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Copper-Catalyzed Chemodivergent Cyclization of N-(*ortho*-alkynyl)aryl-Pyrrole and Indoles

Tengfei Yao, Tong Xia, Wei Yan, Haofeng Xu, Fang Zhang, Yuanjing Xiao, Junliang Zhang,* and Lu Liu*

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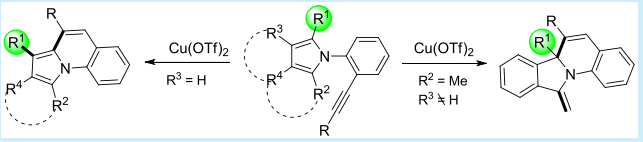
ABSTRACT: Herein, we described an efficient copper-catalyzed chemo-divergent tandem reaction of N-(*ortho*-alkynyl)aryl-pyrrole and (iso)indoles, delivering ring-fused N-heterocycles in good yields in an atom-economical manner. N-(*ortho*-alkynyl)aryl-pyrrole and indoles undergo the tandem cyclization/migration reaction, in which the group at 2-position was migrated to 3-position. In contrast, the dearomative cyclization of N-(ortho-alkynyl)aryl-isoindoles would occur to deliver the N-fused tetracyclic products efficiently.



Nitrogen-containing polycycles are widely present in natural products, bioactive molecules, and materials.[1] Fused pyrrole derivatives, such as Valmerins, Hippadine, alstorisine A, and Isoschizagaline, are often present many useful bioacitivities.[2] In addition, it is found that ring-fused pyrroles have potential application in electronic devices, such as OLEDs (organic light-emitting diodes) and OPVs (organic photovoltaics), as well as energy conversion applications.[3]

With regard to the privileged existing and usefulness of fused N-heterocycles, many efforts have been devoted to this skeleton synthesis.[4] Recently, the cycloisomerization of (hetero)arenes with alkynes to construct cyclic scaffolds has received much attention, because of its atom-economical manner.[5] In this context, the Friedel−Crafts[6] cyclization of N-(*ortho*-alkynyl)aryl-pyrrole and indoles represents one of the most straightforward strategies to construct ring-fused pyrroles and indoles (Scheme 1a), in which the group of 2-position was limited to hydrogen and transferred to the *β*-position of alkyne via protonation of the forming C-metal bond. The pioneering work disclosed by Fürstner showed that various metal salts including $PtCl_2$, AuCl, $GaCl_3$, $InCl_3$, etc. were efficient for achieving this type of transformation.[7] Later, Grätzel, Bolm, Shi, and others disclosed that several different Lewis acids and Bronsted acids were efficient to catalyze this reaction.[8] In continuing with our interest in heterocycle synthesis and alkyne chemistry,[9] we wondered whether the R^1 ($R^1 \neq H$) group at the 2-position of pyrrole or indole would migrate to the *β*-position of alkyne after the cyclization. We disclose herein a copper-catalyzed regioselective and chemodivergent tandem cyclization/migration[10] or dearomative[11] cyclization of N-(*ortho*-alkynyl)aryl-pyrrole and (iso)indoles (Scheme 1b), delivering various ring-fused N-heterocycles in good yields in an atom-economical[12] manner.

2,5-Dimethyl-1-(2-(phenylethynyl)phenyl)-1*H*-pyrrole **1a**, which was readily available by the condensation of hexane-2,5-dione with 2-(phenylethynyl)aniline, under the catalysis of *p*-TsOH, was selected as a model substrate. When the reaction was catalyzed by $Sc(OTf)_3$ in DCE at 90 °C for 12 h, the 1,3-dimethyl-4-phenylpyrrolo[1,2-*a*]quinoline **2a** via 6-*endo*-dig cyclization and the sequential 1,2-migration of methyl group, was observed in 16% NMR yield (Table 1, entry 1). The possible 5-*exo*-dig reaction was not detected in the above-mentioned condition. Encouraged by this result, we screened several different triflate metal salts, including $Bi(OTf)_3$, $In(OTf)_3$, and AgOTf, as well as $Cu(OTf)_2$, in which $Cu(OTf)_2$ displayed the best catalytic efficiency, affording the corresponding product **2a** in the highest yield (see Table 1, entries 2−6). The commonly used catalyst $InCl_3$ for alkyne cyclization reaction also worked in this transformation, but giving the product **2a** in only 48% NMR yield (Table 1, entry 7). Then, various copper salts with different counterion were further tested, and all could not increase the yield, even under higher temperature (Table 1, entries 8−11). Further solvent screening, such as toluene, tetrahydrofuran (THF), and dichloromethane (DCM), could not bring better results either (Table 1, entries 12−16). In this transformation, $Cu(OTf)_2$ should work as a *π*-acid to activate the carbon−carbon triple bond, which could undergo the following nucleophilic addition of the pyrrole ring.

