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Highly Regioselective Domino Benzannulation Reaction of Buta-1,3-diynes to Construct Irregular Nanographenes

Wenlong Yang, Radha Bam, Vincent J. Catalano, and Wesley A. Chalifoux*

Abstract: The properties of nanographenes can be tuned by changing their shapes, therefore the development of new methods that are suitable for the synthesis of various nanographenes is highly desirable. Herein, we describe an intramolecular $InCl_3$-$AgNTf_2$-catalyzed regioselective domino benzannulation reaction of buta-1,3-diynes to build irregular nanographenes. Different nanographene compounds were easily obtained in moderate to high yields through careful design of the precursor compounds. This new domino reaction was successfully applied to a four-fold alkyne benzannulation of dimethoxy-1,1'-binaphthalene derivatives to arrive at novel chiral butterfly ligand precursors. The regioselectivity of the benzannulation reaction was unambiguously confirmed by the X-ray crystallography. Moreover, this new method enables us to synthesize different nanographene isomers and study their optical properties as a function of shape.

Extended polycyclic aromatic hydrocarbons (PAHs), often referred to as nanographenes, have recently received a considerable amount of attention due to their interesting optical and electronic properties.[1] The properties of PAHs can be tuned by changing their degree of π-extension, shape, width, and edge topologies.[2] Bottom-up approaches for the production of well-defined nanographenes have attracted significant interest of chemists.[3] The Scholl reaction,[4] transition-metal-[5] or photo-catalyzed[6] directed intramolecular arylation reactions, and alkyne benzannulation reactions (inter- and intramolecular)[7] are widely used in the key C-C bond-forming reaction of nanographene syntheses. Moreover, the preparation of carbon-rich materials from precursors containing many C-C triple bonds is gaining more attention.[8] For example, Tanaka and coworkers reported the synthesis of helically chiral 1,1′-bitriphenylenes via rhodium-catalyzed double [2+2+2] cycloaddition of biaryl-linked tetraynes with 1,4-diynes.[9] Rubin and coworkers synthesized graphene nanoribbons (GNRs) via a topochemical polymerization and subsequent aromatization of a diacetylene precursors.[10] In 2016, our group reported the bottom-up synthesis of soluble and narrow GNRs using alkyne benzannulations.[11] The multi-fold intramolecular benzannulation reaction of alkynes have been shown to proceed using a variety of π-Lewis acids,[12] Brønsted acids,[13] radical reagents,[14] and other electrophiles.[15] However, we found that almost all of previously reported alkyne benzannulation reactions have been limited to monoyne groups (Figure 1a). Müllen, Feng, and coworkers reported the benzannulation of conjugated buta-1,3-diynes, in which two cyclization events occurred individually (Figure 1b).[16] To the best of our knowledge, the domino benzannulation of conjugated 1,3-diynes has never been reported (Figure 1c). Herein, we report the first domino benzannulation reaction of buta-1,3-diynes catalyzed by $InCl_3$-$AgNTf_2$, to build different irregular nanographenes. This protocol is applicable to efficiently make different nanographene structures through variation of either the building block structures or the substituent positions within the precursors.

