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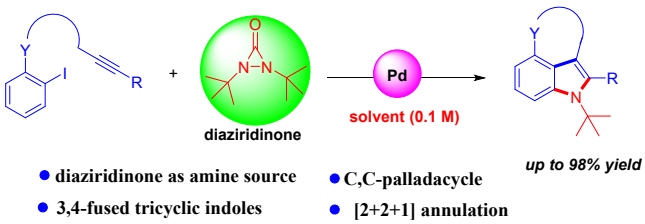
Palladium-Catalyzed [2+2+1] Annulation of Alkyne-tethered Aryl iodides with Diaziridinone：Synthesis of 3,4-Fused Tricyclic Indoles

Lei Zhang[a], Junyu Chen[a], Tianshuo Zhong[a], Xiangyun Zheng[a], Jian Zhou[a], Xinpeng Jiang*[a] and Chuanming Yu*[a]

[a] College of Pharmaceutical Sciences, Zhejiang University of Technology, Hangzhou 310014, PR China

E-mail: Xjiang@zjut.edu.cn; ycm@zjut.edu.cn



Abstract: A novel palladium-catalyzed [2+2+1] annulation of alkyne-tethered aryl iodides with diaziridinone was developed, leading to the formation of 3,4-fused tricyclic indoles. From a mechanistic standpoint, the formation of fused tricyclic indole scaffolds involved C,C-palladacycles, which were synthesized through intramolecular reaction of aryl halides and alkynes. The cascade reaction described herein could be carried out with a broad range of substrate and provided various 3,4-fused tricyclic indoles with yields up to 98%.

Introduction

Indole derivatives represent one of the most widely distributed class of compounds that may be found in various natural products and pharmaceuticals.[1] In particular, 3,4-fused tricyclic indoles have attracted significant interest in the scientific community with wide ranging applications.[2] As shown in **Figure 1**, lysergic acid,[3] produced in the fungus species Claviceps purpurea, features broad biological and pharmacological activities. (-)-Indolactam V[4] and dragmacidin E,[5] isolated from *Streptoverticillium blastmyceticum* NA39-17 and *Spongosortes*, possessing tumor promoting and serine-threonine protein phosphatase inhibitory activities. Rucaparib,[6] a novel PARP inhibitor, may be used to treat breast and ovarian cancers. Therefore, the development of both practical and efficient synthetic methods to produce 3,4-fused tricyclic indoles remains a critical goal in organic synthetic chemistry.

