Facile Synthesis of Diverse Hetero Polyaromatic Hydrocarbons (PAHs) via Styryl Diels-Alder Reaction of Conjugated Diynes

Journal:	*Organic Chemistry Frontiers*
Manuscript ID	QO-RES-04-2022-000644.R1
Article Type:	Research Article
Date Submitted by the Author:	08-Jun-2022
Complete List of Authors:	Wei, Jingwen; University of South Florida, Chemistry Liu, Mengjia; University of South Florida, Chemistry Ye, Xiaohan; University of South Florida, Chemistry Zhang, Shuyao; University of South Florida, Chemistry Sun, Elaine; University of South Florida, Chemistry Shan, Chuan; University of South Florida, chemistry Wojtas, Lukasz; University of South Florida, Department of Chemistry Shi, Xiaodong; University of South Florida, Chemistry

SCHOLARONE™
Manuscripts

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

ARTICLE

Facile Synthesis of Diverse Hetero Polyaromatic Hydrocarbons (PAHs) via Styryl Diels-Alder Reaction of Conjugated Diynes

Jingwen Wei,[a] Mengjia Liu,[a] Xiaohan Ye,[a] Shuyao Zhang,[a] Elaine Sun,[a] Chuan Shan,[a] Lukasz Wojtas,[a] Xiaodong Shi*[a]

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

Introduction

With the continuously uncovering interesting photo and electronic properties, the polyaromatic hydrocarbons (PAHs) have received increasing attention over the past decade from both the chemistry and material research communities.[1] The conjugated π-contact property of PAHs allows charge carrier migration on stacked discotic molecules, and it is being widely used in organic electronic devices, 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 achieve various PAHs with higher efficiency and better functional group diversity.[3] Alkynes, as readily available building blocks that contain high thermal energy and are easy to functionalize, are potentially good starting materials to facilitate new PAHs synthesis.[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 often limits this application in synthesis. One example is the intramolecular styryl dehydro-Diels-Alder (ISDDA) reactions.[5] As shown in **Scheme 1A**, cycloaddition between styrene and alkyne could produce the rapid construction of polyaromatic hydrocarbons as a potentially efficient strategy for the preparation of PAHs. However, styrene dearomatization combined with low alkyne reactivity leads to the 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 complicates the overall transformations, giving the desired ISDDA products in low yields, poor selectivity (**B** and **C**) with limited substrate scope.[7]
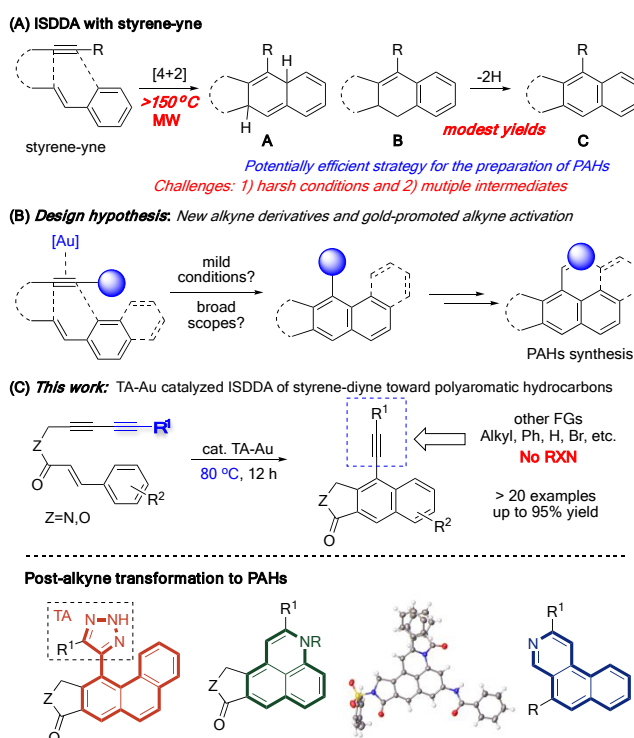
Scheme 1. Achieving polycyclic hydrocarbons via ISDDA.

Despite these challenges, the overall high efficiency of this ISDDA 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 literatures, one typical strategy to achieve this transformation

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

is the application of electro-withdrawing group (EWG) modified alkynes.[9] However, harsh conditions (> 150 °C and microwave irradiation MW) are required with 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 gave rapid decomposition at high temperatures(>80 °C), the 1,2,3-triazole gold catalyst (TA-Au) developed in our lab was able to tolerate high temperature without decomposition at 80 °C for more than 24 hours.[12] The 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 ISDDA reaction with conjugated diyne. While thermal conditions (80 °C) gave the cycloaddition product in 55% yields, the addition of 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 cycloaddition of unactivated alkyne (no EWG) substrate **1a**, high temperature (160 °C) and a long reaction time (**Figure 1A**, Condition A) are needed.[13] Notably, under this condition, the dehydrogenation product **1ab** was minor product and only achieved in 14% yield with the dialin **1aa** separated as the major product. Reducing the temperature to 80 °C gave no conversion. We wonder if gold catalysis can assist cycloaddition of **1a** at low temperature (80 °C). However, it is known in literatures that gold catalyzed enyne cyclization isomerization can occur under mild conditions.[14] As shown in **Figure 1A**, treating substrate **1a** under gold catalyzed conditions (Condition C) produced cyclopropane **1ac** even at room temperature. Clearly, to evaluate if gold catalyst could promote styryl-DA, a modified alkene substrate is needed to avoid the enyne cyclization (accessing styrene reactivity). An 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 catalyzed conditions gave no enyne cyclization. We continued to explore various gold catalyzed conditions with substrate **2a**, hoping to promote 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 temperatures to 100 °C led to the 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 high temperature (160 °C) gave the desired dehydrogenation cycloaddition product **2ab** with 45% yield, and no dialin **2aa** was