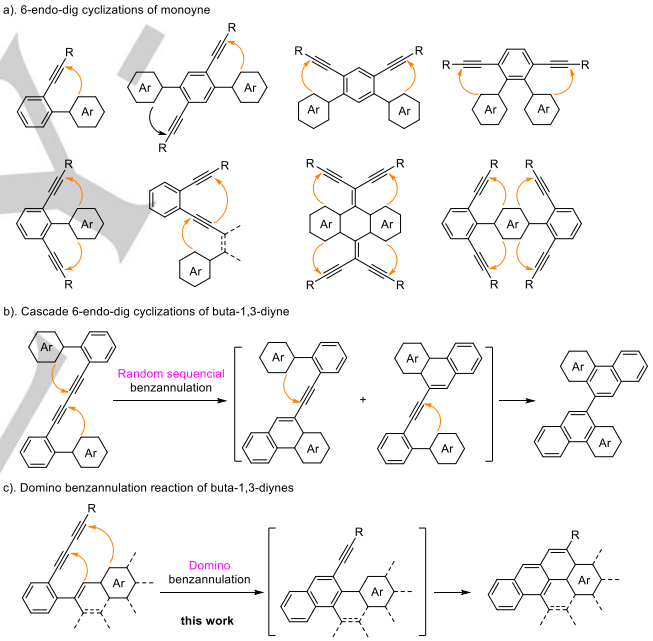

Figure 1. Intramolecular benzannulation reaction of alkynes. (a) 6-endo-dig cyclizations of monoyne moieties. (b) Random sequential 6-endo-dig cyclizations of buta-1,3-diyne. (c) Domino benzannulation reaction of buta-1,3-diynes.

Previous studies have shown that alkyne benzannulation reactions are more facile with electron-rich ethynylaryl groups.[7b, 17] Therefore, we initiated this study by screening suitable catalytic conditions for the domino benzannulation reaction of electron-rich buta-1,3-diyne **1a** as a model substrate with the results summarized in Table 1. Transition metals, such as In(III),[12b, 18] Au(I),[19] Au(III),[12b] and Pt(II),[12b, 20] have been successfully used in the Lewis acid-catalyzed benzannulation reaction of alkynes and these metals have provided a starting point for our study. Recently, we have shown that a wide scope of peropyrenes and teropyrenes could be synthesized through two- and four-fold alkyne benzannulations using $InCl_3$ as a catalyst in toluene at high

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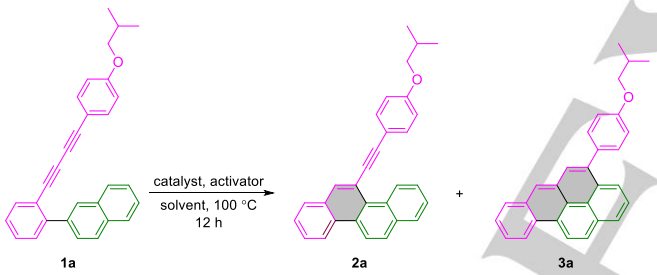
temperature.[17] However, in this case, catalytic amounts of $InCl_3$ only resulted in mono-cyclized intermediate **2a** with no formation of **3a** being detected (entry 1, Table 1). We found that $PtCl_2$ and $AuCl_3$ were less effective with $AuCl(PPh_3)$ giving no conversion at all (entries 2-4). Among all the addition of Ag(I) salts (entries 5-9), addition of $AgNTf_2$ (Tf = trifluoromethanesulfonyl) exhibited highest catalytic ability for this transformation with desired annulated product **3a** being formed exclusively in 83%yields, (entry 9). Compared to using $InCl_3$/AgOTf catalyst system, similar yield was obtained while $In(OTf)_3$ was used as a catalyst (entry 10). The catalytic activity of $InCl_3$/$AgNTf_2$ was high and thus the reaction could even be carried out at a reduced catalyst loading of 10 mol% $InCl_3$ and 10 mol% $AgNTf_2$ to provide improved yield of 94% (entry 12). The reaction resulted in many side products and low yield when conducted in 1,2-dichloroethane (DCE) (entry 13). We conducted a control experiment and no reaction occurred with only $AgNTf_2$ present in the reaction mixture (entry 14). We also explored a Brønsted acid [i.e., triflic acid (TfOH)], and full conversion was observed after stirring **1a** with 2 equivalents of TfOH in dichloromethane (DCM) at –40 ºC for 30 mins giving the target compound **3a** in 51% yield (entry 15). It should be noted that the first alkyne benzannulation is highly regioselective with the structure of **3a** being unambiguously confirmed by X-ray crystallographic analysis (*vide infra*).