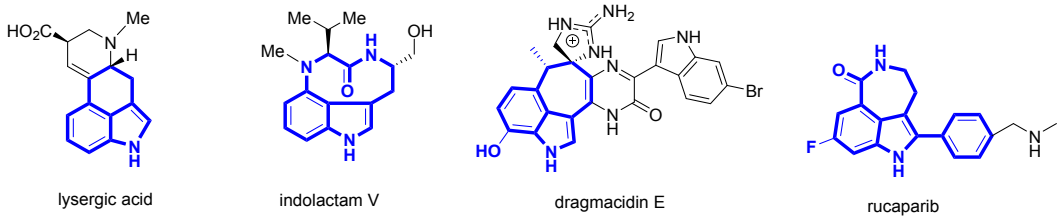
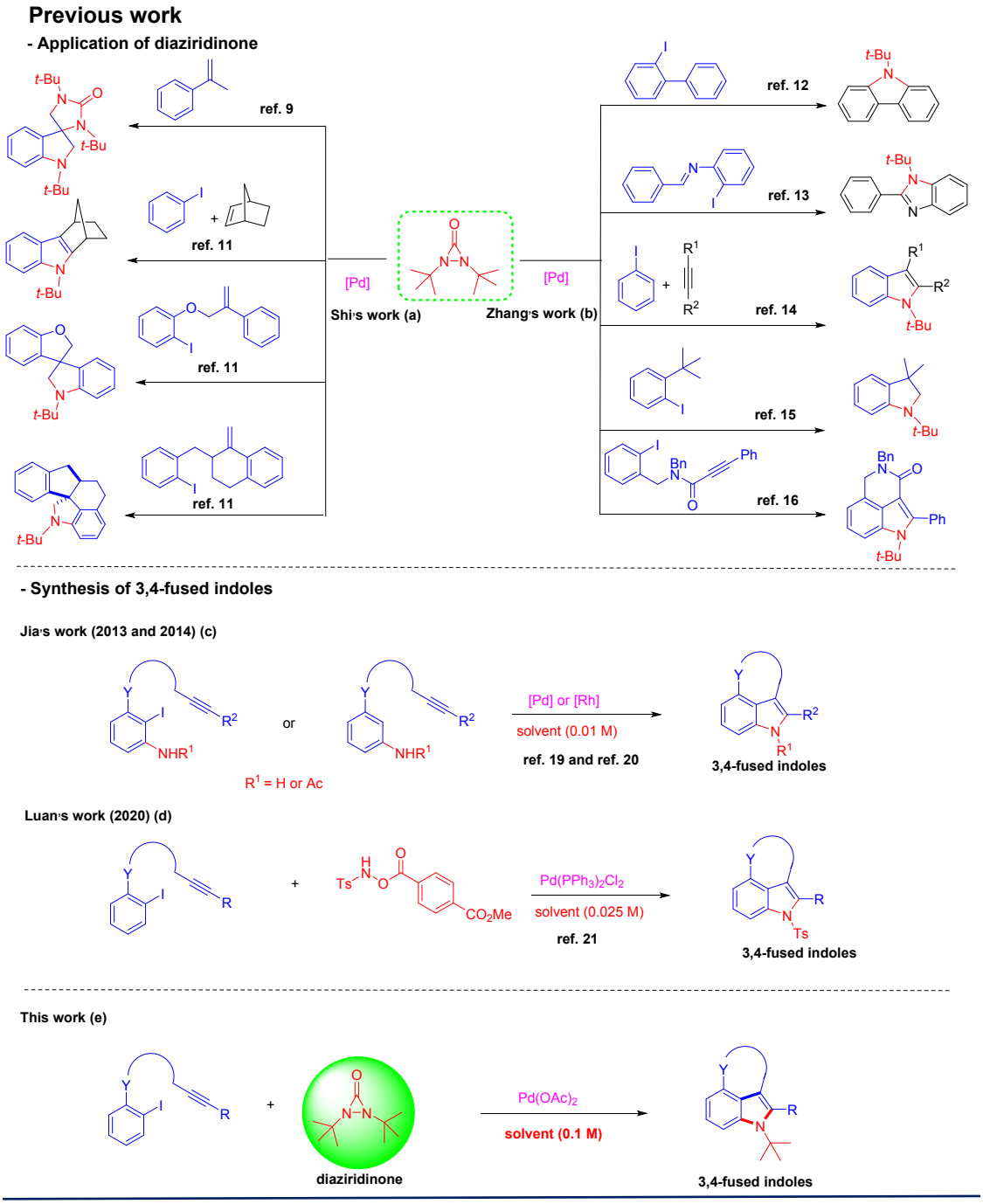


Figure 1. Selected natural products and drug compounds containing 3,4-fused tricyclic indoles.

Scheme 1. Application of diaziridinone and synthesis of 3,4-fused indoles.



Over the past few decades, transition-metal-catalyzed C−H bond activation and functionalization have been utilized for the efficient synthesis of diverse complex compounds through synchronous C−C, C−N, or C−O bond formation.[7] Specifically, C,C-palladacycles, an important class of metallacycles, may be prepared from aryl halides *via* Pd-enabled C(sp^2)−H activation exhibiting unique characteristics resulting in the discovery of novel reactions.[8] In 2013, Shi *et al.* first reported diaziridinones could be used as a new amine source to react with C,C-palladacycles to form indolines[9] via various amination reactions.[10] Moreover, Shi *et al.* also demonstrated the preparation of various indoline and indole derivatives by using important intramolecular design motifs (**Scheme 1a**).[11] Subsequently, the synthetic use of diaziridinone was

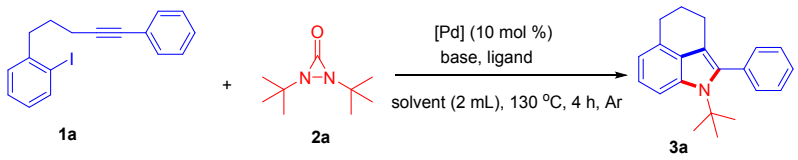
further expanded by Zhang and co-workers using C−H amination reactions to synthesize heterocycles, such as carbazoles,[12] benzimidazoles,[13] and indole derivatives, including substituted indoles,[14] indolines,[15] and 3,4-fused tricyclic indoles[16] (**Scheme 1b**).

Various synthetic methods have been developed thereafter for the construction of indoles through transition-metal-catalysis.[17] However, efficient synthetic methods for the production of the 3,4-fused indole scaffold are still limited.[18] In 2013, Jia and co-workers reported a palladium-catalyzed protocol for the construction of 3,4-fused tricyclic indoles via intramolecular Larock indolization.[19] Subsequently, in 2014 Jia *et al.* reported the rhodium-catalyzed intramolecular annulation of alkyne-tethered acetanilides for the construction of such scaffolds (**Scheme 1c**).[20] In 2020, Luan *et al.* developed a palladium-catalyzed synthesis of 3,4-fused tricyclic indoles with alkyne-tethered aryl iodides and a secondary hydroxylamine (**Scheme 1d**).[21] Based on Luan's work[22] and our preliminary research on metal catalyzed functionalization[23] and indole chemistry,[24] in this paper we report a highly efficient palladium-catalyzed one-pot [2+2+1] annulation reaction of alkyne-tethered aryl iodides with diaziridinone to generate 3,4-fused tricyclic indoles (**Scheme 1e**).

