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Facile synthesis of diverse hetero polyaromatic hydrocarbons (PAHs) *via* the styryl Diels–Alder reaction of conjugated diynes[†]

Jingwen Wei, Mengjia Liu, Xiaohan Ye, Shuyao Zhang, Elaine Sun, Chuan Shan, 🕩 Lukasz Wojtas and Xiaodong Shi 🕩 *

The styryl dehydro-Diels–Alder reaction with a conjugated diyne is reported. While typical alkyne–styrene condensation requires elevated temperatures (>160 °C), the application of a conjugated diyne allowed for effective transformation under milder conditions (80 °C). The thermally stable triazole–gold (TA–Au) catalyst further improved the reaction yields (up to 95%), producing the desired alkynyl–naphthalene in a single step with molecular oxygen as the oxidant. Sequential alkyne activation resulted in various polyaromatic hydrocarbons (PAHs) in excellent yields, highlighting the efficiency of this new strategy for the preparation of PAHs with good functional group tolerance and structural diversity.

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Introduction

With the interesting photo- and electronic properties, polyaromatic hydrocarbons (PAHs) have received increasing attention over the past decade from both the chemistry and materials research communities.¹ The π -contact property of PAHs allows charge carrier migration on stacked discotic molecules, and they are being widely used in organic electronic devices, such as organic field effect transistors (OFETs), organic light-emitting diodes (OLEDs), and photovoltaic devices (OPVs).² The need for new conjugated arene skeletons from simple starting materials calls for the development of new synthetic strategies to obtain various PAHs with higher efficiency and better functional group diversity.³ Alkynes, as readily available building blocks that have high thermal energy and are easy to functionalize, are potentially good starting materials to facilitate the synthesis of new PAHs.⁴ The challenge lies in the high activation barrier associated with the C-C triple bond, which results in the requirement of harsh reaction conditions and this often limits application in synthesis. One example is the intramolecular styryl dehydro-Diels-Alder (ISDDA) reaction.5 As shown in Scheme 1A, cycloaddition between styrene and alkyne could lead to the rapid construction of polyaromatic hydrocarbons, making it a potentially efficient strategy for the

preparation of PAHs. However, styrene dearomatization combined with low alkyne reactivity leads to high activation energy, resulting in the requirement of harsh conditions.⁶ Additionally, the formation of interconvertible intermediates (**A** and **B**) and the problematic dehydrogenation (formation of **C**) further complicate the overall transformations, giving the



Scheme 1 Achieving polycyclic hydrocarbons via the ISDDA reaction.



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Department of Chemistry, University of South Florida, 4202 E. Fowler Avenue, Tampa, Florida 33620, USA. E-mail: xmshi@usf.edu

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desired ISDDA products with low yields, poor selectivity (**B** and **C**) and limited substrate scope.⁷

Despite these challenges, the overall high efficiency of this ISDDA reaction in the construction of polyaromatic hydrocarbon skeletons continues to draw good attention from researchers around the world, with the intent of pursuing a new practical solution for the optimization of this process.⁸ According to the literature, one typical strategy to achieve this transformation is the application of electron-withdrawing group (EWG) modified alkynes.⁹ However, harsh conditions (>150 °C and microwave irradiation, MW) are required and the products were obtained in modest overall yields.¹⁰ Thus, the development of a new strategy allowing this transformation under mild conditions is highly desirable.

Over the past decade, our group has been working on developing new transformations through gold catalyzed alkyne activation.¹¹ Considering that EWG-modified alkynes gave improved reactivity, our initial hypothesis was to determine if this challenging transformation could also be optimized via gold catalyzed alkyne activation (Scheme 1B). While typical [L-Au⁺ catalysts decomposed rapidly at high temperatures (>80 °C), the 1,2,3-triazole gold catalyst (TA-Au) developed in our lab was able to tolerate a high temperature (80 °C) for more than 24 hours without decomposition.¹² This significantly improved thermal stability of TA-Au could potentially assist the reaction when heating is inevitable. After exploring various substituted alkynes, herein, we report the first example of an ISDDA reaction with a conjugated diyne. While thermal conditions (80 °C) gave the cycloaddition product in 55% yield, the addition of the TA-Au catalyst further improved the yield to 95%. Sequential alkyne transformations highlighted this new method as a promising strategy for the construction of diverse PAHs with high efficiency (Scheme 1C).

