Cyclic Alkyne Approach to Heteroatom-Containing Polycyclic Aromatic Hydrocarbon Scaffolds

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ABSTRACT. The chemistry of arynes and cyclic alkynes has undergone a renaissance in recent years. These intermediates, once viewed only as scientific curiosities, have now shown utility in a variety of synthetic applications. One area where cyclic alkyne chemistry could be further developed is in the field of materials chemistry and, specifically, for the synthesis of heteroatom-containing polycyclic aromatic hydrocarbons (PAHs). Such motifs are seen in modern devices, including organic light-emitting diodes (OLEDs). We report a modular synthetic strategy for accessing these important scaffolds that relies on the controlled generation of transient heterocyclic alkynes and arynes. The strained intermediates undergo in situ trapping with readily accessible oxadiazinones. Four sequential pericyclic reactions occur, namely two Diels–Alder / retro-Diels–Alder sequences, which can be performed in a stepwise or one-pot fashion to assemble four new carbon–carbon (C–C) bonds. By employing a variety of strained intermediates and oxadiazinones, products bearing four quadrants of differentiation can be accessed. The new scaffolds accessible by this strategy provide a rapid entryway to new small molecule fluorophores, including solvatochromic compounds, stimuli-responsive materials, and donor–acceptor oligomers. These studies underscore how the use of heterocyclic strained intermediates can be harnessed for the preparation of new organic materials.

INTRODUCTION

Alkynes contained in small rings were once considered only intellectual curiosities. However, in recent years, strained cyclic alkynes have resurfaced and have been widely employed in synthetic methodology studies.[1,2,3,4,5,6,7,8,9,10] Additionally, such efforts have led to a greater understanding of aryne and cyclic alkyne reactivity and regioselectivities, which in turn, has enabled predictions.[11,12,13,14,15,16] The rapid expansion of the field of cyclic alkyne chemistry has led to a host of synthetic applications. For example, arynes and cyclic alkynes have been used as building blocks in the synthesis of catalyst ligands,[17] agrochemicals,[18] pharmaceuticals, and countless natural products.[19,20,21,22,23,24,25] A selection of important arynes and cyclic alkynes, including recently popularized heterocyclic variants, are shown in Figure 1.[26,27,28,29,30,31,32,33,34,35,36,37,38]

One particularly exciting application of arynes and cyclic alkynes lies in materials chemistry. Specifically, arynes have been employed in the synthesis of polymers and polycyclic aromatic hydrocarbons (PAHs).[6,39,40,41,42] Regarding the latter, PAHs have had a remarkable impact on the materials science field[43,44,45,46] and have been employed in widely-used devices, such as organic light-emitting diodes (OLEDs), field effect transistors (OFETs), and photovoltaics (OPVs).[47,48] A particularly interesting subset of PAHs are 9,10-diphenylanthracene derivatives. The parent compound, 9,10-diphenylanthracene (**1**, Figure 1), has been the focus of hundreds of studies since its first disclosure in 1904[49] and has been used in blue glow sticks[50] and OLEDs.[51] Not surprisingly, novel derivatives of 9,10-diphenylanthracene (**1**) have been highly sought after.[52] One promising 'analoging' approach is to prepare variants of **1** that bear heteroatoms, which provides a general means to modulate the properties and potential applications of PAHs. [53,54,55,56] Heteroatoms may be included in the anthracene ring itself or on the C9/C10 substituents, as exemplified by **2**[57,58,59,60,61,62,63] and **3**,[64] respectively (Figure 1), which can have profound effects on the material properties of these compounds.[64] Compounds possessing heteroatoms on both the anthracene ring and C9/C10 substituents have also been prepared, such as **4**, in the context of OLEDs.[65,66] Lastly, more exotic analogs of **1** and **2** have been prepared where the C9/C10

substituents are replaced with heterocycles or substituted aromatics, as demonstrated by **5**[57,63] and **6**,[67,68] respectively. The vast majority of heteroatom-containing derivatives of 9,10-diphenylanthracene (**1**) have been disclosed in the patent literature over the past six years and reflect a rapidly growing area of discovery.[69,70,71,72]