Results and Discussion

Initially, we commenced our study with 1-iodo-2-(5-phenylpent-4-yn-1-yl)benzene **1a** and 1,2-*di-tert*-butyldiaziridin-3-one **2a** in an effort to achieve optimized reaction conditions (**Table 1)**. The substrates were treated with $Pd(OAc)_2$ (10 mol %), Cs_2CO_3 (1 equiv.), and KOAc (1 equiv.) in DMF (2 mL) at 130 °C under Ar for 4 h. The desired product **3a** was obtained in 61% yield (entry 1). Among the various screened catalysts (entries 1-3), $Pd(OAc)_2$ proved to be the most suitable. Different bases such as CsOAc and KOPiv were then investigated, however, no outcome benefits could be observed (entries 4-5). The reaction proceeded with reasonable efficiency when Cs_2CO_3 was used as a base (entry 6). The total yield of **3a** could be improved to 83% when a series of phosphine ligands were added, with PPh_3 demonstrating to be the most effective ligand (entries 7-13). After screening the different solvents such as toluene, *N,N*-dimethylacetamide (DMA), dimethyl sulfoxide (DMSO), tetrahydrofuran (THF), and MeCN, DMF was found to be still the most efficient solvent, providing compound **3a** in 83% yield (entries 14−18). When the amount of Cs_2CO_3 was increased to 2 equiv., the yield of **3a** did not change (entry 19). Control experiments confirmed that the yield of **3a** could be decreased upon lowering the reaction temperature (entry 20) and reducing amount of PPh_3 (entries 21 and 22). Finally, the optimized reaction conditions were determined as follows: **1a** (0.2 mmol), **2a** (2 equiv.), $Pd(OAc)_2$ (10 mol %), Cs_2CO_3 (1 equiv.), and PPh_3 (1 equiv.) in DMF (2.0 mL) at 130 °C for 4 h under Ar atmosphere.

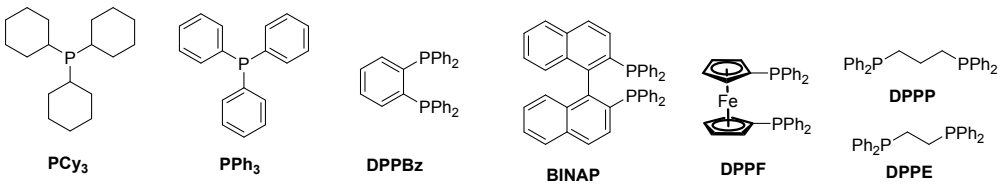
Table 1. Optimization of reaction conditions[a].



