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Atom- and Pot-Economical Consecutive Multi-Step Reaction Approach to Polycyclic Aromatic Hydrocarbons (PAHs)†

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A novel one-pot benzannulation reaction has been developed for the synthesis of substituted polycyclic aromatic hydrocarbons (PAHs) from the direct coupling of propargylic aldehydes/alcohols with 1,1-diarylethanol through an atom-economical uninterrupted three/four-step reaction sequence under mild and metal-free reaction conditions. The strategy involves an acid-catalyzed dehydration and carbon-carbon bond formation followed by DBU-promoted cycloisomerization. Naphthalene and phenanthrene were obtained via mono-benzannulation and chrysene, picene and benzopicene were obtained involving consecutive di-benzannulation reactions in good yields starting from easily accessible starting materials.

The concept of atom-economy introduced by Trost is playing a key role in designing the new chemical strategies, because it seeks to maximize the synthetic efficiency in transforming the starting materials to the target molecule.[1] Similarly, Pot-economy concept pursues the multiple transformations and forming several bonds in single reaction vessel, which minimizes the use of solvents (work-up and purification of intermediates) and address the chemical waste generated.[2] Undoubtedly, synthetic strategies following the combination of both the atom- and pot-economy are extremely attractive.

Polycyclic aromatic hydrocarbon (PAH) derivatives occupy a significant field in organic chemistry due to their wide applications in pharmaceutical chemistry as bio-active molecules,[3] semi-conductors and advanced organic materials.[4, 5] As a result, the construction of substituted PAH architectures has been attracted the attention of several synthetic organic chemists. Among the methods developed for the synthesis of polycyclic aromatic hydrocarbons, mainly naphthalenes, enyne-assisted cycloisomerization reactions have emerged as one of the atom-economical reactions.[6,7] These reactions generally rely on metal-catalysis and require the pre-construction of the desired ene-yne substrates.[7] Hence, the development of new methods with the formation of ene-yne followed by its cycloisomerization in one-pot to the target aromatic hydrocarbon under metal-free conditions, are greatly desirable.

In this direction, we hypothesized that the 1,1-diarylethanol in presence of acid-catalyst will generate the olefin, which acts as a nucleophile to react with propargylic aldehyde under the same reaction conditions would lead to the formation of ene-yne. Subsequently, addition of base in to the same reaction vessel would promote the cycloisomerization reaction to form the benzannulated product. The process of the above consecutive multi-step reaction sequence in one-pot will lead to a novel benzannulation approach to substituted polycyclic aromatic hydrocarbons under atom-economical and metal-free reaction conditions. Herein, we present the results of a novel consecutive reaction strategy for the synthesis of PAHs under mild conditions. To the best of our knowledge there are no examples in the literature neither for the direct coupling of propargylic aldehyde with 1,1-diarylethanol (or alkene) to ene-ynes nor for the cycloisomerization of 1,4-enyne to PAHs.

With this assumption, we set out to examine the reaction of propargylic aldehyde **1a** and 1,1-diphenylethanol (**2a**) in the presence of various acid catalysts to find the optimal conditions (see supporting information, Table S1) for the formation of ene-yne through dehydration (to give **A**) followed by nucleophilic addition (to give **B**). Interestingly, it provided a di-alkenyl product **C** in 94% yield at 80 ^{o}C in presence of *p*TSA in CH_3CN. We presume that initially the aldehyde **1a** underwent nucleophilic addition to **B** followed by immediate nucleophilic substitution with **A** *via* carbocation in the presence of acid catalyst provided **C**, which was isolated and fully characterized. Based on earlier work on cycloisomerization reactions,[8] the conversion of **C** to naphthalene was tested using DBU and found that the reaction proceeded smoothly to give vinylated naphthalene **3a** in 92% yield. A plausible reaction pathway was shown in Scheme 1. DBU promoted isomerization of C affords allene, which undergoes 1,3,5-triene electrocyclization followed by aromatization leads to the benzannulation product **3a**. Further, the reaction conditions [*p*TSA (5 mol%), CH_3CN, 80 ^{o}C, 2h; DBU, r.t., 15 min.] were tested successfully for all the four reactions uninterruptedly in one-pot to obtain the naphthalene **3a** in 87% yield (Table S1).