observed. This result indicated the introduction of carbonyl group provided a more efficient dehydrogenation pathway to the expected naphthalene.
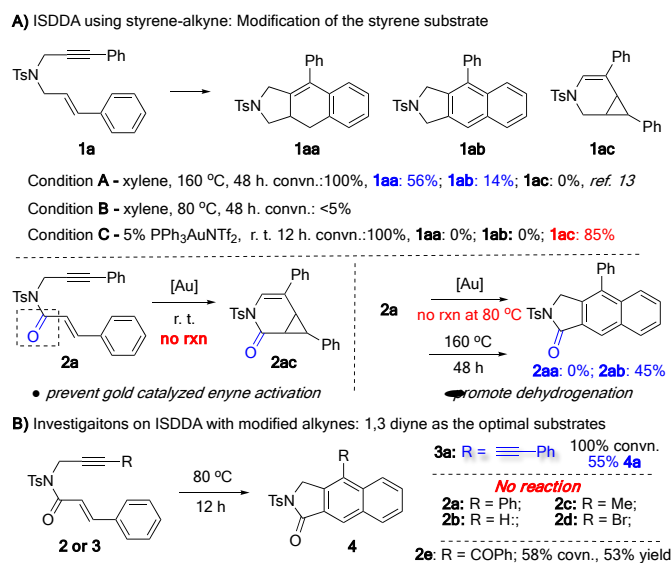
Figure 1. Investigations styryl-yne ISDDA under gold catalysis

In order to solve the high temperature problem, we decided to explore the alkyne substitutions effect. To improve alkyne reactivity, multiple alkyne derivatives (**2a-2e, 3a**) were prepared (**Figure 1B**). Surprisingly, the 1,3-diyne **3a** showed excellent reactivity in the ISDDA reaction. The simple thermal condition at 80 °C have 100% conversion and produced the naphthalene **4a** in 55% yield. Substrates (**2a-2d**) with other substituation groups (Ph, H, Me, Br) had no conversions observed under 80 °C. Substrate **2e** with EWG(COPh) had slower kietic speed with 58% coversion. We assume that both conjugated π system and less stereo hinderance are important in the ISDDA reaction. And conjugated diyne is a good motif that fit both factors. This observation is also consistent with previous reported HDDA works that conjugated diyne can improve the reactivity.[15]

Table 1. Optimization of the reaction conditions.^{a,b}

| 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** (0.2mmol), toluene (10 mL), 10% JohnPhosAu(TA-H)SbF$_6$, 10% Cu(OTf)$_2$,80 °C, 12 h, air, dark. ^{b}Yields are determined by ^{1}H NMR with 1,3,5-trimethoxybenzene as an internal standard. ^{c}reaction performed in glove-box.

This result was exciting as it suggested that: 1) the conjugated diyne is an effective moiety for ISDDA reaction under milder conditions and 2) it is plausible to use gold activation in this concerted cycloaddition process. To further optimize the reaction conditions, various gold catalyzed systems were applied (see details in SI). The TA-Au and Cu cocatalysts were identified as the optimal conditions. The comparison of representative alternative conditions is summarized in **Table 1**.