Next, the substrate scope of this tandem cyclization/migration reaction was investigated (see Scheme 2). The reactions of N-(*ortho*-alkynyl)aryl-pyrrole pyrroles **1b−1n**

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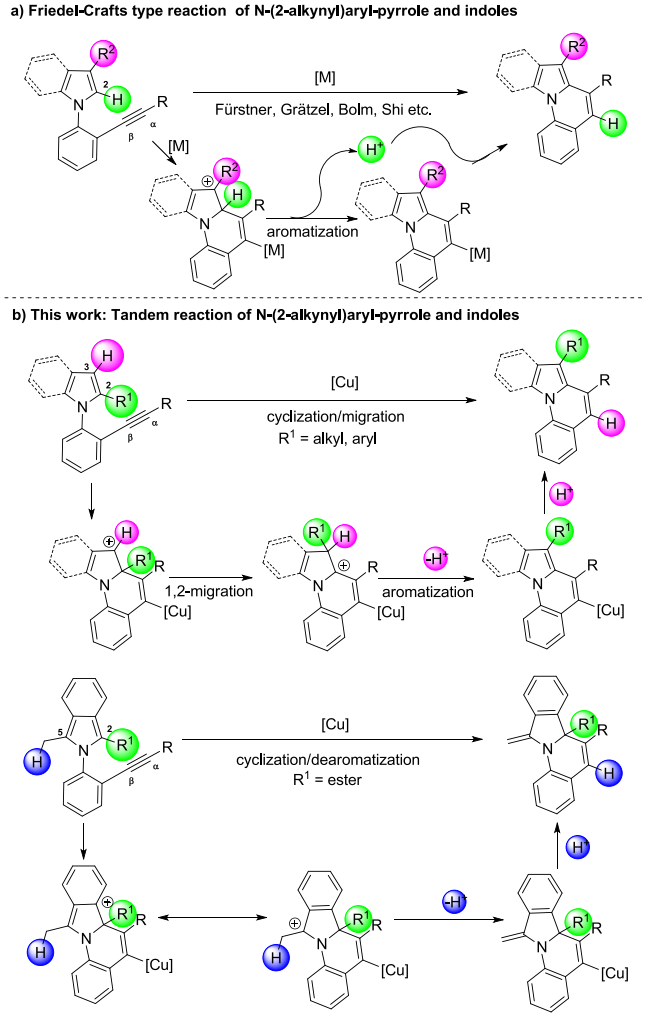
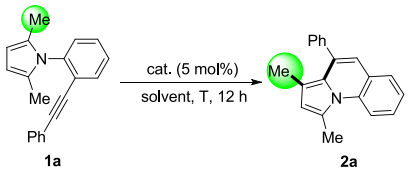
Scheme 1. Intramolecular Cyclization of Pyrroles with Alkynes To Access N-Fused Pyrroles Derivatives



were performed smoothly, which delivered the desired products **2b**−**2n** in excellent yields. These results indicated that the different electron-nature aryl group bearing various electron-withdrawing groups (EWGs) or electron-donating groups (EDGs) at different sites of alkynyl moiety were compatible. The R group could be aliphatic one, i.e., **1o**, in which the product **2o** was given in 81% yield. It is noteworthy that the cycloisomerization of terminal alkyne **1p** succeeded via abnormal anti-Markovnikov addition pathway, because of the aromatic stability of product **2p**. The substituent on N-aryl moiety was also applicable to this transformation (**2q**). We then examined the substituent effect on the migration via the variation of different groups at the 2-positon of pyrrole. To our delight, both alkyl and aryl groups were suitable for this transformation, furnishing the desired cyclization/migration products **2r**−**2w** in excellent yields. Unsymmetric 2-methyl-5-phenyl-pyrrole derived **1x** was amenable to the cyclization smoothly, giving the phenyl migration product **2x** and methyl migration product **2x′** in good yield with 2.4:1 regioselectivity. Furthermore, N-(*ortho*-alkynyl)aryl-indoles **3a**−**3c** were subjected to this catalytic condition, giving the similar cyclization/migration products **4a**−**4c** in good to excellent yields. The exact structure of product **2e** was proved by single-crystal X-ray analysis.

Table 1. Optimization of Reaction Conditions[a]



1a 2a

entry	catalyst	solvent	temperature, T (°C)	yield[b] (%)
1	$Sc(OTf)_3$	DCE	90	16
2	$Bi(OTf)_3$	DCE	90	37
3	$In(OTf)_3$	DCE	90	26
4	$Cu(OAc)_2$	DCE	90	NR[c]
5	AgOTf	DCE	90	29
6	$Cu(OTf)_2$	DCE	90	99 (95)
7	$InCl_3$	DCE	90	48
8	$CuCl_2$	DCE	90	27
9	CuCl	DCE	90	NR[c]
10	CuBr	DCE	90	NR[c]
11	CuI	DCE	90	NR[c]
12	$Cu(OTf)_2$	toluene	110	90
13	$Cu(OTf)_2$	THF	reflux	82
14	$Cu(OTf)_2$	DCM	reflux	6
15	$Cu(OTf)_2$	Et_2O	reflux	4
16	$Cu(OTf)_2$	CH_3CN	reflux	12

[a]Reaction conditions: **1a** (0.1 mmol), cat. (5 mol %), solvent (1 mL), T °C. [b]NMR yield; the number shown in parentheses is the isolated yield. [c]NR = no reaction.