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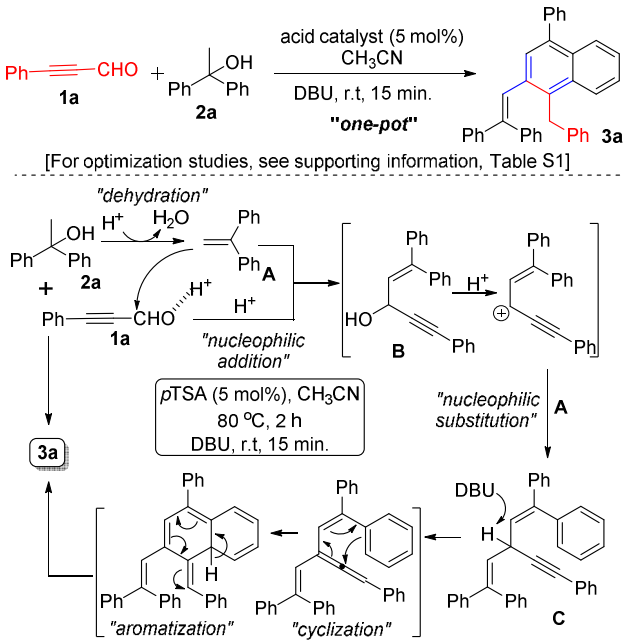
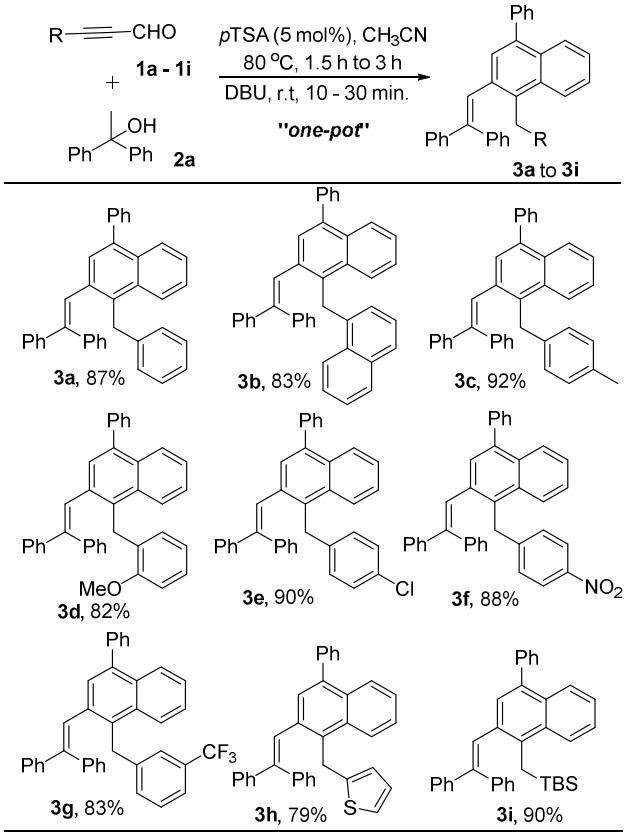
Scheme 1: Possible reaction pathway



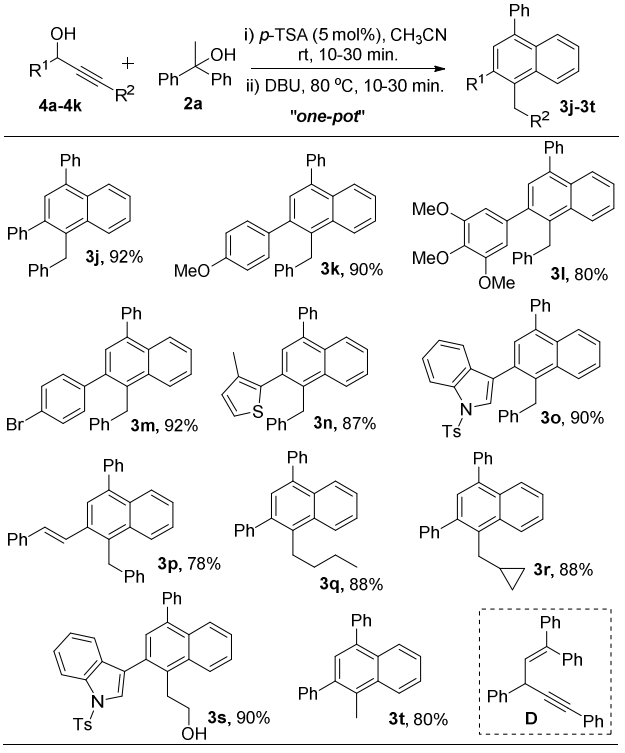
The above success prompted us to study the reaction of **2a** with various propargylic aldehydes as the reaction partner (Scheme 2). The reaction of **1b** with **2a** was investigated in the presence of acid catalyst and subsequent DBU-mediated cycloisomerization offered 2-vinylated naphthalene **3b** in 83% yield. Similarly, other propargylic aldehydes **1c** to **1g** having both electron-donating (4-Me, 2-OMe) and electron-withdrawing substituent (4-Cl, 4-NO_2, 3-CF_3) on the phenyl ring were proved to be competent C2 synthons to generate the corresponding 2-vinylated naphthalenes **3c** to **3g** in good yields. 3-(Thiophen-2-yl)propionaldehyde **1h** worked well, providing the product **3h** in 79% yield. Remarkably, 3-(*tert*-buyldimehylsilyl)-propionaldehyde **1i** was also effective in benzannulation with **2a** to produce the corresponding 2-vinylated naphthalene **3i** in 90% yield with TBDMS group intact in the product (Scheme 2).