As shown in **Table 1**, under the optimal conditions, comprising of 10% JohnPhos(TA-H)AuSbF$_6$ with 10% Cu(OTf)$_2$ under 80 °C for 12 h, the diyne substrate **3a** completely converted to the 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 can still occur with 30% conversion and 26% yield in 12 h (entry 3). The gold catalyst itself could promote this transformation with 84% yield (entry 4,5). In our group prevous work, the Cu(OTf)$_2$ can serve as a Lewis acid to promote the triazole gold catalyst reactivity. The triazole on the gold catalyst served as a dynamic L-ligand and Lewis acid can dissociate the triazole ligand to yield active gold cation for catalysis.[16] The copper co-catalyst itself resulted in a decreased yield of 46%, which indicated this reaction is not catalyzed by Lewis acids (entry 4,6). Lowering gold catalyst loading to 5% caused the 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 diyne hydration (entry 8-9). The primary ligand on gold is also critical. Johnphos was observed as the optimal ligand for this reaction (entry 10). Among 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 achieved through either direct de-hydrogenation or oxidation (such as by O$_2$). To explore this process, this reaction was performed under argon protection. As shown in entry 13, significantly reduced yield was observed (27%). This result clearly ruled-out the dehydrogentaiton pathway. Notably, although it is clear that molecular O$_2$ could be used as the effective oxidant, some product was formed under O$_2$-free condition. In this case, the oxidation was likely achieved with the *in-situ* formed diene, though with lower efficiency and atom economy. Silghtly lower yield was received while conduting the reaction under day light (entry 14, 88%), which is likely associated with the photo initiated styrene decomposition/polymerization. With the optimized reaction conditions developed, we investigated the reaction scopes. The results are summarized in **Table 2**.
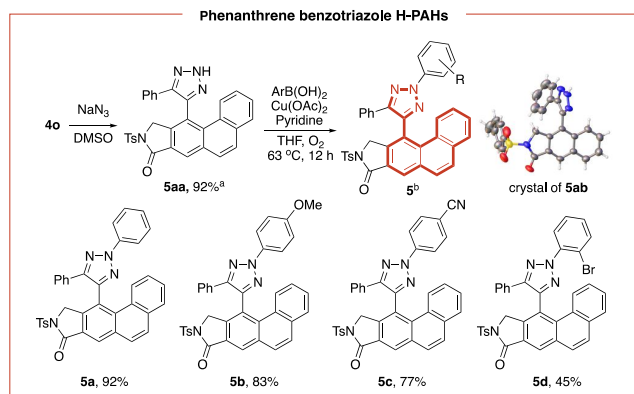
Table 2. Substrate Scope for ISDDA reaction^{a,b}
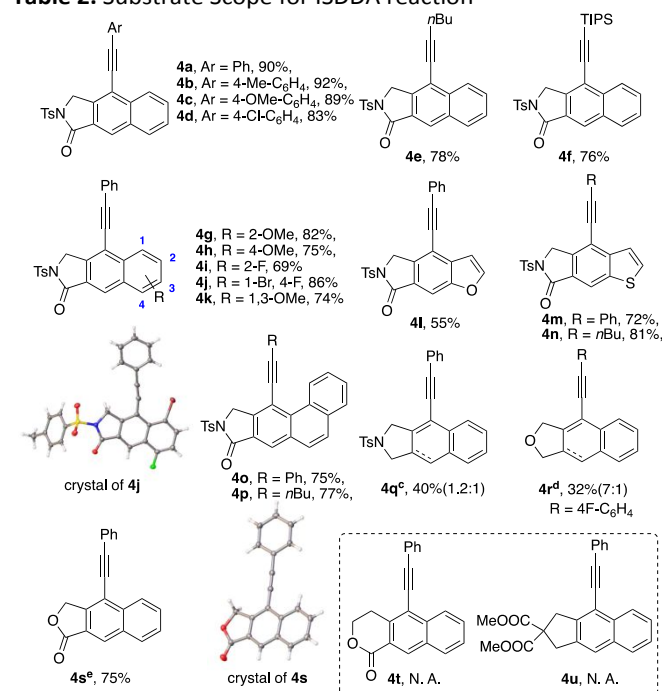
^{a}Standard reaction conditions: substrate (0.2mmol), toluene (10 mL), 10% JohnPhosAu(TA-H)SbF$_6$, 10% Cu(OTf)$_2$, 80 °C ,12 h, dark. ^{b}Isolated yield. ^{c}no [Au], 80 °C, 12h. ^{d}no [Au], 80 °C, 6 h.^{e}10% JohnPhosAu(TA-H)SbF$_6$, 100 °C, 72 h.

To scrutinize the substituent effect of conjugated diynes, substrates with either electron-donating or electron-withdrawing groups were prepared, obtaining the corresponding products in excellent yields (**4a-4d**). Aliphatic and silyl substituted diynes **4e**, **4f** were also amenable, which suggested the good functional group tolerability 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 desired products **4g-4k** in good yields. Notably, the X-ray crystal structure of **4j** showed an interesting stereo repulsion between the alkyne and the bromo at the *peri* position. Impressively, furan and thiophen modified substrates also work in this transformation, giving benzofuran **4l**, benzothiophenes (**4m, 4n**) and phenanthrenes (**4o, 4p**) in one step, which highlights the good efficiency of this method in the construction of various PAHs framework.

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) with low yield (**4q:4qa**=1.2:1, **4q** is the dehydrogenation product, total 40% yield). Similarly, ether-linked substrate 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 long reaction time (72 h) using only TA-Au gave the optimal results with 75% yield. Carbon-linker and longer linkages showed significantly reduced

reactivity with no conversions observed (**4t**,**4u**), indicating the importance of the linkers for this transformation.

Table 3. Phenanthrene benzotriazole H-PAHs synthesis scope

[a]Standard reaction conditions: substrate (0.2mmol), 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.