Table 1. Optimization of the domino benzannulation reaction conditions.

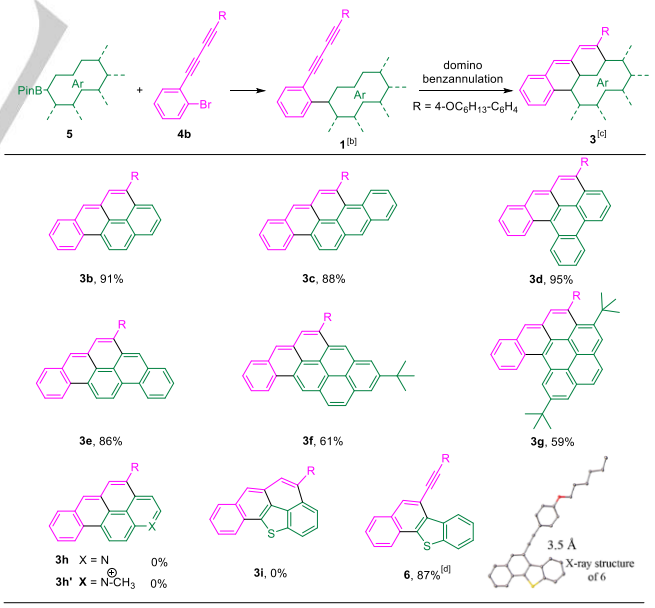


entry	catalyst (mol%)	activator (mol%)	solvent	ratio[a] (**1a**:**2a**:**3a**)	**3a** (%)[b]
1	$InCl_3$ (20)	-	toluene	1:3:0	0
2	$PtCl_2$ (20)	-	toluene	8:1:0	0
3	$AuCl_3$ (20)	-	toluene	22:1:0	0
4	$AuCl(PPh_3)$ (20)	-	toluene	1:0:0	0
5	$InCl_3$ (20)	$AgBF_4$ (60)	toluene	290:1:0	0
6	$InCl_3$ (20)	$AgCO_2CF_3$ (60)	toluene	3:6:1	ND[c]
7	$InCl_3$ (20)	$AgSbF_6$ (60)	toluene	0:0:1	50
8	$InCl_3$ (20)	$AgNTf_2$ (60)	toluene	0:0:1	83
9	$InCl_3$ (20)	AgOTf (60)	toluene	0:0:1	71
10	$In(OTf)_3$ (20)	-	toluene	0:0:1	72
11	$InCl_3$ (10)	$AgNTf_2$ (30)	toluene	0:0:1	85
12	$InCl_3$ (10)	$AgNTf_2$ (10)	toluene	0:0:1	94
13	$InCl_3$ (10)	$AgNTf_2$ (10)	DCE	0:0:1	25[d]
14	-	$AgNTf_2$ (10)	toluene	1:0:0	0
15	TfOH (200)	-	DCM	0:0:1	51[e]

[a] Determined by ^1H NMR. [b] Isolated yield. [c] Not determined. [d] 80°C. [e] Reaction was quenched after 30 minutes.

With optimized reaction conditions in hand (entry 12, Table 1), we turned our attention to exploring the substrate scope of parent PAHs **5** (Table 2). A hexyl chain was incorporated instead of isobutyl group not only to enhance the solubility of both precursors **1** and fully cyclized products **3** but also provide good crystallinity of the products for later possible X-ray analysis. Gratifyingly, naphthalene, anthracene, phenanthrene, and pyrene were all applicable building blocks in this reaction to afford the corresponding larger PAHs in moderate to high yields (**3b-3g**). Heteroaromatic systems were also investigated to further expand the scope. The cyclization of quinoline-based precursors (**1h** and **1h'**) did not produce the desired fully annulated products **3h** and **3h'**. Treating the benzothiophene-containing precursor **1i** to the optimized reaction conditions resulted in no desired doubly cyclized product **3i**. Using $InCl_3$ as a catalyst in DCE gave 87% yield of mono-cyclized intermediate **6**. Subjecting compound **6** to the optimized reaction conditions gave only intractable material. We propose that this is because the distance between the alkyne and aryl carbons are too far apart in **6** to participate in a second 6-endo-dig cyclization reaction (~3.5 Å, insert figure in Table 2).[21]

