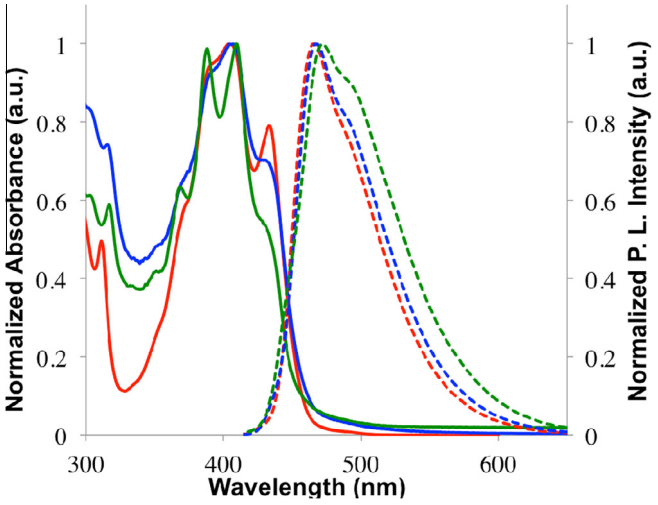


Figure 3. Normalized absorption (solid line) and emission (dotted line) of **1** (red), **2** (blue), and **3** (green) in chloroform.

Table 1
Activation energies for cyclization reactions of **1**–**3**[a]

Molecule	$\Delta G^{\ddagger}$ C^1–C^5[b] (kcal/mol)	$\Delta G^{\ddagger}$ C^1–C^6[c] (kcal/mol)	$\Delta\Delta G^{\ddagger(5-6)}$[d] (kcal/mol)
1	42.73	49.72	−6.99
2	41.70	48.84	−7.14
3	39.01	44.24	−5.23

[a] calculations are performed using B3LYP/6-31G(d) level of theory.
[b] activation energy for C^1–C^5 cyclization.
[c] activation energy for Bergman cyclization.
[d] difference in activation energies for C^1–C^5 and Bergman cyclization.

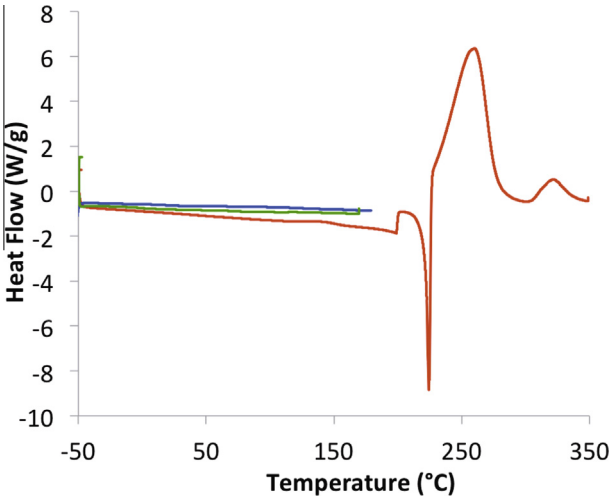
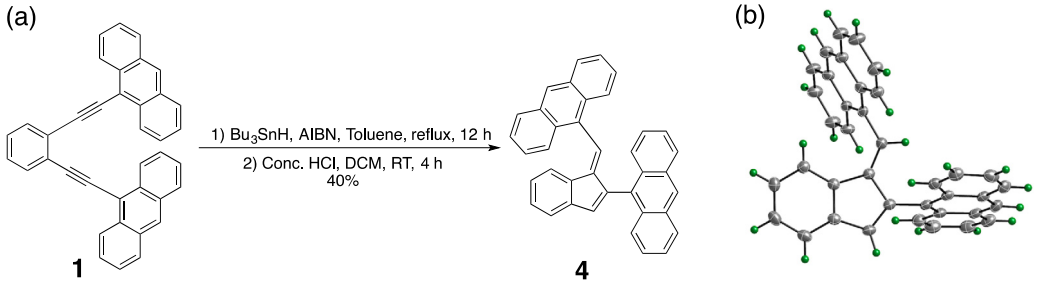


Figure 4. DSC curves of **1** (red), **2** (blue), and **3** (green) (heating rate: 10 °C/min).



Scheme 3. (a) External radical initiated cyclization of **1**; (b) ORTEP view of fulvene product (**4**).

underestimation of the steric effects imparted by the bulky anthracenyl group in the activation energy calculations.