Table 4. Azaphenalene and Isoquinoline H-PAHs synthesis scope
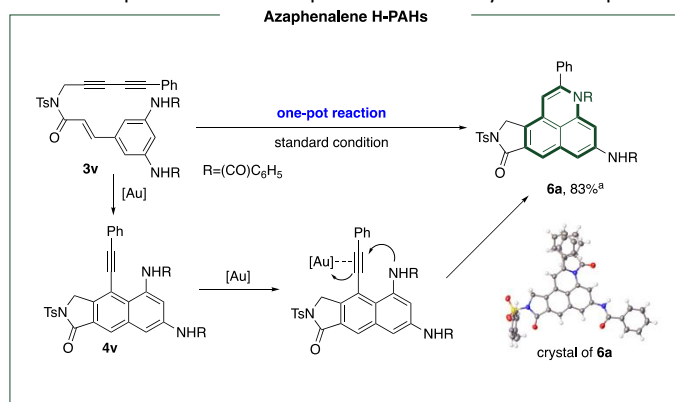
[a]Standard reaction conditions: substrate **3v** (0.2mmol), toluene (10 mL), 10% JohnPhosAu(TA-H)SbF6, 10% Cu(OTf)2, 80 °C ,12 h, air, dark. [b]Standard reaction conditions: substrate **4** (0.2 mmol), THF (2 mL), LiAlH4 (0.4 mmol), 60 °C, 3 h. [c]Standard reaction conditions: substrate **7** (0.2mmol), DCM (2 mL), 10% JohnPhosAu(TA-H)SbF6 for **7a,7b,7d**(10% PPh3AuNTf2 for **7c**), rt., dark, 4h; without purification, DMSO (2 mL), NaOH (1M aq., 0.6 mL), 80 °C, 2 h.
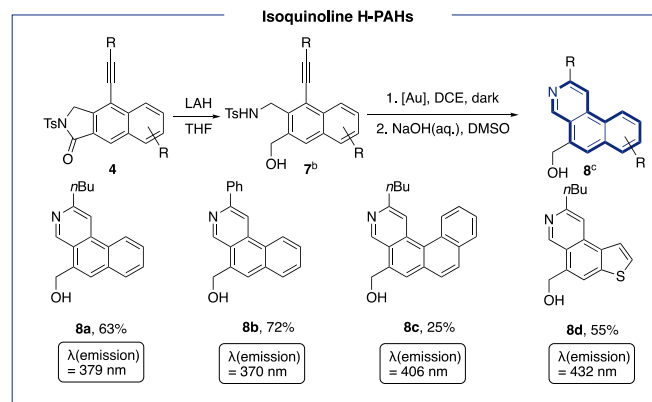
With the ability to incorporate diynes in this ISDDA reaction, the resulting alkyne can be applied for the sequential heteroatom-containing polyaromatic hydrocarbons (H-PAHs). Three H-PAHs synthesis are summarized in **Table 3** and **Table 4** (phenanthrene benzotriazole, azaphenalene, and isoquinoline), which can be achieved based on this practical method. First, the phenanthrene benzotriazole derivatives can be readily prepared in two steps (**Table 3**) through treatment **4o** with NaN3 and sequential N-2 selected triazole arylation. Notably, our group first reported that N-2-aryl-1,2,3-triazole (NAT) is a good fluorophore with strong FL emissions.[17] 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 with excellent yield (83%). The structure of **6a** was confirmed by X-ray crystallography. This result confirmed the feasibility of the cascade sequence for gold catalyzed ISDDA and alkyne activation when proper nucleophiles are present. Finally, while the reaction is rather sensitive to the linkages, the optimal 5-member 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, suggesting the promising applications of these new types of compounds.

Conclusions

In summary, the ISDDA reaction with conjugated diynes is being 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 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 photo properties. Application of this method for the preparation of new H-PAHs cores in natural product synthesis and material development is expected and 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 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.

ARTICLE

Conflicts of interest

There are no conflicts to declare.

Notes and references

1   (*a*) Z. Sun, Q. Ye, C. Y. Chi and J. S. Wu, Low band gap polycyclic hydrocarbons: from closed-shell near infrared dyes and semiconductors to open-shell radicals, *Chem. Soc. Rev.*, 2012, **41**, 7857-7889. (*b*) I. J. Keyte, R. M. Harrison and G. Lammel, Chemical reactivity and long-range transport potential of polycyclic aromatic hydrocarbons - a review, *Chem. Soc. Rev.*, 2013, **42**, 9333-9391. (*c*) A. Narita, X. Y. Wang, X. L. Feng and K. Mullen, New advances in nanographene chemistry, *Chem. Soc. Rev.*, 2015, **44**, 6616-6643. (*d*) B. Schuler, G. Meyer, D. Pena, O. C. Mullins and L. Gross, Unraveling the Molecular Structures of Asphaltenes by Atomic Force Microscopy, *J. Am. Chem. Soc.*, 2015, **137**, 9870-9876. (*e*) K. O. Johansson, M. P. Head-Gordon, P. E. Schrader, K. R. Wilson and H. A. Michelsen, Resonance-stabilized hydrocarbon-radical chain reactions may explain soot inception and growth, *Science*, 2018, **361**, 997-1000. (*f*) H. Ito, Y. Segawa, K. Murakami and K. Itami, Polycyclic Arene Synthesis by Annulative pi-Extension, *J. Am. Chem. Soc.*, 2019, **141**, 3-10. (*g*) M. L. Yang, I. S. Park and T. Yasuda, Full-Color, Narrowband, and High-Efficiency Electroluminescence from Boron and Carbazole Embedded Polycyclic Heteroaromatics, *J. Am. Chem. Soc.*, 2020, **142**, 19468-19472. (*h*) J. He, F. Rauch, M. Finze and T. B. Marder, (Hetero)arene-fused boroles: a broad spectrum of applications, *Chem. Sci.*, 2021, **12**, 128-147.

2   (*a*) L. Schmidt-Mende, A. Fechtenkotter, K. Mullen, E. Moons, R. H. Friend and J. D. MacKenzie, Self-organized discotic liquid crystals for high-efficiency organic photovoltaics, *Science*, 2001, **293**, 1119-1122. (*b*) E. W. Meijer and A. P. H. J. Schenning, Chemistry - Material marriage in electronics, *Nature*, 2002, **419**, 353-354. (*c*) M. Kastler, J. Schmidt, W. Pisula, D. Sebastiani and K. Mullen, From armchair to zigzag peripheries in nanographenes, *J. Am. Chem. Soc.*, 2006, **128**, 9526-9534. (*d*) P. M. Beaujuge and J. M. J. Frechet, Molecular Design and Ordering Effects in pi-Functional Materials for Transistor and Solar Cell Applications, *J. Am. Chem. Soc.*, 2011, **133**, 20009-20029. (*e*) P. Y. Chou, H. H. Chou, Y. H. Chen, T. H. Su, C. Y. Liao, H. W. Lin, W. C. Lin, H. Y. Yen, I. C. Chen and C. H. Cheng, Efficient delayed fluorescence via triplet-triplet annihilation for deep-blue electroluminescence, *Chem. Commun.*, 2014, **50**, 6869-6871. (*f*) E. R. Darzi, J. S. Barber and N. K. Garg, Cyclic Alkyne Approach to Heteroatom-Containing Polycyclic Aromatic Hydrocarbon Scaffolds, *Angew. Chem. Int. Ed.*, 2019, **58**, 9419-9424.