Table 2. Substrate scope with respect to parent PAHs 5.[a]



[a] Reaction conditions: $InCl_3$ (10 mol%), $AgNTf_2$ (10 mol%), toluene, 100 ºC, 12 h. [b] K_2CO_3, $Pd(PPh_3)_4$, THF/H_2O, 80 ºC, 24 h. [c] Isolated yield. [d] $InCl_3$ (10 mol%), DCE, 80 ºC, 12 h.

Recently, we have demonstrated that ethynylthiophene moieties can undergo a facile benzannulation reaction to produce thiophene-functionalized pyrene, peropyrene, and teropyrene

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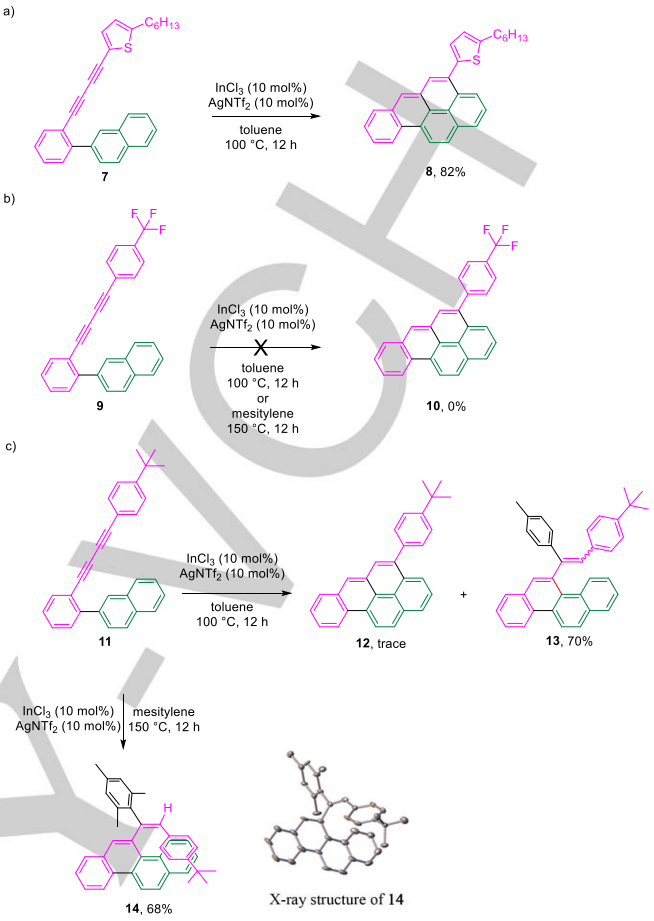
compounds.[22] After treating precursor **7** under optimized reaction conditions the thiophene-functionalized benzo[*a*]pyrene **8** was isolated in 82% yield (Scheme 1a). Summarizing all the above results, we show that electron-rich buta-1,3-diynes work well for the domino benzannulation reaction. We switched to test alkyne substituents terminated with electron-deficient and electron-neutral aryl groups: compounds **9** and **11**, respectively. Unfortunately, no reaction occurred after treating **9** to our optimized reaction conditions, even in mesitylene at 150 °C (Scheme 1b). The electron-neutral precursor **11** gave a trace amount of the desired product **12** when the reaction was carried out at 100 °C (Scheme 1c). Interestingly, the major product was the addition product of molecular toluene to the monocyclized intermediate to provide compound **13**. In an attempt to avoid this side reaction, more sterically hindered mesitylene was used as a solvent. While no reaction occurred while treating the precursor **11** in mesitylene at 100 ºC for 12 hours, full conversion of starting material was observed after keeping the reaction at 150 ºC for 24 hours. The NMR results indicated that mesitylene had added across the remaining triple bond of the monocyclized intermediate to form compound *Z*-**14** with the stereochemistry being unambiguously confirmed by X-ray crystallographic analysis (Scheme 1c). A possible explanation for this solvent trapping reaction is that this is a formal Friedel-Crafts reaction that proceeds through a cationic intermediate, analogous to cationic Au(I)-catalyzed cyclizations.[23] After mono-cyclization of compound **11**, the more stable cation intermediate generated after In(III) complexation would be that which places the positive charge on the carbon next to the newly generated chrysene moiety (see Scheme S7). The two possible outcomes would be either a 5-exo-dig cyclization (not observed) or trapping with a nucleophile (i.e., the solvent). The benzannulation in a non-aromatic solvent (DCE) also failed. It appears that the barrier of the second cyclization step is too high for electron-neutral alkynes, with other pathways – such as solvent trapping being more favorable.