After thermal conditions failed to initiate cyclization, compounds **1**–**3** were subjected to photoinitiated cyclization conditions. The reactions were performed in benzene as solvent and 1,4-cyclohexadiene as a proton source over 24 h using a 150 W light source. All three samples yielded a mixture of products. ^{1}H NMR spectra of the isolated products were complex, making it difficult to deduce structural information of the products. Efforts to grow single crystals of the isolated products as well as the use of different hydrogen sources (methanol and isopropanol) were also unsuccessful. We hypothesize that undesired intramolecular 4+4 cycloaddition (between the anthracenyl groups) and intermolecular 4+2 cycloaddition (between the anthracenyl and the alkyne groups) as well as the intended cyclization reaction are responsible for the observed complex mixture of products.[26,27] Failure to observe cyclized products in **1**–**3** under thermal and photoinitiated conditions compared to other aryl-substituted arenediynes (phenyl, trichlorophenyl, and naphthalenyl derivatives) is likely due to the increased steric demand of the anthracene groups. In the case of naphthalenyl-substituted arenediynes (naphthalen-1-yl, naphthalen-2-yl, and 6-methoxy naphthalen-2-yl derivatives), only the 6-methoxy naphthalen-2-yl derivative resulted in the expected Bergman cyclized product under photoinitiated cyclization.[9] For arenediynes with simple aryl substituents of varying bulkiness (phenyl, naphthalen-1-yl, naphthalen-2-yl, and anthracen-9-yl derivatives), only the phenyl derivative yields the expected cyclized product. Thus, the aryl substituents on the arenediyne play a key role in the photoreactivity of the arenediynes.

As attempts using thermal or photoreaction conditions to initiate cyclization reaction were unsuccessful, compounds **1**–**3** were subjected to radical initiated cyclization reaction conditions. Radical initiated reactions of phenyl-substituted arenediynes are known to preferentially result in the formation of C^1–C^5 cyclized products known as fulvenes.[4,8] Radical initiated cyclization of compounds **1**–**3** was performed by the addition of Bu_3SnH/AIBN (Scheme 3). The reaction mixture was quenched with HCl after 12 h. Compound **1** with no *ortho* substituents yielded the expected fulvene product **4** with an isolated yield of 40% (Scheme 3). The molecular structure of **4** was confirmed by NMR spectroscopy, mass spectrometry, and single crystal structure data. Radical initiated cyclization reactions of **2** and **3** gave a complex mixture of products, which could not be analyzed. In the cases of **2** and **3**, the bulky *ortho* substituents (–CH_3 and –TMS) might have prevented the attack of tributyltin radical onto the alkynyl carbon attached to phenyl. The *ortho* substituents on the phenyl ring seem to play a major role on the external radical initiated cyclization reaction pathway in anthracenyl-substituted arenediynes. Bulky anthracenyl substituents on the alkyne terminus seem to have less of an effect on the radical-mediated cyclization pathway, since **1** yielded the expected fulvene product with an external radical initiator but did not yield the expected cyclized products under thermal or photoinitiated conditions.

To summarize, 9-ethynylanthracenyl arenediynes with different *ortho* substituents were synthesized. Thermal, photo, and radical initiated cyclization reactions were investigated to elucidate the effects of the size of the *ortho* as well as the anthracenyl substituents on the cyclization reactions. Optical absorption spectra of **1**–**3** are red shifted compared to phenyl- and naphthalenyl-substituted arenediynes due to enhanced pi-conjugation. Even though the calculated activation energies for C^1–C^5 cyclization reactions of **1**–**3** are close to the other reported arenediynes, no cyclization products are observed in **1**–**3** upon thermal or photoinitiation. This could be due to the underestimation of the steric effects imparted by the anthracenyl group in the calculations. External radical activated reaction of **1** resulted in the corresponding fulvene product (**4**) whereas the cyclization reactions of **2** and **3** were not successful due to the bulky *ortho* substituents. In the case of external radical initiated reactions, *ortho* substituents played a major role compared to the aryl substituent at the alkyne terminus.

Acknowledgements

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Supplementary data

Crystallographic data for the structures in this Letter have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication. CCDC 1035028 to 1035031 for compounds **1**, **4**, **2**, and **3**, respectively.

Supplementary data (detailed synthetic procedures, ^{1}H and ^{13}C NMR spectra, thermogravimetric analyses of **1**–**3**, absorption and emission spectra of **4**, computational methods, and crystallographic information files (CIF) for **1**–**4**) associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2015.01.011.

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