1a + 2a → 3a

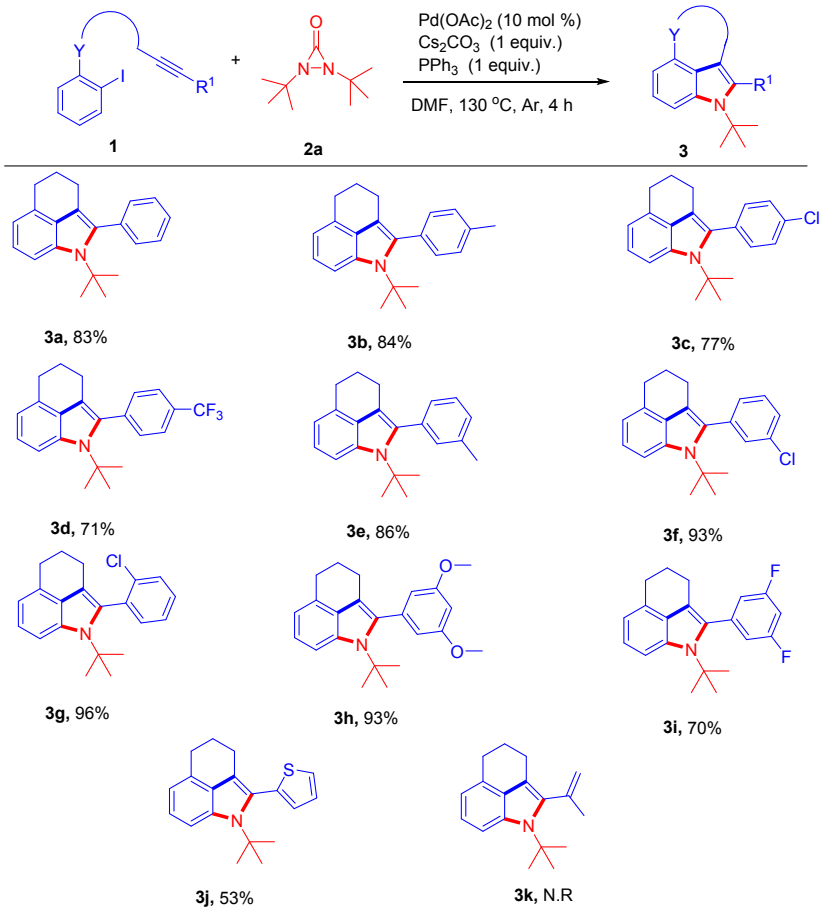
Entry	Catalyst	Base (equiv.)	Ligand	Solvent	Yield[b] (%)
1	$Pd(OAc)_2$	KOAc (1)/Cs_2CO_3 (1)	-	DMF	61
2	$Pd(PPh_3)_4$	KOAc (1)/Cs_2CO_3 (1)	-	DMF	53
3	$Pd(dba)_3$	KOAc (1)/Cs_2CO_3 (1)	-	DMF	46
4	$Pd(OAc)_2$	CsOAc (1)/Cs_2CO_3 (1)	-	DMF	55
5	$Pd(OAc)_2$	KOPiv (1)/Cs_2CO_3 (1)	-	DMF	60
6	$Pd(OAc)_2$	Cs_2CO_3 (1)	-	DMF	63
7	$Pd(OAc)_2$	Cs_2CO_3 (1)	PCy_3	DMF	69
8	***$Pd(OAc)_2$***	***Cs_2CO_3 (1)***	***PPh_3***	***DMF***	***83***
9	$Pd(OAc)_2$	Cs_2CO_3 (1)	DPPBz	DMF	0
10	$Pd(OAc)_2$	Cs_2CO_3 (1)	BINAP	DMF	20
11	$Pd(OAc)_2$	Cs_2CO_3 (1)	DPPF	DMF	15
12	$Pd(OAc)_2$	Cs_2CO_3 (1)	DPPP	DMF	0
13	$Pd(OAc)_2$	Cs_2CO_3 (1)	DPPE	DMF	0
14	$Pd(OAc)_2$	Cs_2CO_3 (1)	PPh_3	toluene	trace
15	$Pd(OAc)_2$	Cs_2CO_3 (1)	PPh_3	DMA	43
16	$Pd(OAc)_2$	Cs_2CO_3 (1)	PPh_3	DMSO	45
17	$Pd(OAc)_2$	Cs_2CO_3 (1)	PPh_3	THF	trace
18	$Pd(OAc)_2$	Cs_2CO_3 (1)	PPh_3	MeCN	trace
19[c]	$Pd(OAc)_2$	Cs_2CO_3 (2)	PPh_3	DMF	83%
20[d]	$Pd(OAc)_2$	Cs_2CO_3 (1)	PPh_3	DMF	80%
21[e]	$Pd(OAc)_2$	Cs_2CO_3 (1)	PPh_3	DMF	53%
22[f]	$Pd(OAc)_2$	Cs_2CO_3 (1)	PPh_3	DMF	70%

[a]Reaction conditions: **1a** (0.2 mmol), **2a** (0.4 mmol), catalyst (10 mol %), base, ligand (1 equiv.), DMF (2 mL), 130 °C, for 4 h, under Ar. [b]Isolated yield. [c]Cs_2CO_3 (2 equiv.). [d]The reaction temperature was 100 °C. [e]PPh_3 (20 mol %). [f]PPh_3 (50 mol %). DMF = *N*,*N*-dimethylformamide, DMA = *N*,*N*-dimethylacetamide, DMSO = dimethyl sulfoxide, THF = tetrahydrofuran.



With these optimized reaction conditions in hand, the scope and limitations of alkyne-tethered aryl iodides **1** were examined as shown in **Scheme 2**. First, the electronic effects of phenyl substituents on the alkynes were examined, including Me-, Cl-, and CF_3-functional groups (**3a**–**3g**). Substrates containing both electron-donating and electron-withdrawing groups in *para* (**3b**–**3d**), *meta* (**3e**–**3f**) and *ortho* (**3g**) positions of the aryl groups on the internal alkyne all displayed high reactivity, providing the desired products in

71-96% yields. Moreover, disubstituted alkynes were found to be well tolerated in this transformation, providing the corresponding products **3h** and **3i** in 93% and 70% yields, respectively. Furthermore, this reaction was not limited to phenyl substrates, giving athiophene ring containing product **3j** in 53% yield. Alkenyl substituents, however, did not provide the desired product **3k** under optimized conditions.