Results and discussion

To achieve the cycloaddition of the unactivated alkyne (no EWG) substrate 1a, a high temperature (160 °C) and a long reaction time (Fig. 1A, Condition A) are needed.¹³ Notably, under these conditions, the dehydrogenation product 1ab was a minor product and was obtained in only 14% yield with dialin 1aa separated as the major product. Reducing the temperature to 80 °C gave no conversion. We wondered if gold catalysis can assist in the cycloaddition of 1a at a low temperature (80 °C). However, it is known in the literature that gold catalyzed enyne cyclization isomerization can occur under mild conditions.¹⁴ As shown in Fig. 1A, treating substrate 1a under gold catalyzed conditions (Condition C) produced cyclopropane 1ac even at room temperature. Clearly, to evaluate if the gold catalyst could promote styryl-DA, a modified alkene substrate is needed to avoid enyne cyclization (accessing styrene reactivity). The enone substrate 2a was prepared with the assumption that gold-catalyzed enyne cyclization would not occur when introducing a carbonyl group linked with styrene. As expected, the conducting substrate 2a under various gold

A) ISDDA using styrene-alkyne: Modification of the styrene substrate



Fig. 1 Investigations of the styryl-yne ISDDA reaction under gold catalysis. (A) Modification of the styrene substrate; (B) Investigations on ISDDA with modified alkynes.

catalyzed conditions did not result in enyne cyclization. We continued to explore various gold catalyzed conditions with substrate 2a, hoping to promote the ISDDA reaction under more practical and milder conditions. Firstly, while TA-Au could survive high temperatures, no reaction occurred at 80 °C after 48 hours. Raising the temperature to 100 °C led to TA-Au decomposition over time with no desired product observed. Clearly, the high activation energy required for non-activated alkyne 2a led to this reaction temperature outside of the practical range for TA-Au catalysis. To our surprise, treating styrene-yne 2a at a high temperature (160 °C) gave the desired dehydrogenation cycloaddition product 2ab in 45% yield, and no dialin 2aa was observed. This result indicated that the introduction of a carbonyl group provided a more efficient dehydrogenation pathway toward the expected naphthalene.

In order to solve the high temperature problem, we decided to explore the alkyne substitution effect. To improve alkyne reactivity, multiple alkyne derivatives (2a-2e and 3a) were prepared (Fig. 1B). Surprisingly, the 1,3-diyne 3a showed excellent reactivity in the ISDDA reaction. The simple thermal conditions at 80 °C resulted in 100% conversion and produced naphthalene 4a in 55% yield. Substrates (2a-2d) with other substitution groups (Ph, H, Me, and Br) showed no conversions at 80 °C. Substrate 2e with an EWG (COPh) had a slower kinetic speed with 58% conversion. We assume that both the conjugated π system and less stereo-hinderance are important in the ISDDA reaction. And a conjugated divne is a good motif that met both these requirements. This observation is also consistent with previously reported studies on the HDDA reaction, which showed that conjugated diynes can improve the reactivity.15

This result was exciting as it suggested that: (1) a conjugated diyne is an effective moiety for the ISDDA reaction under milder conditions and (2) it is plausible to use gold activation

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in this concerted cycloaddition process. To further optimize the reaction conditions, various gold catalyzed systems were applied (see the details in the ESI†). The TA–Au and Cu cocatalysts were identified as the optimal ones. The comparison of representative alternative conditions is summarized in Table 1.

As shown in Table 1, under the optimal conditions, comprising 10% JohnPhos(TA-H)AuSbF₆ and 10% Cu(OTf)₂ at 80 °C for 12 h, the divne substrate 3a was completely converted to product 4a in 95% yield (entry 1). There was no conversion at room temperature (entry 2). Notably, at a lower temperature (60 °C), the reaction could still occur with 30% conversion and 26% yield in 12 h (entry 3). The gold catalyst itself could promote this transformation with 84% yield (entries 4 and 5). In a previous work by our group, $Cu(OTf)_2$ served as a Lewis acid to promote the triazole gold catalyst reactivity. The triazole on the gold catalyst served as a dynamic L-ligand and the Lewis acid dissociated the triazole ligand to yield the active gold cation for catalysis.¹⁶ The copper co-catalyst itself resulted in a decreased yield of 46%, which indicated that this reaction is not catalyzed by Lewis acids (entries 4 and 6). Lowering the loading of the gold catalyst to 5% led to a reduced yield (entry 7). The combination of gold chloride with $AgSbF_6$ or other cationic gold species would give lower yields, likely due to gold decomposition and divne hydration (entries 8 and 9). The primary ligand on gold is also critical. JohnPhos was noted to be the optimal ligand for this reaction (entry 10). Among the Lewis acids (Ga, Zn, Fe and Ag) tested, Cu(OTf)₂ was proved to be the best co-catalyst for TA-Au activation in this case (entry 11). Toluene was found to be the optimal solvent (entry 12). The formation of arene 4a involves oxidation, which could be