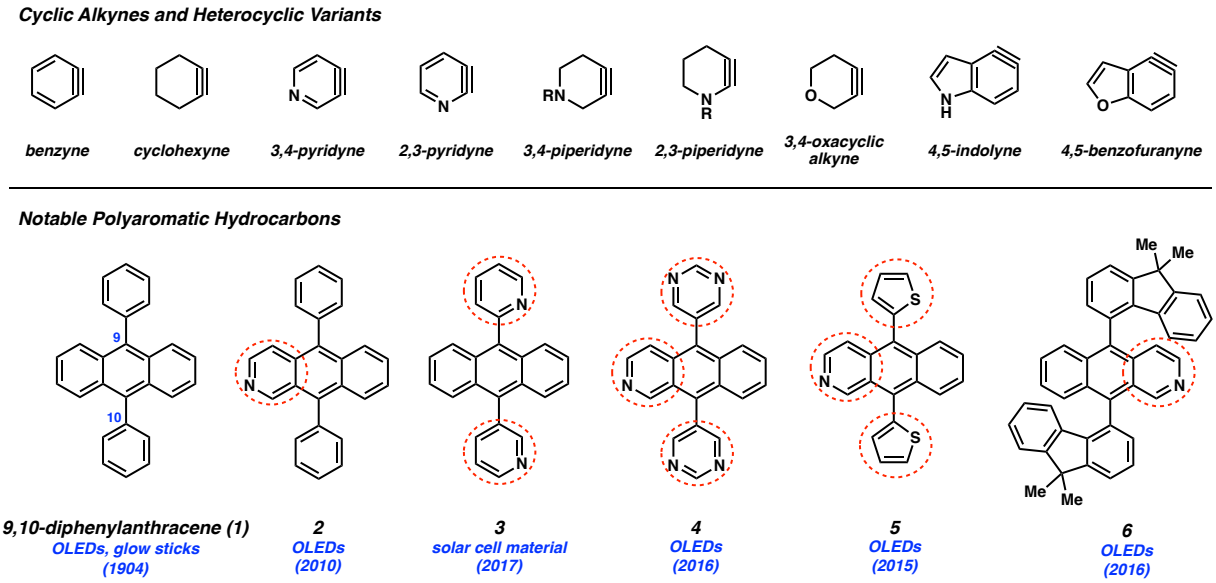

Figure 1. Arynes, cyclic alkynes, and heterocyclic variants (top) and 9,10-diphenylanthracene (**1**) and nitrogen-containing derivatives **2**–**6** (bottom).

Despite the exciting advances in heterocyclic PAHs, synthetic methods to rapidly generate a diverse range of novel heterocyclic PAHs remain limited. For example, the assembly of non-symmetric PAHs that possess multiple functional groups usually requires long linear sequences.[55] Additionally, approaches to arrive at het-anthracene cores typically necessitate harsh reaction conditions, such as high temperatures and strongly acidic or basic conditions, thus limiting functional group compatibility.[55,29] Lastly, variation at C9 and C10 is primarily achieved via the use of strongly basic organometallic reagents or transition metal-catalyzed cross-couplings. However, differentiation at C9 and C10 is challenging using these methods and typically results in symmetric molecules or low yields.[53,73] A modular synthetic approach capable of forming multiple C–C bonds in one step that could allow for up

to four quadrants of differentiation would enable entry to new, tunable, and difficult-to-access derivatives.

With the aforementioned considerations in mind, we targeted the synthesis of scaffold **7** through an ambitious approach, whereby ring fragments **A**–**D** could be united with formation of the central benzene ring (Figure 2a). This conceptual ring-by-ring assembly approach, whether ultimately executed in a stepwise or more direct fashion, would enable access to a diverse range of heterocyclic PAH scaffolds, with the possibility of accessing the desired four quadrants of differentiation. In practice, we questioned if highly reactive strained intermediates, such as arynes and cyclic alkynes (i.e., **8** and **10**), could be used as building blocks **A** and **B** (Figure 2b). Importantly, the use of heterocyclic strained intermediates, such as **8**, would be used strategically to access the desired heteroatom-containing PAHs.[74] With regard to building blocks **C** and **D**, oxadiazinone **9** was identified as a versatile core scaffold. Oxadiazinones are easily prepared from simple precursors[75] and are known to readily undergo one or more Diels–Alder cycloaddition / retro-Diels–Alder cycloaddition reactions (with sequential expulsion of N_2 and CO_2).[76] The success of this approach would hinge on uncovering a means to allow for the controlled generation and trapping of fragments **8** and **10** to ultimately deliver products **7** through the cascade of events suggested in Figure 2b. Key precedent for the desired reaction sequence dates back to the pioneering studies by Steglich in 1977,[77] which demonstrated the double addition of benzyne into oxadiazinones. This approach was also used in the synthesis of conjugated materials by Nuckolls[78] and Wudl.[79] However, a notable limitation in all cases is the inability to introduce two different strained alkynes, instead delivering symmetric products with respect to building blocks **A** and **B**.[80]