A tetrasubstituted pyrrole derivative N-(*ortho*-alkynyl)aryl-*H*-isoindole then attracted our attention. 3-Methyl-2-(2-(phenylethynyl)phenyl)-2*H*-isoindole-1-carboxylate **5**, which could be easily synthesized from the cascade N−H insertion/5-*exo*-dig cyclization of 2-(phenylethynyl)aniline with methyl 2-diazo-2-(2-ethynylphenyl)acetate,[13] was selected to test the intramolecular cycloisomerization. Isoindole **5a** underwent the 6-*endo*-dig cyclization/dearomatization cascade reaction catalyzed by $Cu(OTf)_2$, delivering the N-fused tetracyclic product **6a** in 84% yield. As shown in Scheme 3, various substituents and the end of alkynyl, aryl of aniline, and isoindole moiety had no effect on this transformation, and the corresponding cyclization/dearomatization products **6b**−**6n** were obtained in good to excellent efficiency. The bulky ester groups would decrease the yield slightly, because of the steric hindrance (**6o** and **6p**).

The polycyclic dihydroisoindolo[2,1-*a*]quinolone scaffold could be also obtained directly from the starting 2-(phenylethynyl)aniline with methyl 2-diazo-2-(2-ethynylphenyl)acetate via double copper-catalyzed cycloisomerization (Scheme 4), which provided a highly efficient tool for polyheterocycle synthesis.

This copper-catalyzed tandem cyclization reaction is easy to scale up. The reaction of 4.4 mmol of **1a** was performed, yielding the cyclization product **2a** in 1.08 g and 90% yield (Scheme 5). In order to examine the synthetic value of this protocol, some transformations of **2a** and **6a** were also performed (Scheme 5). Regioselective bromination of **2a** with Br_2 led to dibromosubstituted product **7** with substitutions on the 4-position of pyrrole ring and *para*-position of aniline, which could occur via the following addition reaction with benzaldehyde to give the monoalcohol **8** (Scheme 5b). Meanwhile, the N-fused tetracyclic lactam **9** was obtained in good yield via cleavage oxidation reaction of the C═C double

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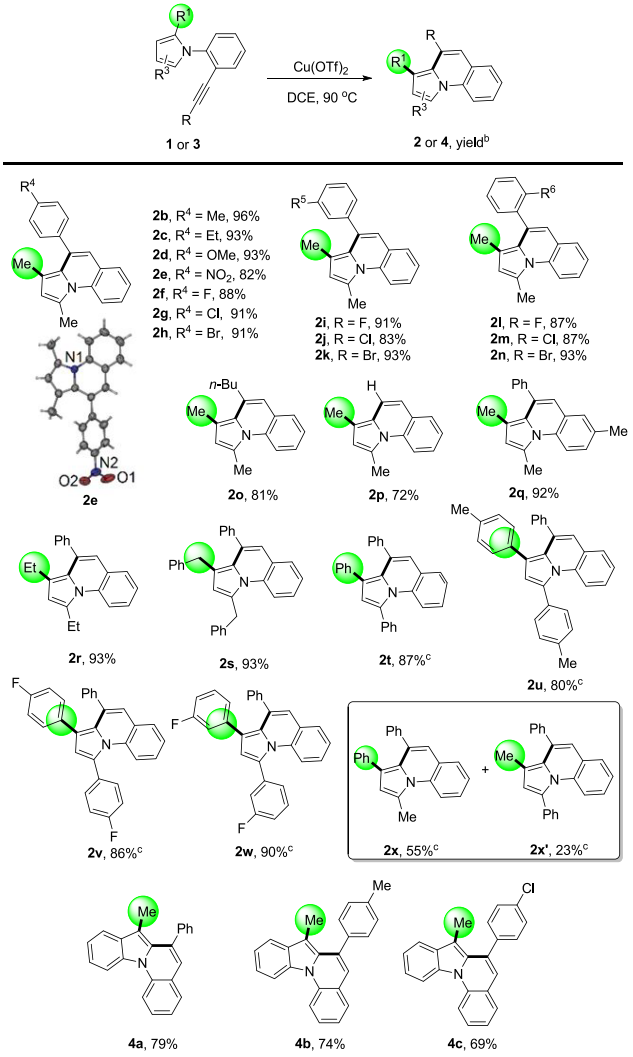
Scheme 2. Intramolecular Cyclization/Migration of Pyrroles and Indoles[a]