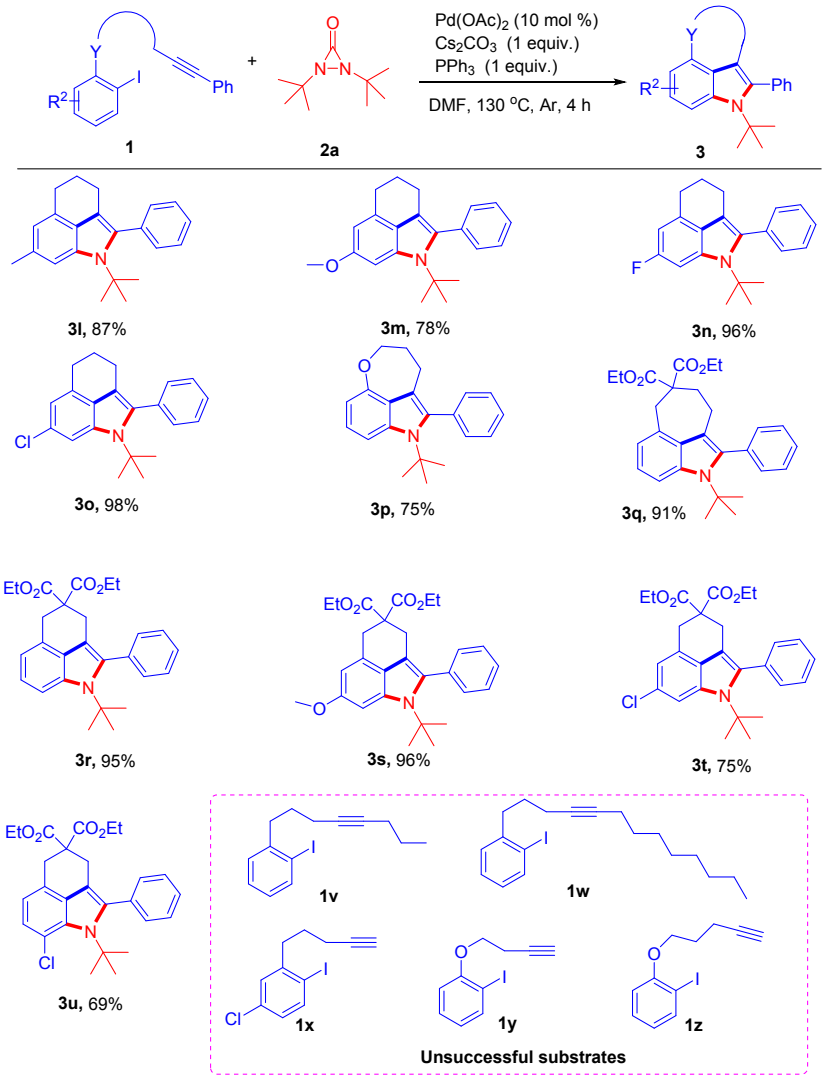


Scheme 2. Substrate scope of phenyl substituents on the alkyne species [a,b]. [a] Reaction conditions: **1** (0.2 mmol), **2a** (0.4 mmol), $Pd(OAc)_2$ (10 mol %), Cs_2CO_3 (1 equiv.) and PPh_3 (1 equiv.) in DMF (2.0 mL) at 130 °C for 4 h under Ar atmosphere. [b] Isolated yield.

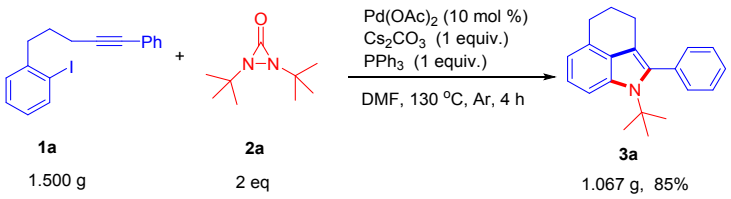
Next, the electronic effects of the aryl iodide moiety were examined (**Scheme 3**, **3l–3o**). Surprisingly, substrates bearing electron-rich (Me and OMe) and electron-deficient (F and Cl) functional groups provided the desired products in good to excellent yields (78-98%). Subsequently, substrates containing a carbon- and oxygen-tether were studied, and the desired 3,4-fused indoles **3p-3u** could be obtained in 69-96% yields. However, alkyl-substituted and unsubstituted alkyne **1v-1z** failed to form the desired product. To demonstrate the synthetic utility of this protocol, a scaled-up reaction of 1-iodo-2-(5-phenylpent-4-yn-1-yl)benzene **1a** and diaziridinone ylide **2a** was carried out under optimized reaction conditions, providing the corresponding product **3a** in 85% yield (**Scheme 4**).