Scheme 1. Scope of buta-1,3-diynes terminated with (a) ethynylthiophene moiety, (b) electron-deficient ethynylphenyl, (c) electron-neutral ethynylphenyl group.

During the investigation of substrate scope, we found that this domino benzannulation reaction also worked well in stilbene derivatives. After treating stilbene derivative **1j** to the optimized reaction conditions, the benz[*a*]anthracene derivative **3j** was obtained in 84% yield (Scheme 2a). Since naphthyl derivatives **1a** and **1b** can cyclize in relative high yield (vide supra), we decided to try applying this method in dimethoxy-1,1'-binaphthalene derivative **1k**. The annulated product **3k** was isolated in 92% yield (Scheme 2b). To our delight, the annulated compound **3m** was obtained in 63% yield after four-fold alkyne benzannulation reaction of bisbuta-1,3-diynes **1m** (Scheme 2c). This demonstrates a new method to afford novel chiral butterfly ligands for use in enantioselective catalysis.

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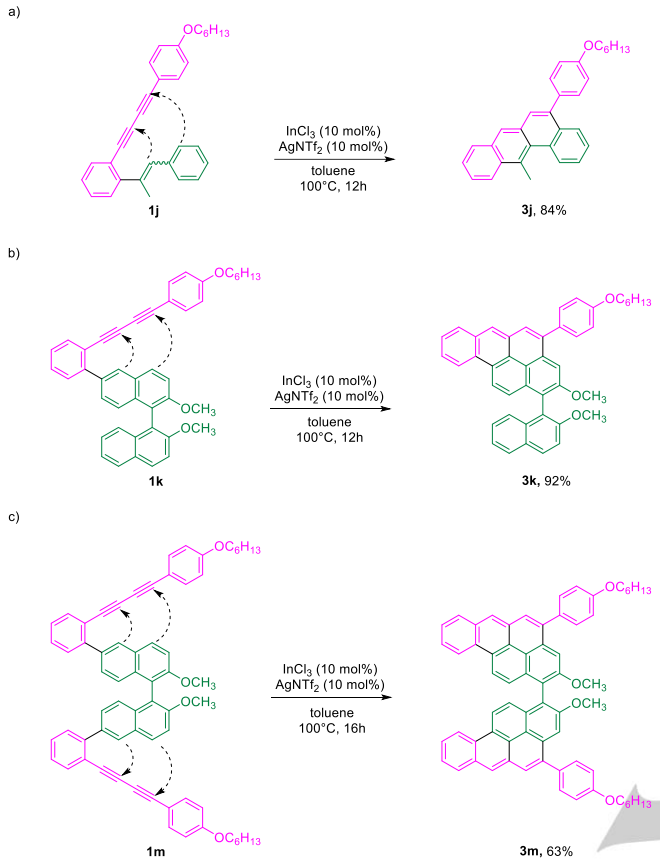

Scheme 2. Domino benzannulation reaction of alkynes in (a) stilbene derivative, (b-c) dimethoxy-1,1'-binaphthalene derivatives.