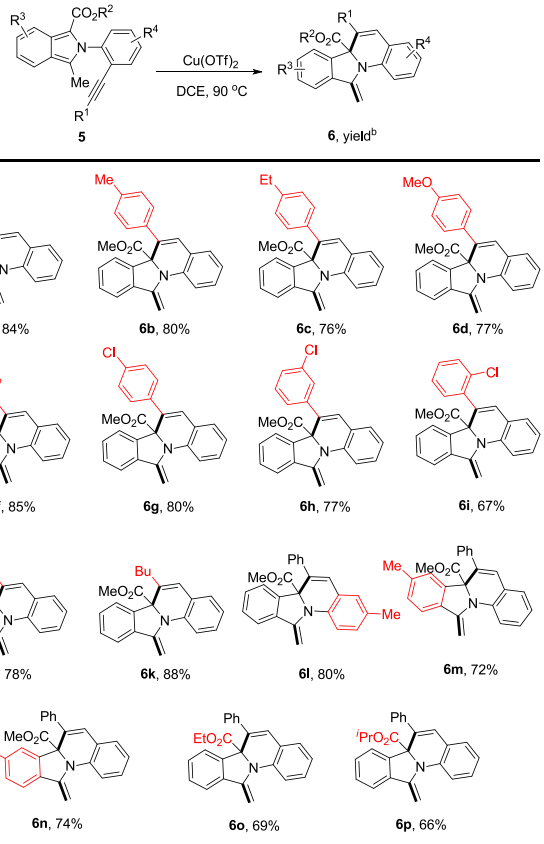
[a]Unless otherwise noted, all reactions were performed with **1** or **3** (0.4 mmol), and $Cu(OTf)_2$ (5 mol %) in DCE (2 mL) at 90 °C for 12 h. [b]Isolated yields. [c]Toluene instead of DCE at 110 °C.

bond when the **6a** was treated with *m*-CPBA. Note that the formal [4 + 2] cycloaddition of **6a** with *o*-QM proceeded smoothly, giving the aza-spiroacetal **10** in 89% yield as a single diastereoisomer. The structures of **9** and **10** were also proved by the single-crystal X-ray analysis.

Finally, to further investigate the promising application of the products, preliminary studies of the photophysical characteristics of selected pyrrole products **2** were performed. The results are summarized in Scheme 6 and Table S3 in the Supporting Information. The fluorescence wavelengths of these compounds ranged from 460 nm to 485 nm, and the quantum efficiencies (Φ) ranged from 0.198 to 0.271. Then, the absorption spectra of **2g** in different solvents were also recorded, which was observed to vary between 370 nm and 372 nm (see the Supporting Information for details). Therefore, the absorption maxima of **2g** in different solvents did not change much.

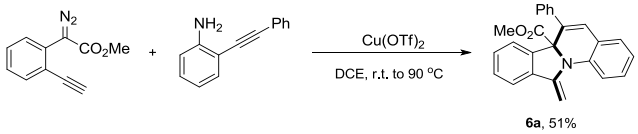
In summary, a chemodivergent intramolecular cascade cyclization/1,2-migration or dearomatization of pyrrole derivatives with alkynes has been realized, which offers a

Scheme 3. Intramolecular Cyclization/Dearomatization of Isoindoles[a]

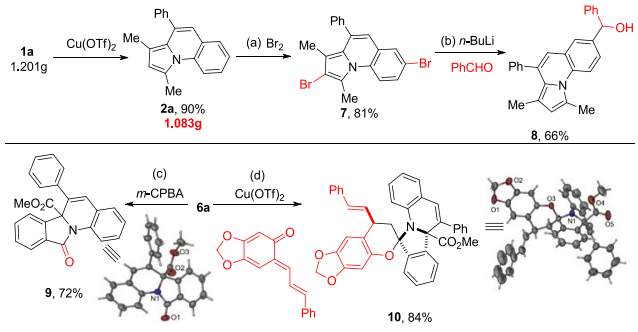


[a]Unless otherwise noted, all reactions were carried out with **5** (0.4 mmol), $Cu(OTf)_2$ (5 mol %) in DCE (2 mL) at 90 °C for 12 h. [b]Isolated yields.

Scheme 4. One-Pot Reaction



Scheme 5. Gram-Scale Reaction and the Transformations of Products



byproduct-free access to various N-containing [5,6,6] tricycle benzopyrrole cores. This transformation posed a broad scope of substrates, mild conditions, atom and step economy, easy operation, inexpensive catalysts, and facile transformations of the products. While the efficiency and scope of the divergent reaction remains to be further improved, the reaction mode

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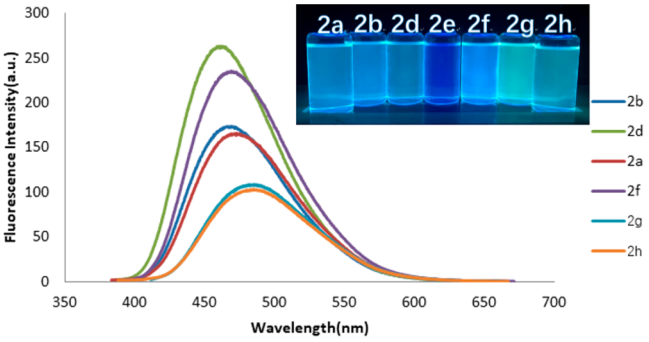
Scheme 6. Fluorescence Spectra of Pyrrolo[1,2-*a*]quinoline 2 in CH_3CN



demonstrated here and the mechanism obtained here should have applications beyond this transformation.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.orglett.0c01519.