3   (*a*) Y. Yano, H. Ito, Y. Segawa and K. Itami, Helically Twisted Tetracene: Synthesis, Crystal Structure, and Photophysical Properties of Hexabenzo[a,c,fg,j,l,op]tetracene, *Synlett*, 2016, **27**, 2081-2084. (*b*) H. Ito, K. Ozaki and K. Itami, Annulative pi-Extension (APEX): Rapid Access to Fused Arenes, Heteroarenes, and Nanographenes, *Angew. Chem. Int. Ed.*, 2017, **56**, 11144-11164. (*c*) R. S. Jordan, Y. L. Li, C. W. Lin, R. D. McCurdy, J. B. Lin, J. L. Brosmer, K. L. Marsh, S. I. Khan, K. N. Houk, R. B. Kaner and Y. Rubin, Synthesis of N=8 Armchair Graphene Nanoribbons from Four Distinct Polydiacetylenes, *J. Am. Chem. Soc.*, 2017, **139**, 15878-15890. (*d*) W. Matsuoka, H. Ito and K. Itami, Rapid Access to Nanographenes and Fused Heteroaromatics by Palladium-Catalyzed Annulative -Extension Reaction of Unfunctionalized Aromatics with Diiodobiaryls, *Angew. Chem. Int. Ed.*, 2017, **56**, 12224-12228. (*e*) H. Kitano, W. Matsuoka, H. Ito and K. Itami, Annulative pi-extension of indoles and pyrroles with diiodobiaryls by Pd catalysis: rapid synthesis of nitrogen-containing polycyclic aromatic compounds, *Chem. Sci.*, 2018, **9**, 7556-7561. (*f*) Y. Koga, T. Kaneda, Y. Saito, K. Murakami and K. Itami, Synthesis of partially and fully fused polyaromatics by annulative chlorophenylene dimerization, *Science*, 2018, **359**, 435-439. (*g*) K. Lin, Y. Jian, P. Zhao, C. S. Zhao, W. D. Pan and S. Liu, A rapid construction of a specific quino[4,3-b] carbazolone system and its application for the synthesis of calothrixin B, *Org. Chem. Front.*, 2018, **5**, 590-594. (*h*) C. D. Zhu, D. Wang, D. Y. Wang, Y. Zhao, W. Y. Sun and Z. Z. Shi, Bottom-up Construction of -Extended Arenes by a Palladium-Catalyzed Annulative Dimerization of o-Iodobiaryl Compounds, *Angew. Chem. Int. Ed.*, 2018, **57**, 8848-8853.

4   (*a*) T. K. Shah, J. M. Medina and N. K. Garg, Expanding the Strained Alkyne Toolbox: Generation and Utility of Oxygen-Containing Strained Alkynes, *J. Am. Chem. Soc.*, 2016, **138**, 4948-4954. (*b*) S. E. Suh, S. M. Chen, K. N. Houk and D. M. Chenoweth, The mechanism of the triple aryne-tetrazine reaction cascade: theory and experiment, *Chem. Sci.*, 2018, **9**, 7688-7693. (*c*) X. Xiao and T. R. Hoye, The domino hexadehydro-Diels-Alder reaction transforms polyynes to benzynes to naphthynes to anthracynes to tetracynes (and beyond?), *Nat. Chem.,* 2018, **10**, 838-844. (*d*) E. R. Darzi, J. S. Barber and N. K. Garg, Cyclic Alkyne Approach to Heteroatom-Containing Polycyclic Aromatic Hydrocarbon Scaffolds, *Angew. Chem. Int. Ed.*, 2019, **58**, 9419-9424. (*e*) C C. B. Ritts and T. R. Hoye, Sulfurane [S(IV)]-Mediated Fusion of Benzynes Leads to Helical Dibenzofurans, *J. Am. Chem. Soc.*, 2021, **143**, 13501-13506.

5   (*a*) L. S. Kocsis, H. N. Kagalwala, S. Mutto, B. Godugu, S. Bernhard, D. J. Tantillo and K. M. Brummond, Mechanistic Insight into the Dehydro-Diels-Alder Reaction of Styrene-Ynes, *J. Org. Chem.*, 2015, **80**, 11686-11698. (*b*) A. E. Bober, J. T. Proto and K. M. Brummond, Intramolecular Didehydro-Diels-Alder Reaction for the Synthesis of Benzo-and Dihydrobenzo-Fused Heterocycles, *Org. Lett.*, 2017, **19**, 1500-1503.