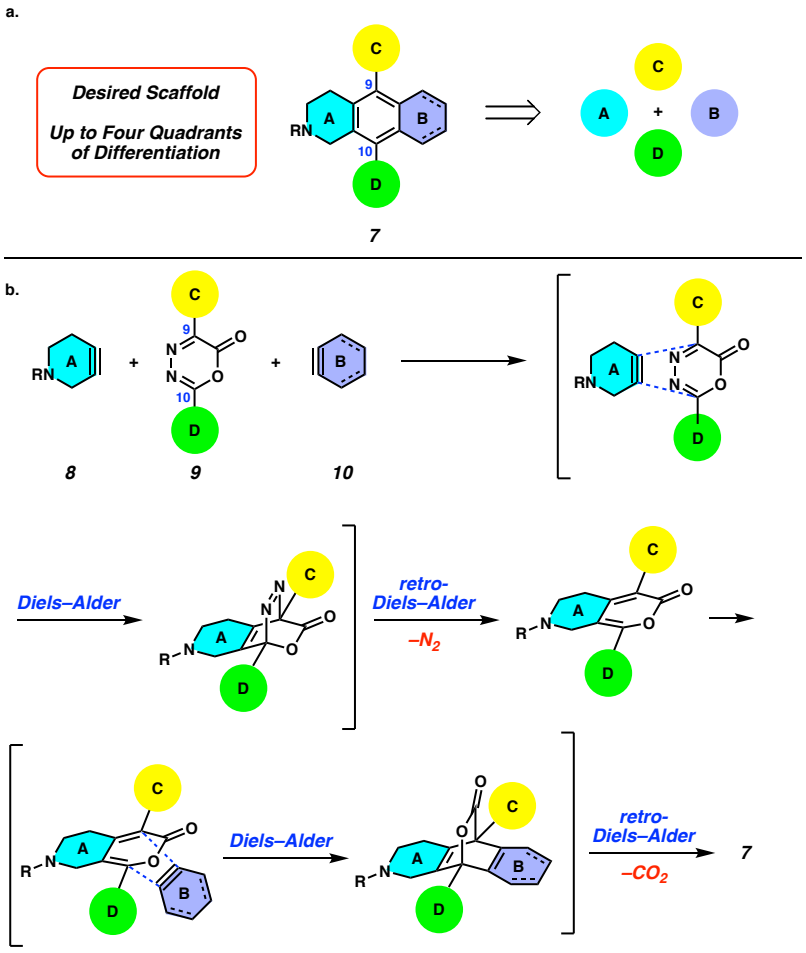

Figure 2. Proposed strategy to access a diverse range of heteroatom-containing PAHs **7** using simple fragments **8**, **9**, and **10**.

We report the successful development of the synthetic sequence shown in Figure 2b, which provides a modular and rapid means to synthesize a diverse range of heteroatom-containing PAHs. The trapping of in situ-generated strained intermediates with oxadiazinones, demonstrated in both stepwise and one-pot fashions, furnishes the desired structural frameworks. This includes products with four quadrants of differentiation, which are accessed by leveraging the controlled formation of four new carbon–carbon (C–C) bonds. Small molecule fluorophores, including solvatochromic compounds and stimuli-responsive materials, as well as donor–acceptor oligomers can be accessed from this strategy. These studies demonstrate that heterocyclic strained intermediates can be leveraged for the preparation of new organic materials.

RESULTS AND DISCUSSION

Discovery and Scope of Methodology.

With the ultimate goal of synthesizing heterocyclic PAHs bearing four quadrants of differentiation, we initiated our studies by pursuing a stepwise variant of our designed approach to prepare heterocyclic 9,10-anthracene-type cores (Figure 3). As mentioned above, arynes are known to undergo oxadiazinone trapping, but the intermediate benzopyrone directly undergoes trapping with a second equivalent of the aryne, precluding the opportunity to introduce two different strained alkyne fragments. When using benzyne in our initial studies, attempts to intercept the intermediate benzopyrone by varying the stoichiometry were unsuccessful, and only resulted in double addition to form 9,10-diphenylanthracene (**1**). We hypothesized that the intermediate benzopyrone was more reactive than the oxadiazinone and therefore, prevented isolation or second addition of a different aryne. We questioned if a cyclic alkyne could be used to isolate the corresponding pyrone intermediate based on prior studies by Sauer and co-workers using cyclooctyne.[81] Thus, rather than using an aryne for the initial oxadiazinone cycloaddition, we opted to pursue the use of a heterocyclic alkyne derived from commercially available silyl triflate **11**.[29] Two key results are shown in Figure 3, illustrating the ability to modulate the product distribution through facile alteration of the stoichiometry of the reaction. When silyl triflate **11** was employed in excess (2 equiv relative to **12**), the major products are adducts **14**, which result from double addition of the intermediate piperidyne, consistent with the results previously seen in aryne/oxadiazinone reactions.[76,77,78] Formation of the intermediate pyrones **13** was not observed under these conditions. However, when a 1 : 2 ratio of **11** and **12** was utilized, the desired pyrones **13**, arising from a single Diels–Alder / retro-Diels–Alder reaction, were isolated in 74% yield under optimized conditions, without formation of double addition products **14**. Of note, pyrone **13** is produced as a mixture of regioisomers **13a** and **13b**. It was found that treatment of excess CsF under oxidative conditions selectively decomposed **13b** leaving **13a** untouched. Products **13** possess the desired heterocyclic **A** ring. This reactivity is reminiscent of oxadiazinone Diels–Alder reactivity for most

species other than arynes.[76] Several points should be noted: a) our results provide the first example of a Diels–Alder cycloaddition featuring an oxadiazinone and a strained intermediate derived from a Kobayashi silyl triflate precursor,[82] b) the reactions occur at ambient temperature under exceptionally mild reaction conditions, c) the desired reaction produces mixtures of pyrone isomers **13a** and **13b**, which may generally be viewed as both a strength and limitation (additional analogs, yet not selective), and d) isomer **13a**, the key lynchpin to the success of our synthetic strategy, was ultimately accessible as a single isomer (see Supporting Information for details) and employed in subsequent experiments.