As the formaion of intermediate **C** from propargylic aldehyde is assumed through the nucleophilic substitution of propargylic alcolhol **B** with insitu generated nucleophile **A** (as shown Scheme 1), we next investigated the feasibility of propargylic alcohols[9] as an alternative reaction partners in place of propargylic aldehydes (Scheme 3). Firstly, the reaction of propargylic alcohol **4a** with 1,1-diphenylethanol (**2a**) was examined under the optimal reaction conditions. To our delight, one-pot benzannulation proceeded smoothly to provide the desired naphthalene **3j** in 92% yield *via* the enyne **D**, which was isolated and fully characterized. Noteworthy to mention that the dehydration/propargylation were proceeded at room temperature, while the cycloisomerization required 80 °C for faster reaction (at room temperature the reaction time was more than 8 h). Next, the reactivity of various propargylic alcohols using 1,1-diphenylethanol (**2a**) as the reaction partner was investigated (Scheme 3). In the cases of 1-aryl propargylic alcohols (R^1 = aryl), different substitutions on

Scheme 2: Reaction of **2a** with propargylic aldehydes



Scheme 3: Scope of propargylic alcohols in benzannulation with **2a**[a]



[a]Structures of propargylic alcohols **4a** to **4K** were shown in supporting information

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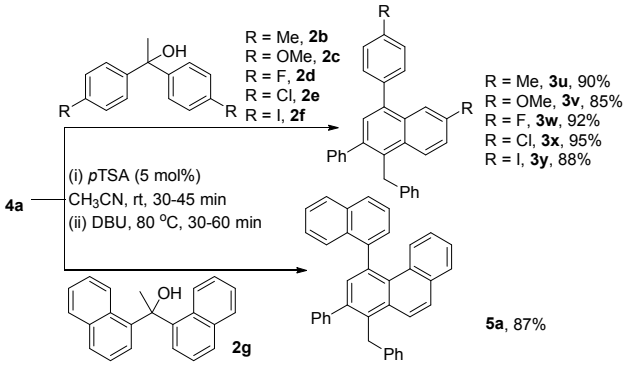
the aryl ring were tolerated well. For example, *p*-OMe, 3,4,5-$(MeO)_3$ and *p*-Br substituted phenyl propargylic alcohols underwent the one-pot three-step reaction smoothly to afford the corresponding naphthalenes **3k** to **3m** in 80-92% yields. 1-Heteroaryl propargylic alcohols having 3-methyl-2-thienyl and 3-indolyl substitution were also compatible in this reaction, furnishing **3n** and **3o** in 87% and 90% yields, respectively. Interestingly, 1-alkenyl substituted propargylic alcohol (obtained by the reaction of cinnamaldehyde with phenyl acetylene), was also suitable in reacting with **2a** to afford the expected **3p** in 78% yield. The nature of R^2 substitution had no influence on the reaction, as it can be seen by the formation of naphthalenes when R^2 was aryl groups (**3j** to **3p**) as well as alkyl groups (**3q** to **3s**). Notably, the propargylic alcohol having R^1 = Ph and R^2 = TMS underwent the one-pot reaction well to provide the desilylated product **3t** in 80% yield.