6   (*a*) L. H. Klemm and K. W. Gopinath, An Intramolecular Diels-Alder Reaction - a Simple Synthesis of Gamma-Apopicropodophyllin, *Tetrahedron Lett.*, 1963, 1243-1245. (*b*) L. H. Klemm, R. A. Klemm, P. S. Santhanam and D. V. White, Intramolecular Diels-Alder Reactions .VI. Syntheses of 3-Hydroxymethyl-2-Naphthoic Acid Lactones, *J. Org. Chem.*, 1971, **36**, 2169-2172. (*c*) L. S. Kocsis and K. M. Brummond, Intramolecular Dehydro-Diels-Ader Reaction Affords Selective Entry to Arylnaphthalene or Aryldihydronaphthalene Lignans,

Org. Lett., 2014, **16**, 4158-4161. (*d*) D. I. Saavedra, B. D. Rencher, D. H. Kwon, S. J. Smith, D. H. Ess and M. B. Andrus, Synthesis and Computational Studies Demonstrate the Utility of an Intramolecular Styryl Diels Alder Reaction and Di-t-butylhydroxytoluene Assisted [1,3]-Shift to Construct Anticancer dl-Deoxypodophyllotoxin, *J. Org. Chem.*, 2018, **83**, 2018-2026.

7   S. S. Chackalamannil, D. Doller, M. Clasby, Y. Xia, K. Eagen, Y. Lin, H. A. Tsai and A. T. McPhail, A facile Diels-Alder route to dihydronaphthofuranones, *Tetrahedron Lett.*, 2000, **41**, 4043-4047.

8   (*a*) L. S. Kocsis, E. Benedetti and K. M. Brummond, A Thermal Dehydrogenative Diels-Alder Reaction of Styrenes for the Concise Synthesis of Functionalized Naphthalenes, *Org. Lett.*, 2012, **14**, 4430-4433. (*b*) E. Benedetti, A. B. E. Veliz, M. Charpenay, L. S. Kocsis and K. M. Brummond, Attachable Solvatochromic Fluorophores and Bioconjugation Studies, *Org. Lett.*, 2013, **15**, 2578-2581. (*c*) L. S. Kocsis, H. N. Kagalwala, S. Mutto, B. Godugu, S. Bernhard, D. J. Tantillo and K. M. Brummond, Mechanistic Insight into the Dehydro-Diels-Alder Reaction of Styrene-Ynes, *J. Org. Chem.*, 2015, **80**, 11686-11698. (*d*) Z. X. Fang, Y. Liu, B. D. Barry, P. Q. Liao and X. H. Bi, Formation of Benzo[f]-1-indanone Frameworks by Regulable Intramolecular Annulations of gem-Dialkylthio Trienynes, *Org. Lett.*, 2015, **17**, 782-785. (*e*) L. S. Kocsis, K. M. Elbel, B. A. Hardigree, K. M. Brummond, M. A. Haidekker and E. A. Theodorakis, Cyclopenta[b]naphthalene cyanoacrylate dyes: synthesis and evaluation as fluorescent molecular rotors, *Org. Biomol. Chem.*, 2015, **13**, 2965-2973. (*f*) J. Zhang, H. Wang, S. B. Ren, W. Zhang and Y. K. Liu, Cu(0)/Selectfluor System-Mediated Mild Synthesis of Fluorinated Fluorenones from Nonaromatic Precursors (1,6-Enynes) Involving C-C Single Bond Cleavage, *Org. Lett.*, 2015, **17**, 2920-2923. (*g*) J. Zhang, H. F. Zhang, D. D. Shi, H. W. Jin and Y. K. Liu, Facile and Diverse Synthesis of Benzo[b]fluorenone Derivatives through a Copper/Selectfluor-Catalyzed Tandem Annulation of 1,6-Enynes, *Eur. J. Org. Chem.*, 2016, **2016**, 5545-5558. (*h*) W. Xu, G. N. Wang, X. Xie and Y. H. Liu, Gold(I)-Catalyzed Formal Intramolecular Dehydro-Diels-Alder Reaction of Ynamide-ynes: Synthesis of Functionalized Benzo[b]carbazoles, *Org. Lett.*, 2018, **20**, 3273-3277. (*i*) Q. Zhao, D. F. Leon Rayo, D. Campeau, M. Daenen and F. Gagosz, Gold-Catalyzed Formal Dehydro-Diels-Alder Reactions of Ene-Ynamide Derivatives Bearing Terminal Alkyne Chains: Scope and Mechanistic Studies, *Angew. Chem. Int. Ed.*, 2018, **57**, 13603-13607. (*j*) N. Camedda, M. Lanzi, F. Bigi, R. Maggi and G. Maestri, Ambient Synthesis of Tricyclic Naphthalenes via Stepwise Styryl-yne Dearomative Diels-Alder Cyclization, *Org. Lett.*, 2021, **23**, 6536-6541. (*k*) H. F. Wang, L. N.

Guo, Z. B. Fan, T. H. Tang and W. W. Zi, Gold-Catalyzed Formal Hexahydro-Diels-Alder/Carboalkoxylation Reaction Cascades, *Org. Lett.*, 2021, **23**, 2676-2681. (*l*) L. M. Zheng, H. Xue, B. W. Zhou, S. P. Luo, H. W. Jin and Y. K. Liu, Single Cu(I)-Photosensitizer Enabling Combination of Energy-Transfer and Photoredox Catalysis for the Synthesis of Benzo[b]fluorenols from 1,6-Enynes, *Org. Lett.*, 2021, **23**, 4478-4482.