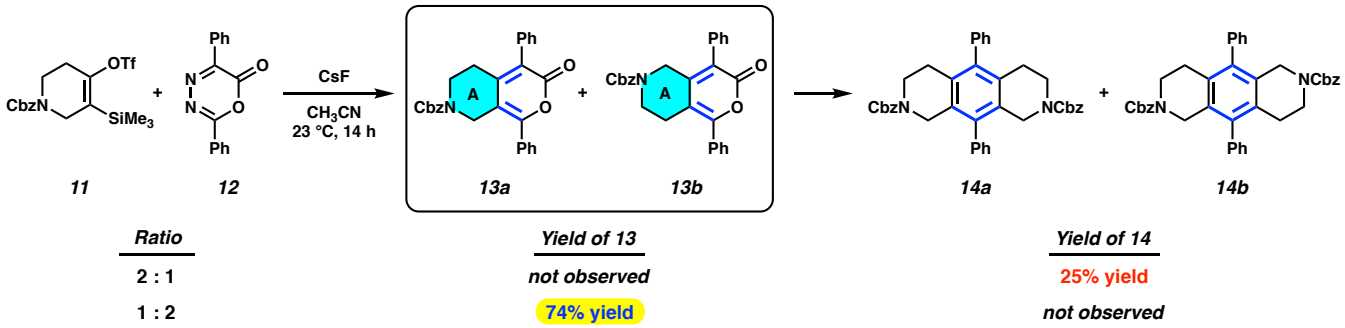

Figure 3. Optimization of a sequential Diels–Alder / retro-Diels–Alder to form pyrones **13**.

After establishing a suitable method to access pyrone **13a**, we turned our attention towards introducing and modulating the **B** ring. As shown in Figure 4, we found that pyrone **13a** readily undergoes a Diels–Alder / retro-Diels–Alder reaction sequence, with loss of CO_2, in the presence of arynes or non-aromatic cyclic alkynes (generated from silyl triflate precursors **15**) at ambient temperature. In each case, the transformation proceeds with formation of two new C–C bonds and delivers non-symmetric heterocyclic PAH skeletons **16** with variation in the **B** ring. The use of benzyne (**17**),[82] for example, afforded tricycle **18** in 83% yield (entry 1). The other arynes tested, 1,2-naphthalyne (**19**)[83] and 4,5-indolyne (**21**),[37] also performed well, giving rise to products **20** and **22** in 89% and 70% yield, respectively (entries 2 and 3). In these latter cases, we observed a mixture of the two possible regioisomers, which is expected given the unsymmetrical nature of both pyrone **13a** and the aryne intermediates. Switching to cyclic alkynes, as a means to introduce greater sp^3-character and potentially provide access to increasingly soluble PAHs, we first evaluated cyclohexyne (**23**), which gave rise to **24**

in 71% yield (entry 4). Heterocyclic strained cyclic alkynes **25**[29] and **26**[33] could also be employed to assemble multi-heterocyclic frameworks **14** and **27**, respectively (entries 5 and 6). Of note, silyl triflate precursors to **17**, **19**, **21**, and **25** are all commercially available.[84] With regard to regioselectivities (entries 2, 5, and 6), we surmise that the major product arises from initial bond formation occurring between the more electron-rich carbon adjacent to the carbonyl group of the pyrone[85] and the more distorted carbon of the strained intermediate in a concerted asynchronous fashion.[15,29,33]