Furthermore, the *tert*-butyl group could be easily removed to form the unprotected 3,4- fused tricyclic indole product **3a'** in 75% yield under acidic conditions (**Scheme 5**).[25] Various indole derivatives could then be formed thereafter. Moreover, a competitive experiment was carried out between two alkyne-tethered aryl iodides with differing electronic effects. The ratio of two

corresponding products (**3c**/**3b** = 1.3 and **3o**/**3l** = 1.3) suggested that the electron-withdrawing alkyne-tethered aryl iodides exhibited a slightly higher reactivity (**Scheme 6**).

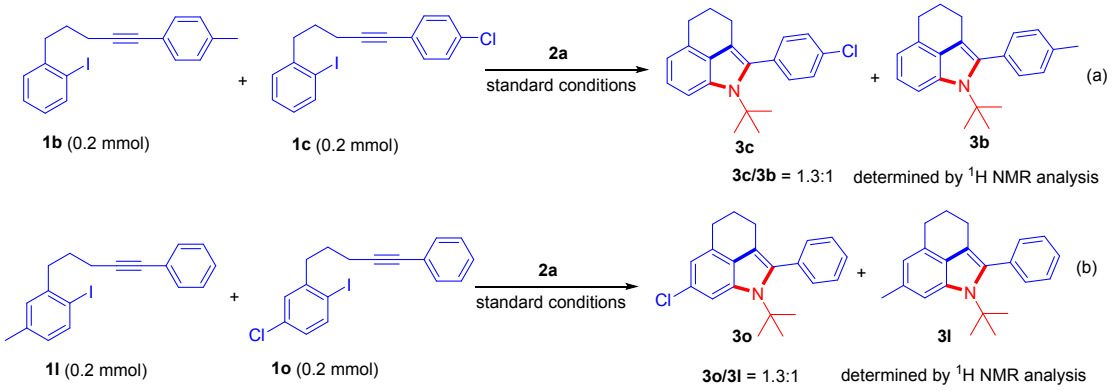


Scheme 3. Substrate scope of alkyne-tethered aryl iodides[a,b]. [a] Reaction conditions: **1** (0.2 mmol), **2a** (0.4 mmol), $Pd(OAc)_2$ (10 mol %), Cs_2CO_3 (1 equiv.) and PPh_3 (1 equiv.) in DMF (2.0 mL) at 130 °C for 4 h under Ar atmosphere. [b] Isolated yield.



Scheme 4. Gram-scale reaction.

Scheme 5. Removal of the *tert*-butyl group from compound **3a**.