Experimental procedures and characterization data (PDF)

Accession Codes

CCDC 1936280−1936282 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

■ AUTHOR INFORMATION

Corresponding Authors

Junliang Zhang − *Department of Chemistry, Fudan University, Shanghai 200438, People's Republic of China;* orcid.org/0000-0002-4636-2846; Email: junliangzhang@fudan.edu.cn

Lu Liu − *School of Chemistry and Molecular Engineering and Shanghai Engineering Research Center of Molecular Therapeutics and New Drug Development, East China Normal University, Shanghai 200241, People's Republic of China;* orcid.org/0000-0003-2151-891X; Email: lliu@chem.ecnu.edu.cn

Authors

Tengfei Yao − *School of Chemistry and Molecular Engineering, East China Normal University, Shanghai 200241, People's Republic of China*

Tong Xia − *School of Chemistry and Molecular Engineering, East China Normal University, Shanghai 200241, People's Republic of China*

Wei Yan − *School of Chemistry and Molecular Engineering, East China Normal University, Shanghai 200241, People's Republic of China*

Haofeng Xu − *School of Chemistry and Molecular Engineering, East China Normal University, Shanghai 200241, People's Republic of China*

Fang Zhang − *School of Chemistry and Molecular Engineering, East China Normal University, Shanghai 200241, People's Republic of China*

Yuanjing Xiao − *School of Chemistry and Molecular Engineering, East China Normal University, Shanghai 200241, People's Republic of China;* orcid.org/0000-0002-0185-1961

Complete contact information is available at: https://pubs.acs.org/10.1021/acs.orglett.0c01519

Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) For selected books and reviews, see: (a) *Heterocyclic Chemistry*, Gilchrist, T. L., Ed.; Longman: London, 1998. (b) *The Chemistry of Heterocycles*, Eicher, T.; Hauptmann, S., Ed.; Wiley−VCH: Weinheim, Germany, 2003.

(2) (a) Boulahjar, R.; Ouach, A.; Matteo, C.; Bourg, S.; Ravache, M.; le Guevel, R.; Marionneau, S.; Oullier, T.; Lozach, O.; Meijer, L.; Guguen-Guillouzo, C.; Lazar, S.; Akssira, M.; Troin, Y.; Guillaumet, G.; Routier, S. Novel Tetrahydropyrido[1,2-*a*]isoindolone Derivatives (Valmerins): Potent Cyclin-Dependent Kinase/Glycogen Synthase Kinase 3 Inhibitors with Antiproliferative Activities and Antitumor Effects in Human Tumor Xenografts. *J. Med. Chem.* **2012**, *55*, 9589−9606. (b) Suyavaran, A.; Ramamurthy, C.; Mareeswaran, R.; Shanthi, Y. V.; Selvakumar, J.; Mangalaraj, S.; Kumar, M. S.; Ramanathan, C. R.; Thirunavukkarasu, C. Synthesis and biological evaluation of isoindoloisoquinolinone, pyroloisoquinolinone and benzoquinazolinone derivatives as poly(ADP-ribose) polymerase-1 inhibitors. *Bioorg. Med. Chem.* **2015**, *23*, 488−498. (c) Cho, N.; Du, Y.; Valenciano, A. L.; Fernández-Murga, M. L.; Goetz, M.; Clement, J.; Cassera, M. B.; Kingston, D. G. I. Antiplasmodial alkaloids from bulbs of Amaryllis belladonna Steud. *Bioorg. Med. Chem. Lett.* **2018**, *28*, 40−42. (d) Chen, Y.; Yang, J.; Yang, X.; Khan, A.; Liu, L.; Wang, B.; Zhao, Y.; Liu, Y.; Ding, Z.; Luo, X. A Alstorisine, a nor-monoterpenoid indole alkaloid from cecidogenous leaves of Alstonia scholaris. *Tetrahedron Lett.* **2016**, *57*, 1754−1757. (e) Almerico, A. M.; Mingoia, F.; Diana, P.; Barraja, P.; Montalbano, A.; Lauria, A.; Loddo, R.; Sanna, L.; Delpiano, D.; Setzu, M. G.; Musiu, C. Pyrrolo[1,2-*f*]phenanthridines and related non-rigid analogues as antiviral agents. *Eur. J. Med. Chem.* **2002**, *37*, 3−10. (f) Kariba, R. M.; Houghton, P. J.; Yenesew, A. Antimicrobial Activities of a New Schizozygane Indoline Alkaloid from Schizozygia coffaeoides and the Revised Structure of Isoschizogaline. *J. Nat. Prod.* **2002**, *65*, 566−569.