Single crystals of **3a**, **3d**, **3e**, and **3f** suitable for X-ray crystallographic analysis were obtained by solvent diffusion methods, which unambiguously confirmed the regioselectivity of the domino benzannulation reaction of buta-1,3-diynes.[24] Their structures and corresponding crystal packing are shown in Figure 2. Compounds **3a** and **3e** showed slip-stacking (Figure 2b, 2g) while **3f** showed face-to-face packing (Figure 2j) due to its relative larger planar backbone, with a close interplanar spacings of ~3.4-3.5 Å for these compounds (Figure 2c, 2h, and 2k). Compound **3d** showed distorted structure because of its helical backbone (Figure 2d-2e) and exhibited a face-to-face packing with a distance of 3.8 Å (Figure 2e).

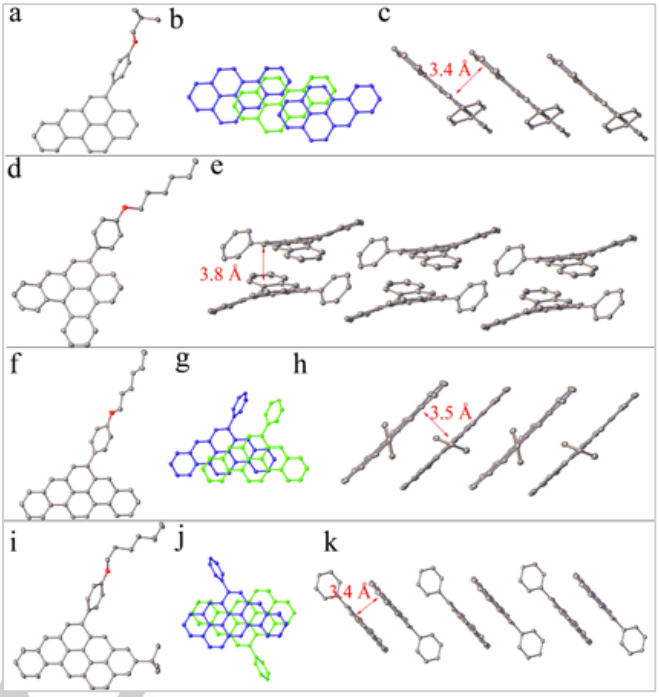

Figure 2. X-ray structures (ellipsoids at 50% probability, hydrogens removed for clarity) and packing structures (hydrogens and side chains removed for clarity) of (a-c) **3a**, (d-e) **3d**, (f-h) **3e**, and (i-k) **3f**.

The UV-Vis absorption and emission spectra of selected compounds **3c**, **3d**, **3e**, **3f**, and **3g** are shown in Figure 3. All of these compounds display vibrational fine structure in their respective UV-vis spectra. The observed emission spectra are mirror images of the absorption spectra, which indicates that the same states are involved in absorption and emission. Interestingly, compounds **3c**, **3d**, and **3e** are dibenzochrysene structural isomers, with the same number of fused rings, but show very different absorption and emission profiles (Figure 3a). Compared to compounds **3d** and **3e** (λ_{max} = 396 and 401 nm, respectively), a dramatic bathochromic shift of ~60 nm for compound **3c** was observed (λ_{max} = 459 nm) with a smaller Stokes shift. Similarly, compounds **3f** and **3g** can also be considered as anthrapyrene isomers, both having seven fused benzene rings. However, compared to compound **3f** with planar backbone, twisted compound **3g** showed broad absorption and emission spectra with a relatively small bathochromic shift being observed (Figure 3b).