9   (*a*) E. Ruijter, J. Garcia-Hartjes, F. Hoffmann, L. T. M. van Wandelen, F. J. J. de Kanter, E. Janssen and R. V. A. Orru, Synthesis of Polycyclic Alkaloid-Type Compounds by an N-Acyliminium Pictet-Spengler/Diels-Alder Sequence, *Synlett*, 2010, **16**, 2485-2489. (*b*) K. M. Brummond and L. S. Kocsis, Intramolecular Didehydro-Diels-Alder Reaction and Its Impact on the Structure-Function Properties of Environmentally Sensitive Fluorophores, *Acc. Chem. Res.*, 2015, **48**, 2320-2329.

10   H. J. Mun, E. Y. Seong, K. H. Ahn and E. J. Kang, Fe(II)/Fe(III)-Catalyzed Intramolecular Didehydro-Diels-Alder Reaction of Styrene-ynes, *J. Org. Chem.*, 2018, **83**, 1196-1203.

11   (*a*) J. Wang, S. Y. Zhang, C. Xu, L. Wojtas, N. G. Akhmedov, H. Chen and X. D. Shi, Highly Efficient and Stereoselective Thioallylation of Alkynes: Possible Gold Redox Catalysis with No Need for a Strong Oxidant, *Angew. Chem. Int. Ed.*, 2018, **57**, 6915-6920. (*b*) X. H. Ye, H. H. Peng, C. Y. Wei, T. Yuan, L. Wojtas and X. D. Shi, Gold-Catalyzed Oxidative Coupling of Alkynes toward the Synthesis of Cyclic Conjugated Diynes, *Chem*, 2018, **4**, 1983-1993. (*c*) X. H. Ye, P. Y. Zhao, S. Y. Zhang, Y. B. Zhang, Q. L. Wang, C. Shan, L. Wojtas, H. Guo, H. Chen and X. D. Shi, Facilitating Gold Redox Catalysis with Electrochemistry: An Efficient Chemical-Oxidant-Free Approach, *Angew. Chem. Int. Ed.*, 2019, **58**, 17226-17230. (*d*) J. Wang, C. Y. Wei, X. M. Li, P. Y. Zhao, C. Shan, L. Wojtas, H. Chen and X. D. Shi, Gold Redox Catalysis with a Selenium Cation as a Mild Oxidant, *Chem. Eur. J.*, 2020, **26**, 5946-5950. (*e*) T. Yuan, X. H. Ye, P. Y. Zhao, S. Teng, Y. P. Yi, J. Wang, C. Shan, L. Wojtas, J. Jean, H. Chen and X. Shi, Regioselective Crossed Aldol Reactions under Mild Conditions via Synergistic Gold-Iron Catalysis, *Chem*, 2020, **6**, 1420-1431. (*f*) S. Y. Zhang, C. H. Wang, X. H. Ye and X. D. Shi, Intermolecular Alkene Difunctionalization via Gold-Catalyzed Oxyarylation, *Angew. Chem. Int. Ed.*, 2020, **59**, 20470-20474. (*g*) T. Yuan, Q. Tang, C. Shan, X. H. Ye, J. Wang, P. Y. Zhao, L. Wojtas, N. Hadler, H. Chen and X. D. Shi, Alkyne Trifunctionalization via Divergent Gold Catalysis: Combining pi-Acid Activation, Vinyl-Gold Addition, and Redox Catalysis, *J. Am. Chem. Soc.*, 2021, **143**, 4074-4082.

12   (*a*) S. E. Motika, Q. Y. Wang, X. H. Ye and X. D. Shi, Ambient Synthesis of Dienals via Triazole-Gold and Amine Catalysis Relay, *Org. Lett.*, 2015, **17**, 290-293. (*b*) S. Hosseyni, L. Wojtas, M. Y. Li and X. D. Shi, Intermolecular Homopropargyl Alcohol Addition to Alkyne and a Sequential 1,6-Enyne Cycloisomerization with Triazole-Gold Catalyst, *J. Am. Chem. Soc.*, 2016, **138**, 3994-3997. (*c*) S. E. Motika, Q. Y. Wang, N. G. Akhmedov, L. Wojtas and X. D. Shi, Regioselective Amine-Borane Cyclization: Towards the Synthesis of 1,2-BN-3-Cyclohexene by Copper-Assisted Triazole/Gold Catalysis, *Angew. Chem. Int. Ed.*, 2016, **55**, 11582-11586. (*d*) R. Cai, X. H. Ye, Q. Sun, Q. He, Y. He, S. Q. Ma and X. D. Shi, Anchoring Triazole-Gold(I) Complex into Porous Organic Polymer To Boost the Stability and Reactivity of Gold(I) Catalyst, *ACS Catal.*, 2017, **7**, 1087-1092. (*e*) F. S. Zhang, Q. Lai, X. D. Shi

and Z. G. Song, Triazole-gold (TAAu) catalyzed three-component coupling (A3 reaction) towards the synthesis of 2, 4-disubstituted quinoline derivatives, *Chin. Chem. Lett.*, 2019, **30**, 392-394. (*f*) T. Jia, S. Y. Fan, F. M. Li, X. H. Ye, W. K. Zhang, Z. G. Song and X. D. Shi, Achieving Aliphatic Amine Addition to Arylalkynes via the Lewis Acid Assisted Triazole-Gold (TA-Au) Catalyst System, *Org. Lett.*, 2021, **23**, 6019-6023.