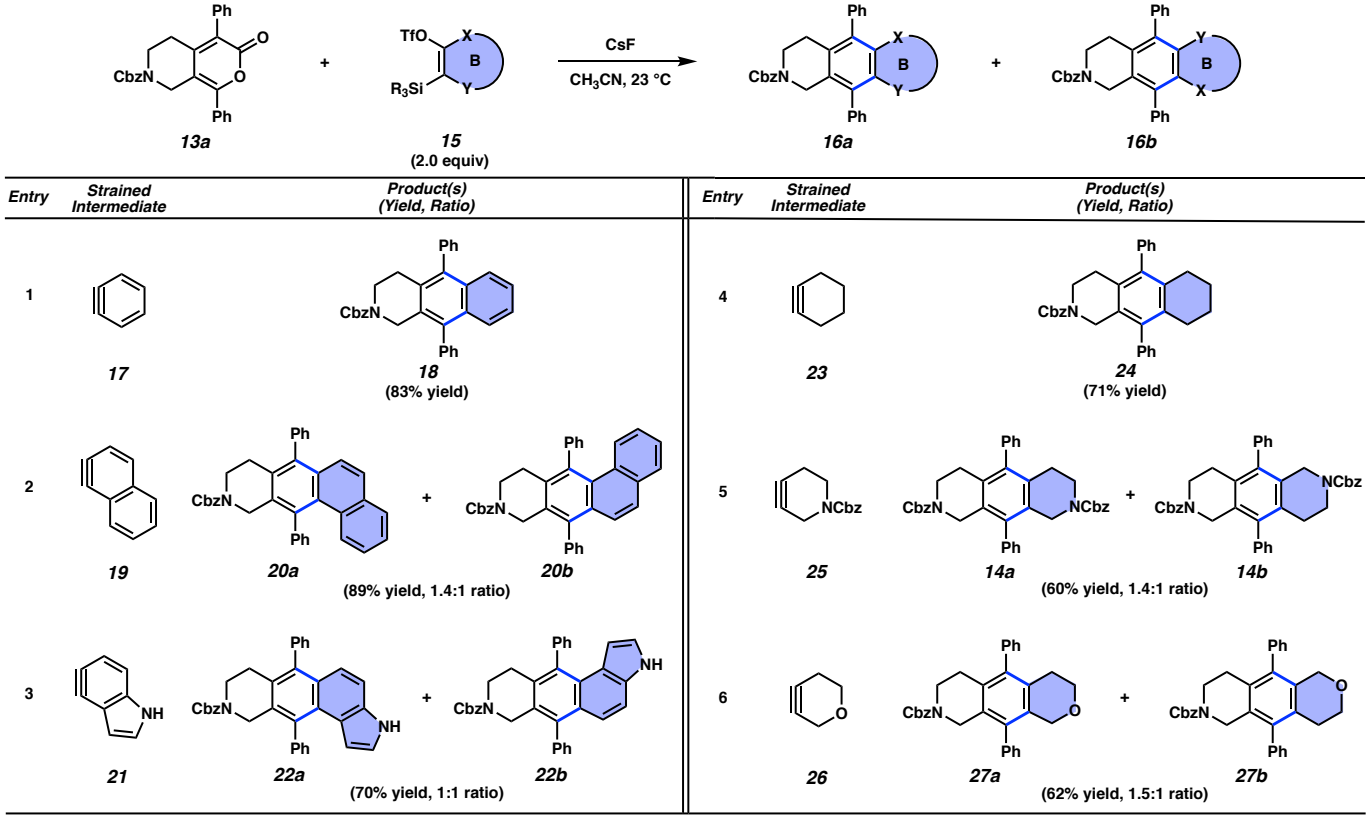

Figure 4. The second Diels–Alder / retro-Diels–Alder reaction using pyrone intermediate **13a**. Conditions unless otherwise stated: CsF (5.0 equiv), CH_3CN (0.1 M), 23 °C, 14 h. Yields reflect the average of two isolation experiments.

With a controlled means to access PAH scaffolds with variable **A** and **B** rings, we sought to access products bearing differing **C** and **D** rings. As noted earlier, in most routes to 9,10-anthracene derivatives, the **C** and **D** rings are introduced through a double cross-coupling or by the double addition of an organometallic reagent, allowing for the formation of only symmetric products with limited functional group compatibility.[55,53] Our approach utilizing an oxadiazinone obviates this problem. A

series of differentially-substituted oxadiazinones were prepared using established chemistry[75] and subjected to silyl triflate **11** under our standard reaction conditions (Figure 5). The desired Diels–Alder / retro-Diels–Alder sequence took place to efficiently deliver pyrone isomers **28**–**31** in yields ranging from 66 to 84%. In all cases, it was possible to separate the depicted pyrone isomer, which was then subjected to benzyne precursor **32** under our standard conditions. The desired products **33**–**36** were obtained in good to excellent yields. The **C** ring in all cases was a phenyl ring, whereas the **D** ring was varied to give a product bearing an electron-donating *para*-methoxyphenyl group and an electron withdrawing *para*-nitrophenyl group (**33** and **34**, respectively). Likewise, a product bearing a *para*-bromophenyl **D** ring was obtained (**35**), which provides a cross-coupling handle for further elaboration. Lastly, a thiophene unit was incorporated to give **36**, which is notable given the prevalence of thiophenes in organic electronics.[53]

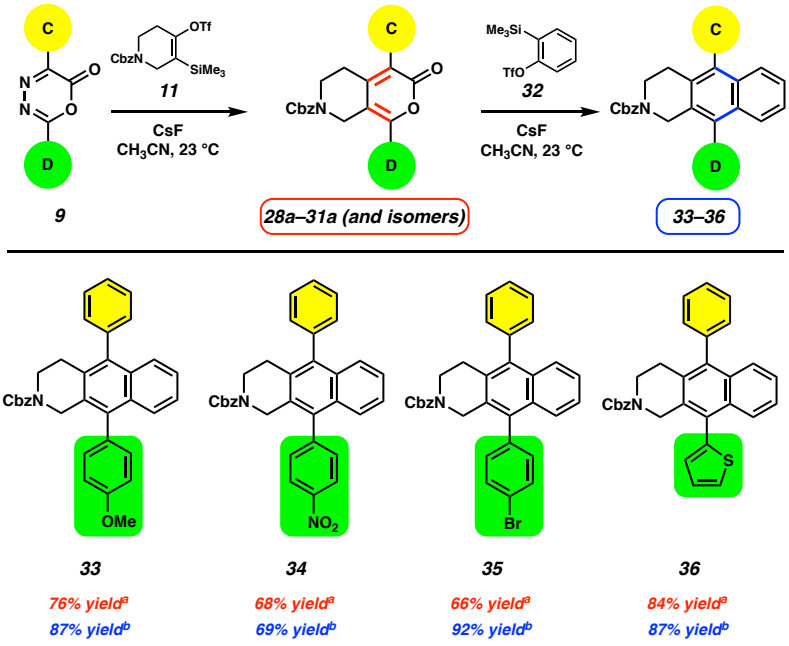

Figure 5. Reaction scope of oxadiazinone core. [a] Yield of the pyrone intermediates **28**–**31**. Yields reflect the average of two isolation experiments. Conditions for piperidyne cycloaddition: oxadiazinone **9** (2.0 equiv), silyl triflate **11** (1.0 equiv), CsF (2.0 equiv), CH_3CN (0.1 M), 23 °C, 14–18 h. [b] Yield of products **33**–**36**. Yields reflect the average of two isolation experiments. Conditions for benzyne cycloaddition: pyrone **28a**–**31a** (1.0 equiv), silyl triflate **32** (2.0 equiv), CsF (5.0 equiv), CH_3CN (0.1 M), 23 °C, 18 h.