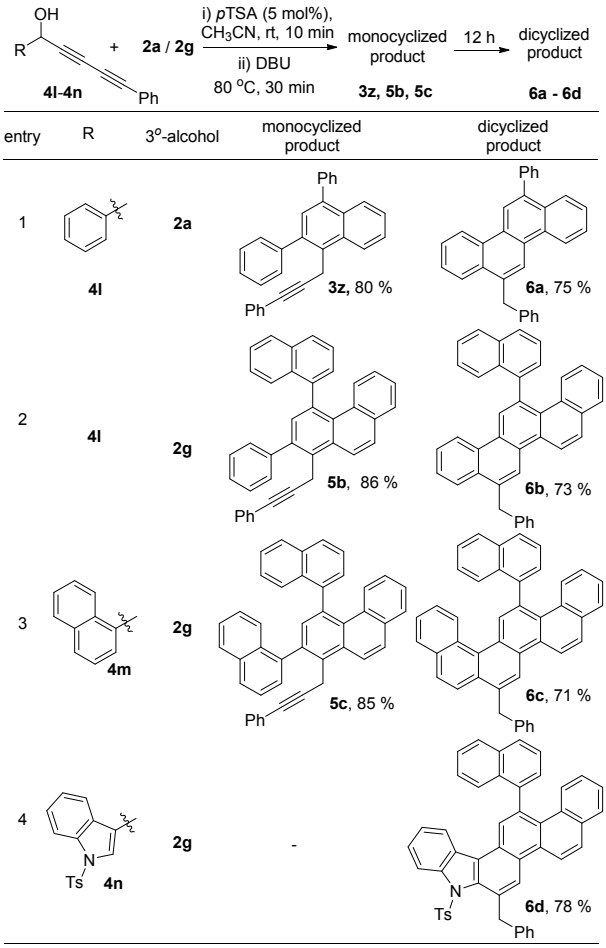
Furthermore, the scope of 1,1-diarylethan-1-ols **2** using 1,3-diphenylprop-2-yn-1ol (**4a**) as the reaction partner was also tested (Scheme 4). In general, it was observed that 1,1-diphenylethan-1-ols, **2b** to **2f**, having both of the electron-donating (*p*-Me, *p*-MeO) as well as electron-withdrawing (*p*-F, *p*-Cl, *p*-I) substitution, were successfully reacted with **4a** to give the corresponding naphthalenes **3u** to **3y** in good yields. Employment of 1,1-di(naphthalene-1-yl)ethan-1-ol (**2g**) in the present one-pot reaction with **4a** provided substituted phenanthrene **5a** in 87% yield.

Scheme 4: Reactivity of 1,1-diarylethan-1-ols



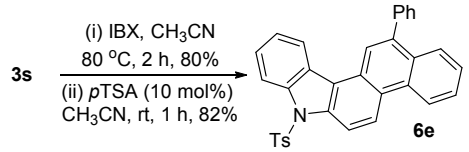
Further, the applicability of this consecutive process was verified towards the synthesis of higher-membered aromatic hydrocarbons such as chrysene, picene and benzopicene, valuable motifs with numerous applications.[5] In general, the synthesis of PAHs involved the multi-step and metal-mediated reactions.[10] We assumed that the use of 2,4-diyn-1-ols in reaction with 1,1-diarylethan-1-ols (Table 1) will undergo a consecutive reaction sequence involving an acid-catalyzed dehydration and propargylation followed by DBU-promoted double cycloisomerization (dibenzannulation) to provide the higher-membered aromatic hydrocarbons. First, we attempted the annulation of 1,5-diphenylpenta-2,4-diyn-1-ol (**4l**) with **2a** in the presence of *p*TSA followed by DBU in acetonitrile. Gratifyingly, the formation of alkynyl-naphthalene **3z** was observed in 30 min. at 80 °C which subsequently underwent second cyclization in 12 h at 80 °C to provide the 6-benzyl-12-phenylchrysene (**6a**) in 75% yield (entry 1, Table 1). Similarly, the reaction of **4l** with **2g** was also successful in providing the double cyclization product, picene **6b** in 73% yield through the monocyclized intermediate **5b** (entry 2). In addition, when we extended the substrate scope, 1-(naphthalen-1-yl)-5-phenylpenta-2,4-diyn-1-ol (**4m**), the corresponding benzo[*a*]picene **6c** was isolated in 71% yield *via* the mono-cyclized phenanthrene **5c** (entry 3). A similar one-pot uninterrupted multi-step process was also observed to give the novel dibenzannulated product, phenanthro[1,2-*c*]carbazole **6d** (78% yield) from the reaction of **4n** with **2g**, wherein we could not isolate the monocyclized product (entry 4, Table 1).

Table 1. Synthesis of PAHs *via* di-benzannulation[a]



To further explore the applicability of the present method, we explored the transformation of the obtained naphthalene **3s**. The alcohol group of naphthalene **3s** was oxidized using IBX in acetonitrile to obtain the aldehyde, which upon treatment

Scheme 5: Conversion of **3s** to naphtho[1,2-*c*]carbazole **6e**



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with *p*TSA (10 mol%) in acetonitrile at room temperature gave 13-phenyl-7-tosyl-7*H*-naphtho[1,2-*c*]carbazoles **6e** in 82% yield (Scheme 5).

In summary, we have developed a simple and metal-free novel tandem reaction for the synthesis of diverse aromatic compounds from readily accessible propargylic aldehydes/alcohols and diaryl ethanols under mild reaction conditions. The developed strategy proved to be effective for the rapid construction of various polycyclic aromatic hydrocarbons such as chrysene, picene, benzopicene and phenanthrocarbazole through the dibenzannulaion reaction. The effectiveness of present method in the synthesis of diversely substituted PAHs is under progress to study their physical properties towards further applications.

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