13 T. Ozawa, T. Kurahashi and S. Matsubara, Dehydrogenative Diels-Alder Reaction, *Org. Lett.*, 2011, **13**, 5390-5393.

14 (*a*) C. Nieto-Oberhuber, M. P. Munoz, E. Bunuel, C. Nevado, D. J. Cardenas and A. M. Echavarren, Cationic gold(I) complexes: Highly alkynophilic catalysts for the exo- and endo-cyclization of enynes, *Angew. Chem. Int. Ed.*, 2004, **43**, 2402-2406. (*b*) C. Nieto-Oberhuber, P. Perez-Galan, E. Herrero-Gomez, T. Lauterbach, C. Rodriguez, S. Lopez, C. Bour, A. Rosellon, D. J. Cardenas and A. M. Echavarren, Gold(I)-catalyzed intramolecular [4+2] cycloadditions of arylalkynes or 1,3-enynes with alkenes: Scope and mechanism, *J. Am. Chem. Soc.*, 2008, **130**, 269-279. (*c*) A. S. K. Hashmi, W. B. Yang, F. Rominger and C. Invest, Gold(I)-Catalyzed Formation of Benzo[b]furans from 3-Silyloxy-1,5-enynes, *Angew. Chem. Int. Ed.*, 2011, **50**, 5761-5764. (*d*) J. F. Brazeau, S. Y. Zhang, I. Colomer, B. K. Corkey and F. D. Toste, Enantioselective Cyclizations of Silyloxyenynes Catalyzed by Cationic Metal Phosphine Complexes, *J. Am. Chem. Soc.*, 2012, **134**, 2742-2749. (*e*) A. Escribano-Cuesta, P. Perez-Galan, E. Herrero-Gomez, M. Sekine, A. A. C. Braga, F. Maseras and A. M. Echavarren, The role of cyclobutenes in gold(I)-catalysed skeletal rearrangement of 1,6-enynes, *Org. Biomol. Chem.*, 2012, **10**, 6105-6111. (*f*) P. J. Cai, Y. Wang, C. H. Liu and Z. X. Yu, Gold(I)-Catalyzed Polycyclization of Linear Dienediynes to Seven-Membered Ring-Containing Polycycles via Tandem Cyclopropanation/Cope Rearrangement/C-H Activation, *Org. Lett.*, 2014, **16**, 5898-5901. (*g*) M. C. B. Jaimes, F. Rominger, M. M. Pereira, R. M. B. Carrilho, S. A. C. Carabineiro and A. S. K. Hashmi, Highly active phosphite gold(I) catalysts for intramolecular hydroalkoxylation, enyne cyclization and furanyne cyclization, *Chem. Commun.*, 2014, **50**, 4937-4940. (*h*) R. Dorel and A. M. Echavarren, Gold(I)-Catalyzed Activation of Alkynes for the Construction of Molecular Complexity, *Chem. Rev.*, 2015, **115**, 9028-9072. (*i*) Z. Xu, H. Y. Chen, Z. X. Wang, A. G. Ying and L. M. Zhang, One-Pot Synthesis of Benzene-Fused Medium-Ring Ketones: Gold Catalysis-Enabled Enolate Umpolung Reactivity, *J. Am. Chem. Soc.*, 2016, **138**, 5515-5518. (*j*) J. G. Mayans, J. S. Suppo and A. M. Echavarren, Photoredox-Assisted Gold-Catalyzed Arylative Alkoxycyclization of 1,6-Enynes, *Org. Lett.*, 2020, **22**, 3045-3049.

15 (*a*) Y. Liang, X. Hong, P. Y. Yu and K. N. Houk, Why Alkynyl Substituents Dramatically Accelerate Hexadehydro-Diels-Alder (HDDA) Reactions: Stepwise Mechanisms of HDDA Cycloadditions, *Org. Lett.,* 2014, **16**, 5702-5705. (*b*) L. L. Fluegel and T. R. Hoye, Hexadehydro-Diels-Alder Reaction: Benzyne Generation via Cycloisomerization of Tethered Triynes, *Chem. Rev.,* 2021, **121**, 2413-2444.

16 Y. M. Xi, Q. Y. Wang, Y. J. Su, M. Y. Li and X. D. Shi, Quantitative kinetic investigation of triazole-gold(I) complex catalyzed [3,3]-rearrangement of propargyl ester, *Chem. Commun.*, 2014, **50**, 2158-2160.

17 (*a*) R. Cai, D. W. Wang, Y. F. Chen, W. M. Yan, N. R. Geise, S. Sharma, H. Y. Li, J. L. Petersen, M. Y. Li and X. D. Shi, Facile

synthesis of fluorescent active triazapentalenes through gold-catalyzed triazole-alkyne cyclization, *Chem. Commun.*, 2014, **50**, 7303-7305. (*b*) Y. W. Zhang, X. H. Ye, J. L. Petersen, M. Y. Li and X. D. Shi, Synthesis and Characterization of Bis-N-2-Aryl Triazole as a Fluorophore, *J. Org. Chem.*, 2015, **80**, 3664-3669. (*c*) Q. Lai, Q. Liu, K. Zhao, C. Shan, L. Wojtas, Q. C. Zheng, X. D. Shi and Z. G. Song, Rational design and synthesis of yellow-light emitting triazole fluorophores with AIE and mechanochromic properties, *Chem. Commun.*, 2019, **55**, 4603-4606.