As an additional test of this methodology for the assembly of heterocycle-containing PAH scaffolds, we performed a three-component coupling of two different silyl triflates, **11** and **32**, and oxadiazinone **12**. Operationally, CsF was added to an equimolar solution of the three reactants. After stirring at room temperature for 18 hours, the desired product **18** was obtained in 56% yield along with pyrone intermediate **13** accounting for the majority of the remaining mass balance. This constitutes a rare example of a three-component reaction involving the union of two different transiently generated strained alkynes. Notably, the products of double piperidyne or benzyne addition were not observed, suggesting high selectivity for the controlled formation and reaction of the two strained intermediates generated in situ. We posit that silyl triflate **11** more readily undergoes fluoride-mediated elimination to form the corresponding alkyne compared to benzyne precursor **32** as a result of the lower strain energy associated with 3,4-piperidyne compared to benzyne.[86] Nonetheless, the transformation proceeds by way of four consecutive pericyclic reactions to ultimately create four new C–C bonds and deliver a heterocyclic PAH scaffold in one-pot, under exceedingly mild reaction conditions.

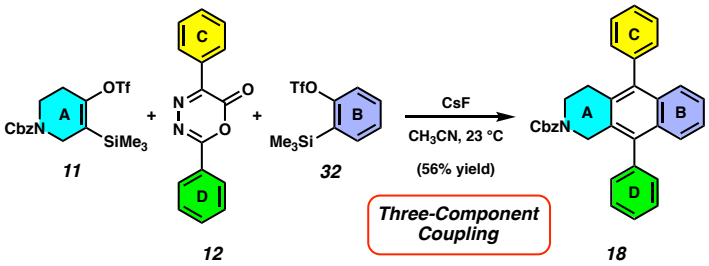

Figure 6. The controlled one-pot, three-component coupling of **11**, **12**, and **32**. Conditions: silyl triflate **11** (1.0 equiv), oxadiazinone **12** (1.0 equiv), silyl triflate **32** (1.0 equiv), CsF (3.0 equiv), CH_3CN (0.1 M), 23 °C, 14 h.

Further Synthetic Applications and Materials-Related Properties.

Having developed the parent methodology, we pursued several synthetic applications with a focus on incorporating motifs commonly utilized in materials chemistry, including donor–acceptor fluorophores and conjugate oligomers. One such endeavor is summarized in Figure 7, in which we targeted a heterocyclic PAH scaffold reminiscent of 9,10-diphenylanthracene (**1**), albeit with four

unique quadrants of substitution. Oxadiazinone **37**, readily prepared from the corresponding hydrazide and glyoxylic acid fragments, was treated with silyl triflate **11** in the presence of CsF. This furnished pyrone **38**, which, in turn, was reacted with silyl triflate **39** under our typical reaction conditions to afford the corresponding product of the Diels–Alder / retro-Diels–Alder sequence. Silyl protection of the indole nitrogen provided separable isomers **40a** and **40b**. X-ray analysis of **40a** allowed us to unambiguously establish the structure, as shown in Figure 7b. Access to a fully aromatic framework was then achieved via removal of the Cbz-protecting group and subsequent MnO_2-mediated oxidation. The product obtained through this facile and concise sequence, **41a**, is reminiscent of 9,10-diphenylanthracene (**1**), but bears three heterocycles (i.e., thiophene, indole, pyridine) and a *para*-methoxyphenyl motif in place of standard phenyl units. Of note, **41a** was found to exhibit pH-responsive fluorescence switching properties. Specifically, **41a** displayed a blue-green fluorescence emission. Upon addition of trifluoroacetic acid, the pyridine nitrogen underwent protonation to afford **42a**, which displayed a red fluorescence emission. Addition of triethylamine to **42a** returned **41a** and restored the blue-green emission. This effort showcases the utility of our methodology for accessing stimuli responsive materials, which are thought to be important for a host of materials-related applications such as pH fluorescence sensors[87,88] and solid-state fluorescent switches.[89]