Table 1	Optimization of the reaction conditions ^{a,b}	
TsN	Ph 10% [JohnPhosAu(TA-H)]SbF ₆ 10% Cu(OTf) ₂ 80 °C, Toluene, air, 12 h 3a	TsN 0 4a
Entry	Variation from "standard conditions"	Yield of 4a (%)
1	None	95
2	Room temperature	0
3	60 °C	26
4	No [TA–Au], no [Cu]	55
5	Only [TA-Au], no [Cu]	84
6	Only [Cu], no [TA-Au]	46
7	5% [TA–Au], 5% [Cu]	75
8	$[Au]: LAuCl + AgSbF_6$	<50
9	[Au]: [LAu(MeCN)]SbF ₆	<20
10	$[Au]: [LAu(TA)]SbF_6 (L = PPh_3, XPhos, etc.)$	<75
11	Other LA than [Cu]: Ga, Zn, Ag, etc.	<77
12	Other solvents: DCE, DMF, DMSO, CH ₃ CN	<67
13 ^c	Under argon	27
14	Under light	88

^{*a*} Standard reaction conditions: **3a** (0.2 mmol), toluene (10 mL), 10% JohnPhosAu(TA–H)SbF₆, 10% Cu(OTf)₂, 80 °C, 12 h, air, dark. ^{*b*} Yields are determined by ¹H NMR with 1,3,5-trimethoxybenzene as an internal standard. ^{*c*} Reaction performed in a glove box.

achieved through either direct dehydrogenation or oxidation (such as with O_2). To explore this process, this reaction was performed under argon protection. As shown in entry 13, a significantly reduced yield was observed (27%). This result clearly ruled out the dehydrogenation pathway. Notably, although it is clear that molecular O_2 could be used as an effective oxidant, some products were formed under O_2 -free conditions. In this case, the oxidation was likely achieved with the *in situ* formed diene, although with lower efficiency and atom economy. A slightly lower yield was obtained while conducting the reaction under daylight (entry 14, 88%), which is likely associated with the photo-initiated styrene decomposition/polymerization. With the optimized reaction conditions in hand, we investigated the reaction scopes. The results are summarized in Table 2.

To scrutinize the substituent effect of conjugated diynes, substrates with either electron-donating or electron-withdrawing groups were prepared and the corresponding products were obtained in excellent yields (4a-4d). Aliphatic and silyl substituted diynes 4e and 4f were also amenable, which suggested good functional group tolerance on the diynes. The substrate scopes of the styryl part were also explored. The 2-OMe, 4-OMe and 2-F substituted arenes and disubstituted arenes all worked well, giving the desired products 4g-4k in good yields. Notably, the X-ray crystal structure of 4j showed an interesting stereorepulsion between the alkyne and the bromo at the *peri*-position. Impressively, furan and thiophene modified substrates also worked in this transformation, giving

Table 2 Substrate scope of the ISDDA reaction^{a,b}



^{*a*} Standard reaction conditions: substrate (0.2 mmol), toluene (10 mL), 10% JohnPhosAu(TA-H)SbF₆, 10% Cu(OTf)₂, 80 °C, 12 h, dark. ^{*b*} Isolated yield. ^{*c*} No [Au], 80 °C, 12 h. ^{*d*} No [Au], 80 °C, 6 h. ^{*e*} 10% JohnPhosAu(TA-H)SbF₆, 100 °C, 72 h.

benzofuran 4l, benzothiophenes 4m and 4n and phenanthrenes 4o and 4p in one step, which highlights the good efficiency of this method in the construction of various PAH frameworks.