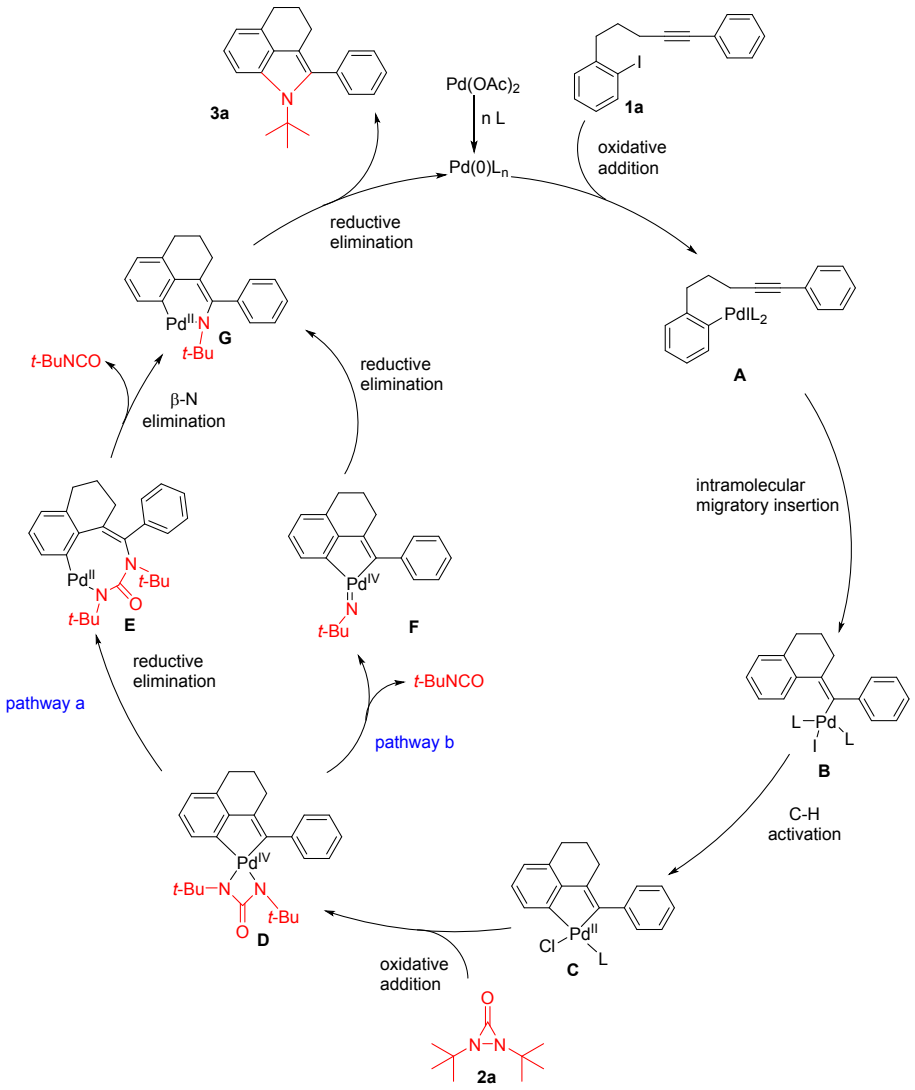


Scheme 6. Competition experiments.

On the basis of various reports found in the literature,[11, 21-22, 26] a plausible reaction mechanism could be proposed (**Scheme 7**). Initially, via oxidative addition of the carbon-halogen bond in 1-iodo-2-(5-phenylpent-4-yn-1-yl)benzene **1a** to Pd(0) forms intermediate **A**, which undergoes an intramolecular migratoy insertion, generating a primary vinylpalladium complex species **B**. Then, intermediate **B** undergoes intramolecular C−H activation to generate C,C-pallada-cycle **C**. Next, the pallada(IV)cycle **D** is obtained due to **B** insertion into the N-N bond of diaziridinone **2a** *via* oxidative addition. Subsequently, intermediate **D** to **G** may undergo two possible pathways, one is the reductive elimination of **D** to afford intermediate **E**. Species **G** may be formed by *β*-N elimination (pathway a) or via a Pd(IV)-nitrene pathway (pathway b). The final product **3a** is formed by reductive elimination and regeneration of the Pd(0)-catalytic species, completing this catalytic cycle.

Conclusions

In conclusion, we have developed a cascade reaction to generate various functionalized 3,4-fused tricyclic indoles *via* palladium-catalyzed [2+2+1] annulation between alkyne-tethered aryl iodides and diaziridinone, in which C,C-palladacycles may act as key intermediates. The protocol proved to be useful for the preparation of diverse 3,4-fused tricyclic indole species due to high atom economy, good to excellent yields, and suitable functional group tolerance. Moreover, further chemical transformations of the desired products enhance the overall synthetic value. Further studies on the applicability of 3,4-fused tricyclic indoles for the synthesis of natural products are currently ongoing in our laboratory.



Scheme 7. Plausible reaction mechanism.

Experimental Section

General methods. All commercials obtained from commercial sources were used as received unless otherwise noted. The progress of the reactions was monitored by TLC with silica gel plates, and the visualization was carried out under UV light (254 nm). Melting points were determined using a Büchi B-540 capillary melting point apparatus. NMR spectra were recorded on 400 MHz and 600 MHz spectrometers in the solvent indicated. Chemical shifts are reported downfield from TMS (= 0) for ^{1}H NMR. For ^{13}C NMR, chemical shifts are reported in the scale relative to $CDCl_3$ (= 77.0), DMSO-d_6 (= 40.0) and Benzene-d_6 (= 128.0). Mass spectra were measured with a low-resolution MS instrument using ESI ionization. HRMS spectra were recorded on an electrospray ionization quadrupole time-of-flight (ESI-Q-TOF) mass spectrometer.

Preparation of Substrates.The substrates (**1a−1o, 1v-1w**),[26d, 27] **1p**,[26d, 28] (**1q-1u**),[26d, 29] **1x**,[27a] **1y-1z**,[30] **2a**[31] were prepared using the literature procedures, and the NMR data of all these compounds were compared with the corresponding reported data.

*1-iodo-2-(5-phenylpent-4-yn-1-yl)benzene (**1a**)*. Eluent in chromatography: petroleum ether, **1a** was isolated as a colorless oil (1.30 g, 75%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, J = 7.6 Hz, 1H), 7.44 – 7.39 (m, 2H), 7.33 – 7.22 (m, 5H), 6.94 – 6.84 (m, 1H), 2.98 – 2.83 (m, 2H), 2.48 (t, J = 6.8 Hz, 2H), 1.95 – 1.86 (m, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 144.2, 139.5, 131.6, 129.6, 128.3, 128.2, 127.8, 127.6, 123.9, 100.5, 89.6, 81.3, 39.8, 29.0, 19.0. HRMS (EI) *m/z* calcd for $C_{17}H_{15}I$ $[M]^+$ 346.0218, found 346.0197.