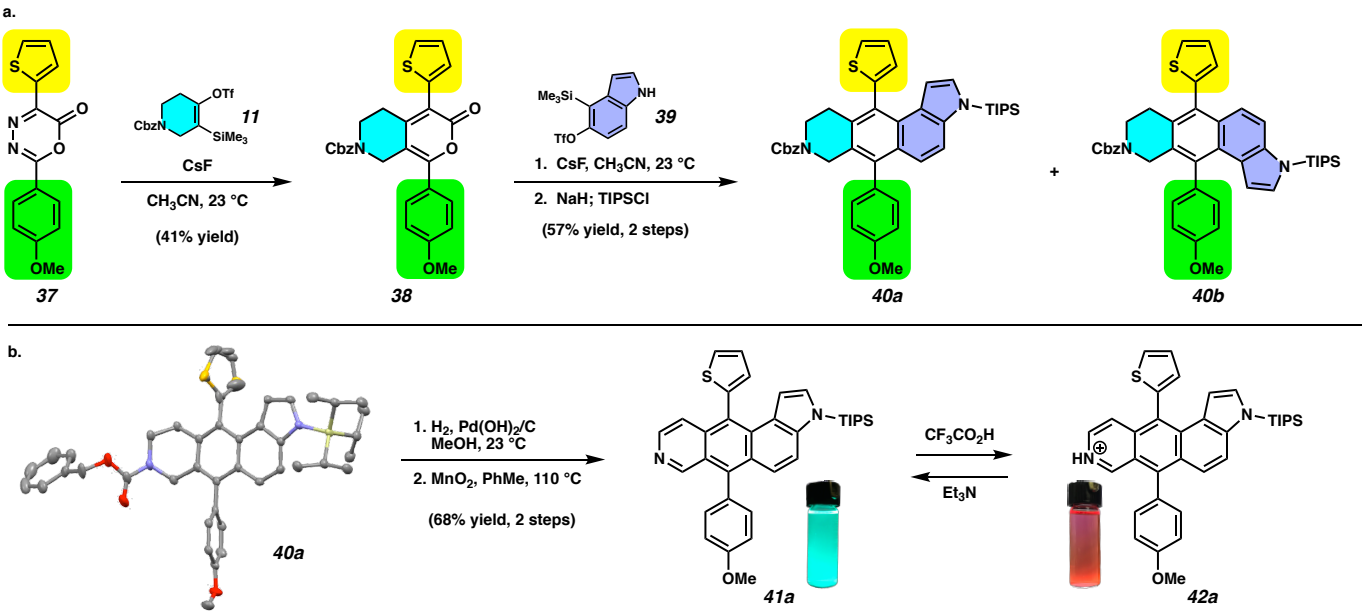

Figure 7. a. Strategic synthesis of **40**, bearing four unique axes of substitution. **b. 40a** was elaborated to **41a**, a pH-responsive fluorophore.

By leveraging the orthogonality of our methodology to palladium-catalyzed cross-couplings, we were able to access additional fluorescent materials (Figure 8). We first carried out the one-pot, three-component coupling of silyl triflates **11** and **32** with dichlorooxadiazinone **43** (Figure 8a). Analogous to the one-pot transformation shown earlier (see Figure 6), this transformation led to the controlled formation of four C–C bonds to deliver pentacycle **44** in 58% yield. The aryl chlorides present in **44** then underwent Pd-catalyzed Miyaura borylation to give (bis)boronic ester **45**. Subsequent Suzuki–Miyaura cross-coupling with 4-bromobenzothiadiazole (**46**) afforded the donor–acceptor fluorophore **47** in 95% yield. The HOMO of **47** is thought to be localized on the central acene core, whereas the LUMO is believed to be concentrated on the electron-poor benzothiadiazoles (see Supporting Information for DFT orbital density maps). **47** was found to be solvatochromic,[90] indicative of a donor–acceptor system (Figure 8b).

As shown in Figure 8c, bis(boronate) **45** could be employed as a building block for polymer synthesis. Suzuki–Miyaura polymerization[91] between diboronic ester **45** and 4,7-dibromobenzothiadiazole (**48**) provided donor–acceptor oligomer **49** in 86% yield. **49** was found to have a polydispersity index (PDI) of 1.3 and a number average molecular wight (M_n) of 1.7 kDa. The absorption and emission spectra for **47** and **49** in THF are shown in Figure 8d. The donor–acceptor oligomer **49** displays a red-shifted absorbance and emission relative to **47** with a longest-wavelength absorption maximum of λ = 391 nm and an emission maximum of λ = 491 nm. The chromatographic shifts can be attributed to the extended conjugation present in oligomer **49** compared to **47**. Ultimately, the results shown in Figure 8 demonstrate how a common adduct obtained from a one-pot, three-component variant of our synthetic methodology (i.e. **44**) can be used to rapidly access donor–acceptor monomers and oligomers displaying differing photophysical properties.