(3) (a) Ito, S.; Tokimaru, Y.; Nozaki, K. Benzene-Fused Azacorannulene Bearing an Internal Nitrogen Atom. *Angew. Chem., Int. Ed.* **2015**, *54*, 7256−7260. (b) Yokoi, H.; Hiraoka, Y.; Hiroto, S.; Sakamaki, D.; Seki, S.; Shinokubo, H. Nitrogen-embedded buckybowl and its assembly with C_{60}. *Nat. Commun.* **2015**, *6*, 8215. (c) Gao, X.; Zhang, S. B.; Zhao, Y.; Nagase, S. A Nanoscale Jigsaw-Puzzle Approach to Large π-Conjugated Systems. *Angew. Chem., Int. Ed.* **2010**, *49*, 6764. (d) Cheng, Y. J.; Yang, S. H.; Hsu, C. S. Synthesis of Conjugated Polymers for Organic Solar Cell Applications. *Chem. Rev.* **2009**, *109*, 5868. (e) Hains, A. W.; Liang, Z.; Woodhouse, M. A.; Gregg, B. A. Molecular Semiconductors in Organic Photovoltaic Cells. *Chem. Rev.* **2010**, *110*, 6689. (f) Dou, L.; Liu, Y.; Hong, Z.; Li, G.; Yang, Y. Low-Bandgap Near-IR Conjugated Polymers/Molecules for Organic Electronics. *Chem. Rev.* **2015**, *115*, 12633. (g) Zhu, M.; Yang, C. Blue fluorescent emitters: design tactics and applications in organic light-emitting diodes. *Chem. Soc. Rev.* **2013**, *42*, 4963. (h) Dong, H.; Fu, X.; Liu, J.; Wang, Z.; Hu, W. 25th Anniversary Article: Key Points for High-Mobility Organic Field-Effect Transistors. *Adv. Mater.* **2013**, *25*, 6158.

https://dx.doi.org/10.1021/acs.orglett.0c01519
Org. Lett. XXXX, XXX, XXX−XXX

(4) For selected recent reviews, see: (a) Chung, L. H.; Wong, C. Y. Ruthenium-Induced Alkyne Cycloisomerization: Construction of Metalated Heterocycles, Revelation of Unconventional Reaction Pathways, and Exploration of Functional Applications. *Chem. - Eur. J.* **2019**, *25*, 2889−2897. (b) Sadowski, B.; Klajn, J.; Gryko, D. T. Recent advances in the synthesis of indolizines and their π-expanded analogues. *Org. Biomol. Chem.* **2016**, *14*, 7804−7828. (c) Kim, E.; Lee, Y.; Lee, S.; Park, S. B. Discovery, Understanding, and Bioapplication of Organic Fluorophore: A Case Study with an Indolizine-Based Novel Fluorophore, Seoul-Fluor. *Acc. Chem. Res.* **2015**, *48*, 538−547. (d) Zhang, Y.; Nie, B.; Zhang, J. Progress in the Research of Copper Promoted C—H Functionalizations for the Synthesis of Fused Heterocycles Bearing Bridgehead Nitrogen. *Youji Huaxue* **2015**, *35*, 2067−2085.

(5) For selected books and reviews, see: (a) Larock, R. C. In *Acetylene Chemistry. Chemistry, Biology and Material Science*; Diederich, F.; Stang, P. J.; Tykwinski, R. R., Eds.; Wiley−VCH: New York, 2005; pp 51−99. (b) Trost, B. M.; Krische, M. J. Transition Metal Catalyzed Cycloisomerizations. *Synlett* **1998**, *1998*, 1−16. (c) Zeni, G.; Larock, R. C. Synthesis of Heterocycles via Palladium π-Olefin and π-Alkyne Chemistry. *Chem. Rev.* **2004**, *104*, 2285−2310. (d) Dénès, F.; Pérez-Luna, A.; Chemla, F. Addition of Metal Enolate Derivatives to Unactivated Carbon−Carbon Multiple Bonds. *Chem. Rev.* **2010**, *110*, 2366. (e) Gulevich, A. V.; Dudnik, A. S.; Chernyak, N.; Gevorgyan, V. Transition Metal-Mediated Synthesis of Monocyclic Aromatic Heterocycles. *Chem. Rev.* **2013**, *113*, 3084−3213. (f) Chinchilla, R.; Nájera, C. Chemicals from Alkynes with Palladium Catalysts. *Chem. Rev.* **2014**, *114*, 1783−1826. (g) Yamamoto, Y. Synthesis of heterocycles via transition-metal-catalyzed hydroarylation of alkynes. *Chem. Soc. Rev.* **2014**, *43*, 1575−1600. (h) Boyarskiy, V. P.; Ryabukhin, D. S.; Bokach, N. A.; Vasilyev, A. V. Alkenylation of Arenes and Heteroarenes with Alkynes. *Chem. Rev.* **2016**, *116*, 5894−5986.

(6) (a) *Friedel-Crafts and Related Reactions*; Olah, G. A., Ed.; Wiley, 1964. (b) *Electrophilic Aromatic Substitution*, Taylor, R., Ed.; John Wiley & Sons, 1990. (c) Gore, P. H. The Friedel-Crafts Acylation Reaction and its Application to Polycyclic Aromatic Hydrocarbons. *Chem. Rev.* **1955**, *55*, 229−281. (d) You, S.-L.; Cai, Q.; Zeng, M. Chiral Brønsted acid catalyzed Friedel−Crafts alkylation reactions. *Chem. Soc. Rev.* **2009**, *38*, 2190−2201. (e) Evano, G.; Theunissen, C. Beyond Friedel and Crafts: Innate Alkylation of C−H Bonds in Arenes. *Angew. Chem., Int. Ed.* **2019**, *58*, 7558−7598.