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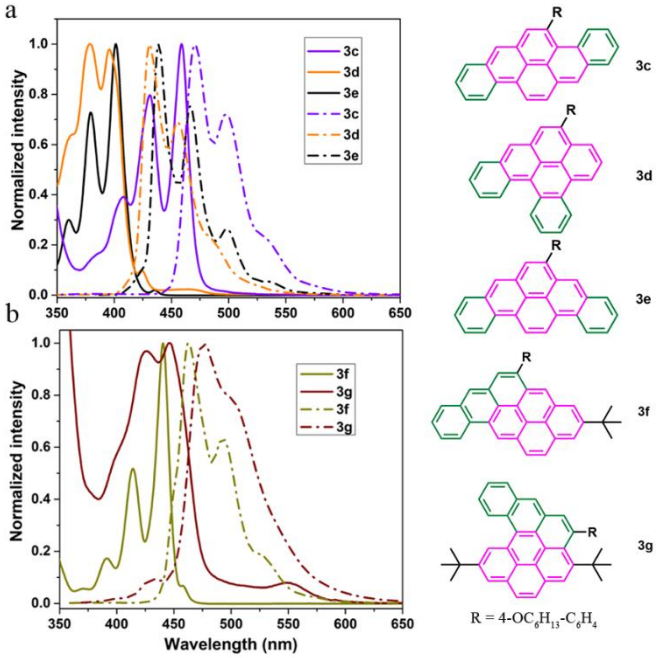

Figure 3. The UV-Vis absorption (solid line) and emission (dash-dot line) spectra of selected (a) dibenzochrysene compounds **3c**, **3d**, **3e** and (b) compounds **3f** and **3g** in toluene at 298 K.

In summary, we have developed the first domino benzannulation reaction of buta-1,3-diynes catalyzed by $InCl_3$-$AgNTf_2$. A series of irregular PAHs were successfully synthesized through this new strategy. Moreover, we can use this method to produce a broad scope of nanographene isomers efficiently, which allows one to study their interesting optical properties. An electron-donating group attached to the buta-1,3-diyne precursors was crucial for the second benzannulation reaction to occur. The double 6-endo-dig cyclization reaction was favored and the regioselectivity of the first alkyne benzannulation reaction was unambiguously confirmed by the X-ray crystallographic analysis of the resulting PAH products. The benzannulation reaction of buta-1,3-diynes was also applicable in stilbene and dimethoxy-1,1'-binaphthalene derivatives, allowing for the synthesis of novel chiral butterfly ligand precursors. The domino benzannulation reaction of buta-1,3-diynes described here has immense potential for application towards the precise synthesis of large PAHs with irregular shapes.

Acknowledgements

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Keywords: domino • benzannulation • alkyne • nanographenes • regioselectivity

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[24] CCDC 1843508, 1843509, 1843513, 1843510, 1843511, and 1843512 (**3a**, **3d**, **3e**, **3f**, **6**, and **14**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre.

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Entry for the Table of Contents
Layout 1:

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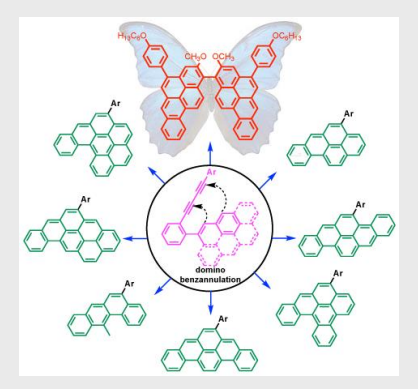
A series of irregular nanographenes were synthesized by $InCl_3$-$AgNTf_2$-catalyzed highly regioselective domino benzannulation of conjugated diynes. A novel chiral butterfly ligand precursor was successfully obtained through this strategy after a four-fold alkyne benzannulation.



*Wenlong Yang, Radha Bam, Vincent J. Catalano, and Wesley A. Chalifoux**

Page No. – Page No.

Highly Regioselective Domino Benzannulation Reaction of Buta-1,3-diynes to Construct Irregular Nanographenes