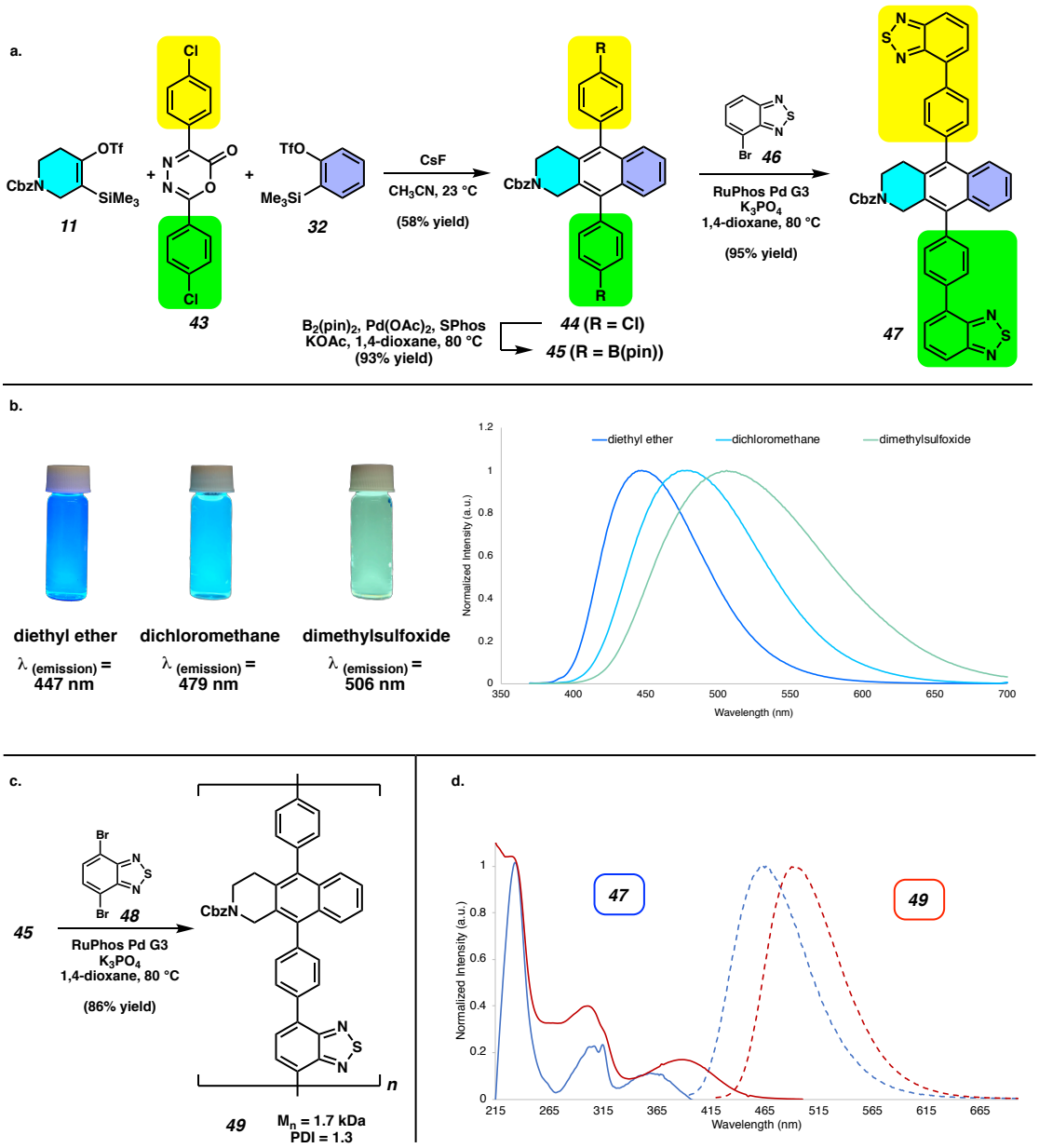

Figure 8. a. A tactical one-pot, three-component reaction towards donor–acceptor fluorophore **47**. **b.** Solvatochromism of fluorophore **47**. **c.** Suzuki–Miyaura polymerization using 4,7-dibromobenzothiadiazole (**48**) delivered oligomer **49**. **d.** UV/Vis and fluorescence spectra with oligomer **49** displaying red-shifted absorbance (red solid line) and emission (red dashed line) relative to **47** (blue solid and dashed lines).

CONCLUSIONS

We have discovered a modular synthetic platform that leverages strained cyclic alkynes and arynes to access new heteroatom-containing PAH scaffolds. Two strained intermediates are ultimately united with an oxadiazinone coupling partner via two Diels–Alder / retro-Diels–Alder sequences

(performed operationally in either a stepwise or one-pot fashion) to rapidly construct four new C–C bonds. An array of heterocyclic PAH frameworks reminiscent of 9,10-diphenylanthracene (**1**) can be accessed, including unique products that bear four different quadrants of substitution around the phenyl core. The utility of this methodology is underscored by the synthesis of new small molecule fluorophores, including a solvatochromic compound, a stimuli-responsive material, and a donor–acceptor oligomer. These studies demonstrate that heterocyclic strained intermediates can be strategically harnessed for the preparation of new organic compounds with materials-related properties.

ASSOCIATED CONTENT

Supporting Information Available. Detailed experimental procedures, compound characterization data, and computational analysis. This material is available free of charge via the Internet at http://pubs.acs.org.

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ACKNOWLEDGMENT

The authors are grateful to the University of California, Los Angeles for financial support. We are grateful to the NIH-NIGMS (R01 GM123299 to N.K.G. and F32-GM122245 to E.R.D.), the UCLA Graduate Division (Dissertation Year Fellowship to J.S.B.), and the Chemistry-Biology Interface training program (J.S.B., USPHS National Research Service Award 5T32GM008496-20). We thank the Sletten and Nelson laboratories (UCLA) for the use of their instrumentation and Dr. Scott Virgil (Caltech) for carrying out preparative separations. These studies were supported by shared

instrumentation grants from the NSF (CHE-1048804) and the National Center for Research Resources (S10RR025631). This work used computational and storage services associated with the Hoffman2 Shared Cluster provided by the UCLA Institute for Digital Research and Education's Research Technology Group.

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