(7) (a) Fürstner, A.; Mamane, V. Flexible Synthesis of Phenanthrenes by a $PtCl_2$-Catalyzed Cycloisomerization Reaction. *J. Org. Chem.* **2002**, *67*, 6264. (b) Mamane, V.; Hannen, P.; Fürstner, A. Synthesis of Phenanthrenes and Polycyclic Heteroarenes by Transition-Metal Catalyzed Cycloisomerization Reactions. *Chem. - Eur. J.* **2004**, *10*, 4556−4575.

(8) (a) Delcamp, J. H.; Yella, A.; Holcombe, T. W.; Nazeeruddin, M. K.; Grätzel, M. The Molecular Engineering of Organic Sensitizers for Solar-Cell Applications. *Angew. Chem., Int. Ed.* **2013**, *52*, 376. (b) Boldt, S.; Parpart, S.; Villinger, A.; Ehlers, P.; Langer, P. Synthesis and Properties of Aza-ullazines. *Angew. Chem., Int. Ed.* **2017**, *56*, 4575−4578. (c) Petuškova, J.; Bruns, H.; Alcarazo, M. Cyclopropenylylidene-Stabilized Diaryl and Dialkyl Phosphenium Cations: Applications in Homogeneous Gold Catalysis. *Angew. Chem., Int. Ed.* **2011**, *50*, 3799−3802. (d) Liu, R.; Wang, Q.; Wei, Y.; Shi, M. Synthesis of indolizine derivatives containing eight-membered rings via a gold-catalyzed two-fold hydroarylation of diynes. *Chem. Commun.* **2018**, *54*, 1225−1228. (e) Kiruthika, S. E.; Nandakumar, A.; Perumal, P. T. Synthesis of Pyrrolo-/Indolo[1,2-*a*]quinolines and Naphtho[2,1-*b*]thiophenes from gem-Dibromovinyls and Sulphonamides. *Org. Lett.* **2014**, *16*, 4424−4427. (f) Sarkar, S.; Bera, K.; Jalal, S.; Jana, U. Synthesis of Structurally Diverse Polyfunctional Pyrrolo[1,2-a]quinolines by Sequential Iron-Catalyzed Three-Component Coupling and Gold-Catalyzed Hydroarylation Reactions. *Eur. J. Org. Chem.* **2013**, *2013*, 6055−6061. (g) Li, X.; Zhao, J.; Xie, X.; Liu, Y. Synthesis of functionalized indolizines via gold(i)-catalyzed intramolecular hydroarylation/aromatization of pyrrole-ynes. *Org. Biomol. Chem.* **2017**, *15*, 8119−8133. (h) Pirwerdjan, R.; Becker, P.; Bolm, C. Exploring the Reactivity of N-Alkynylated Sulfoximines: Acid-Catalyzed Cyclizations. *Org. Lett.* **2016**, *18*, 3307−3309.

(9) For selected examples from our group, see: (a) Liu, L.; Zhang, J. Selectivity Control in Lewis Acid Catalyzed Regiodivergent Tandem Cationic Cyclization/Ring Expansion Terminated by Pinacol Rearrangement. *Angew. Chem., Int. Ed.* **2009**, *48*, 6093−6096. (b) Liu, L.; Wei, L.; Lu, Y.; Zhang, J. One-Pot Tandem Catalysis: A Concise Route to Fused Bicyclic Scaffolds from Acyclic β-Ketoesters and Alkynyl Aldehydes. *Chem. - Eur. J.* **2010**, *16*, 11813−11817. (c) Yu, Z.; Liu, L.; Zhang, J. Triflic Acid-Catalyzed Enynes Cyclization: A New Strategy beyond Electrophilic π-Activation. *Chem. - Eur. J.* **2016**, *22*, 8488−8492. (d) Zhou, L.; Zhang, M.; Li, W.; Zhang, J. Furan-Based *o*-Quinodimethanes by Gold-Catalyzed Dehydrogenative Heterocyclization of 2-(1-Alkynyl)-2-alken-1-ones: A Modular Entry to 2,3-Furan-Fused Carbocycles. *Angew. Chem., Int. Ed.* **2014**, *53*, 6542−6545. (e) Qian, D.; Hu, H.; Liu, F.; Tang, B.; Ye, W.; Wang, Y.; Zhang, J. Gold(I)-Catalyzed Highly Diastereo- and Enantioselective Alkyne Oxidation/Cyclopropanation of 1,6-Enynes. *Angew. Chem., Int. Ed.* **2014**, *53*, 13751−13755. (f) Feng, J.; Lin, T.; Wu, H.; Zhang, J. Transfer of Chirality in the Rhodium-Catalyzed Intramolecular Formal Hetero-[5 + 2] Cycloaddition of Vinyl Aziridines and Alkynes: Stereoselective Synthesis of Fused Azepine Derivatives. *J. Am. Chem. Soc.* **2015**, *137*, 3787−3790. (g) Wang, Y.; Zhang, P.; Qian, D.; Zhang, J. Highly Regio-, Diastereo-, and Enantioselective Gold(I)-Catalyzed Intermolecular Annulations with N-Allenamides at the Proximal C = C Bond. *Angew. Chem., Int. Ed.* **2015**, *54*, 14849−14852. (h) Feng, J.; Lin, T.; Zhu, C.; Wang, H.; Wu, H.; Zhang, J. The Divergent Synthesis of Nitrogen Heterocycles by Rhodium(I)-Catalyzed Intermolecular Cycloadditions of Vinyl Aziridines and Alkynes. *J. Am. Chem. Soc.* **2016**, *138*, 2178−2181. (i) Wang, Y.; Zhang, P.; Di, X.; Dai, Q.; Zhang, Z.; Zhang, J. Gold-Catalyzed Asymmetric Intramolecular Cyclization of N-Allenamides for the Synthesis of Chiral Tetrahydrocarbolines. *Angew. Chem., Int. Ed.* **2017**, *56*, 15905−15909. (j) Xu, S.; Zhang, Z.; Xu, B.; Liu, B.; Liu, Y.; Zhang, J. Enantioselective Regiodivergent Synthesis of Chiral Pyrrolidines with Two Quaternary Stereocenters via Ligand-Controlled Copper(I)-Catalyzed Asymmetric 1,3-Dipolar Cycloadditions. *J. Am. Chem. Soc.* **2018**, *140*, 2272−2283. (k) Zhang, Z.-M.; Xu, B.; Qian, Y.; Wu, L.; Wu, Y.; Zhou, L.; Liu, Y.; Zhang, J. Palladium-Catalyzed Enantioselective Reductive Heck Reactions: Convenient Access to 3,3-Disubstituted 2,3-Dihydrobenzofuran. *Angew. Chem., Int. Ed.* **2018**, *57*, 10373−10377. (l) Zhang, Z.-M.; Xu, B.; Wu, L.; Zhou, L.; Ji, D.; Liu, Y.; Li, Z.; Zhang, J. Palladium/XuPhos-Catalyzed Enantioselective Carboiodination of Olefin-Tethered Aryl Iodides. *J. Am. Chem. Soc.* **2019**, *141*, 8110−8115. (m) Zhang, P.-C.; Han, J.; Zhang, J. Pd/PC-Phos-Catalyzed Enantioselective Intermolecular Denitrogenative Cyclization of Benzotriazoles with Allenes and N-Allenamides. *Angew. Chem., Int. Ed.* **2019**, *58*, 11444−1144.