The styrene–diyne linkers were also explored. As discussed above, amine-linked substrates gave mixtures of naphthalene and dialin under the thermal conditions (no gold) in a low yield (4q:4qa = 1.2:1, 4q is the dehydrogenation product, total 40% yield). Similarly, ether-linked substrates gave 4r(dehydrogenation product) and 4ra (7:1) in 32% yield with full conversion in 6 h. Both results suggested the important role of gold catalysis in this transformation over alternative thermal conditions. The ester linked substrate gave a slow reaction (4s) at 80 °C. In addition, Cu(OTf)₂ caused product decomposition. Conducting the reaction at 100 °C with a longer reaction time

 Table 3
 Synthesis scope of phenanthrene benzotriazole H-PAHs



^{*a*} Standard reaction conditions: substrate (0.2 mmol), DMSO (2 mL), NaN₃ (0.4 mmol), 120 °C, 12 h. ^{*b*} Standard reaction conditions: triazole substrate (0.2 mmol), THF (2 mL), ArB(OH)₂ (0.4 mmol), pyridine (0.4 mmol), Cu(OAc)₂ (0.02 mmol), 63 °C, O₂, 12 h.

(72 h) using only TA-Au gave the optimal results with 75% yield. Carbon-linkers and longer linkages showed significantly reduced reactivity with no conversions observed (4t and 4u), indicating the importance of the linkers for this transformation.

With the ability to incorporate diynes in this ISDDA reaction, the resulting alkyne can be applied for the syntheses of sequential heteroatom-containing polyaromatic hydrocarbons (H-PAHs). The syntheses of three H-PAHs are summarized in Tables 3 and 4 (phenanthrene benzotriazole, azaphenalene, and isoquinoline), which can be achieved based on this practical method. First, the phenanthrene benzotriazole derivatives can be readily prepared in two steps (Table 3) through the treatment of **40** with NaN₃ and sequential *N*-2 selected triazole arylation. Notably, our group first reported that *N*-2-aryl-1,2,3triazole (NAT) is a good fluorophore with strong FL emissions.¹⁷ The integration of NAT with PAHs will likely lead to the discovery of new H-PAHs with interesting photo- and electronic properties, which is currently under investigation in our lab.

Second, under gold catalyzed alkyne activation conditions, azaphenalene could also be readily prepared with modified arene substrates. As shown in Table 4, the application of 1,3-di-amide substituted styrene-diyne **3v** gave **6a** in one pot in an excellent yield (83%). The structure of **6a** was confirmed by X-ray crystallography. This result confirmed the feasibility of the cascade sequence for the gold catalyzed ISDDA reaction and alkyne activation when suitable nucleophiles are present. Finally, while the reaction is rather sensitive to the linkages, the optimal 5-membered amide linker provided a potential *N*-nucleophile for sequential alkyne addition to construct isoquinoline H-PAHs. A two-step sequence was developed through gold catalyzed alkyne addition, followed by tosyl elimination, giving the desired isoquinoline with high efficiency (Table 4). Notably, all these H-PAHs give excellent FL emission,



^{*a*} Standard reaction conditions: substrate **3v** (0.2 mmol), toluene (10 mL), 10% JohnPhosAu(TA-H)SbF₆, 10% Cu(OTf)₂, 80 °C, 12 h, air, dark. ^{*b*} Standard reaction conditions: substrate **4** (0.2 mmol), THF (2 mL), LiAlH₄ (0.4 mmol), 60 °C, 3 h. ^{*c*} Standard reaction conditions: substrate **7** (0.2 mmol), DCM (2 mL), 10% JohnPhosAu(TA-H)SbF₆ for **7a**, **7b**, and **7d** (10% PPh₃AuNTf₂ for **7c**), rt, dark, 4 h; without purification, DMSO (2 mL), NaOH (1 M aq., 0.6 mL), 80 °C, 2 h.

suggesting the promising applications of these new types of compounds.

Conclusions

In summary, the ISDDA reaction with conjugated diynes is reported for the first time and the sequential alkyne activation allows easy construction of various PAHs with high efficiency. Compared to simple alkynes, diyne substrates showed significantly improved reactivity, allowing the reaction to proceed at a lower temperature. The application of the thermally stable TA-Au catalyst further improved the performance of this transformation, giving the desired products in excellent yields. The resulting alkyne of the ISDDA products allowed for easy transformations into various H-PAHs with high efficiency and interesting photoproperties. The application of this method for the preparation of new H-PAH cores in natural product synthesis and materials development is anticipated and is currently under investigation in our lab.

Author contributions

J. W. and X. S. conceived the project. J. W., M. L. and E. S. performed the experimental work. J. W. and M. L. collected and analysed the spectroscopic data. C. S. and L. W. collected and analysed the X-ray diffraction data. J. W., M. L., X. Y., S. Z. and X. S. wrote the manuscript. All of the authors discussed the results and contributed to the preparation of the manuscript.

Conflicts of interest

There are no conflicts to declare.

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