(10) For recent cyclization and migration reactions of pyrroles and indoles, see: (a) Zhuo, C.-X.; Wu, Q.-F.; Zhao, Q.; Xu, Q.-L.; You, S.-L. Enantioselective Functionalization of Indoles and Pyrroles via an in Situ-Formed Spiro Intermediate. *J. Am. Chem. Soc.* **2013**, *135*, 8169−8172. (b) Zhuo, C.-X.; Cheng, Q.; Liu, W.-B.; Zhao, Q.; You, S.-L. Enantioselective Synthesis of Pyrrole-Based Spiro- and Polycyclic Derivatives by Iridium-Catalyzed Asymmetric Allylic Dearomatization and Controllable Migration Reactions. *Angew. Chem., Int. Ed.* **2015**, *54*, 8475−8479. (c) Zhao, H.-P.; Liang, G.-C.; Nie, S.-M.; Lu, X.; Pan, C.-X.; Zhong, X.-X.; Su, G.-F.; Mo, D.-L. Metal-free graphene oxide-catalyzed azasemipinacol rearrangement to prepare 2-(indol2-yl)-phenols and benzofuro[3,2-b]indolines containing quaternary carbon centers. *Green Chem.* **2020**, *22*, 404−410. (d) Zhao, H.-P.; Ma, X.-P.; Nie, S.-M.; Xiao, Y.; Mo, D.-L. Synthesis of chromeno[4,3-b]quinolines and spirobenzofuran-3,3′-quinolines through silver-mediated Appel reaction/C−Br bond cleavage/double selective rearrangement sequence. *Org. Chem. Front.* **2019**, *6*, 2334−2338.

(11) For a recent intramolecular dearomative Heck reaction of pyrrole, see: Yang, P.; You, S.-L. Palladium-Catalyzed Asymmetric

https://dx.doi.org/10.1021/acs.orglett.0c01519
Org. Lett. XXXX, XXX, XXX−XXX

Intramolecular Dearomative Heck Reaction of Pyrrole Derivatives. *Org. Lett.* **2018**, *20*, 7684−7688.
(12) Trost, B. M. The atom economy-a search for synthetic efficiency. *Science* **1991**, *254*, 1471−1477.
(13) (a) Peng, C.; Cheng, J.; Wang, J. Sequential Copper(I)-Catalyzed Reaction of Amines with *o*-Acetylenyl-Substituted Phenyldiazoacetates. *Adv. Synth. Catal.* **2008**, *350*, 2359−2364. (b) Ma, B.; Wu, Z.; Huang, B.; Liu, L.; Zhang, J. Gold-catalysed facile access to indene scaffolds via sequential C−H functionalization and 5-endo-dig carbocyclization. *Chem. Commun.* **2016**, *52*, 9351−9354.

https://dx.doi.org/10.1021/acs.orglett.0c01519
Org. Lett. XXXX, XXX, XXX−XXX