*1-iodo-2-(5-(p-tolyl)pent-4-yn-1-yl)benzene (**1b**)*. Eluent in chromatography: petroleum ether, **1b** was isolated as a light yellow liquid (1.40 g, 78%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, J = 8.0 Hz, 1H), 7.31 (d, J = 8.2 Hz, 2H), 7.29 – 7.19 (m, 2H), 7.09 (d, J = 7.8 Hz, 2H), 6.90 – 6.84 (m, 1H), 2.93 – 2.83 (m, 2H), 2.46 (t, J = 6.8 Hz, 2H), 2.33 (s, 3H), 1.94 – 1.85 (m, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 144.2, 139.5, 137.5, 131.4, 129.6, 128.9, 128.3, 127.8, 120.8, 100.5, 88.8, 81.3, 39.8, 29.1, 21.4, 19.0. HRMS (EI) *m/z* calcd for $C_{18}H_{17}I$ $[M]^+$ 360.0375, found 360.0388.

*1-(5-(4-chlorophenyl)pent-4-yn-1-yl)-2-iodobenzene (**1c**)*. Eluent in chromatography: petroleum ether, **1c** was isolated as a yellow liquid (1.52 g, 80%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, J = 7.8 Hz, 1H), 7.38 – 7.32 (m, 2H), 7.30 – 7.20 (m, 4H), 6.92 – 6.85 (m, 1H), 2.94 – 2.82 (m, 2H), 2.46 (t, J = 7.0 Hz, 2H), 1.94 – 1.85 (m, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 144.1, 139.6, 133.5, 132.8, 129.5, 128.5, 128.3, 127.9, 122.4, 100.5, 90.7, 80.3, 39.8, 28.9, 19.0. HRMS (EI) *m/z* calcd for $C_{17}H_{14}ClI$ $[M]^+$ 379.9829, found 379.9820.

*1-iodo-2-(5-(4-(trifluoromethyl)phenyl)pent-4-yn-1-yl)benzene (**1d**)*. Eluent in chromatography: petroleum ether, **1d** was isolated as a yellow liquid (1.45 g, 70%); ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.85 (d, J = 7.6 Hz, 1H), 7.75 – 7.60 (m, 4H), 7.39 – 7.33 (m, 2H), 7.01 – 6.95 (m, 1H), 2.86 – 2.82 (m, 2H), 2.57 – 2.50 (m, , 2H), 1.90 – 1.77 (m, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 144.0, 139.6, 131.8, 129.5, 129.2, 128.3, 127.9, 127.8, 125.1 (q, $J_{C\text{-}F}$ = 3.8 Hz), 122.6, 100.5, 92.5, 80.2, 39.8, 28.9, 19.0. ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.72. HRMS (EI) *m/z* calcd for $C_{18}H_{14}F_3I$ $[M]^+$ 414.0092, found 414.0088.

*1-iodo-2-(5-(m-tolyl)pent-4-yn-1-yl)benzene (**1e**)*. Eluent in chromatography: petroleum ether, **1e** was isolated as a yellow liquid (1.48 g, 82%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, J = 7.6 Hz, 1H), 7.31 – 7.21 (m, 4H), 7.17 (t, J = 7.6 Hz, 1H), 7.08 (d, J = 7.4 Hz, 1H), 6.92 – 6.82 (m, 1H), 2.94 – 2.83 (m, 2H), 2.47 (t, J = 6.8 Hz, 2H), 2.31 (s, 3H), 1.95 –1.85 (m, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 144.2, 139.5, 137.8, 132.2, 129.6, 128.6, 128.5, 128.3, 128.1, 127.8, 123.7, 100.5, 89.2, 81.4, 39.8, 29.0, 21.2, 18.9. HRMS (EI) *m/z* calcd for $C_{18}H_{17}I$ $[M]^+$ 360.0375, found 360.0364.

*1-(5-(3-chlorophenyl)pent-4-yn-1-yl)-2-iodobenzene (**1f**)*. Eluent in chromatography: petroleum ether, **1f** was isolated as a colorless oil (1.44 g, 76%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, J = 8.8 Hz, 1H), 7.41 – 7.38 (m, 1H), 7.32 – 7.23 (m, 4H), 7.23 – 7.17 (m, 1H), 6.97 – 6.79 (m, 1H), 2.98 – 2.82 (m, 2H), 2.47 (t, J = 8.0 Hz, 2H), 1.96 – 1.82 (m, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 144.0, 139.6,

134.0, 131.5, 129.7, 129.6, 129.4, 128.3, 127.9, 127.9, 125.6, 100.5, 91.1, 80.1, 39.8, 28.9, 18.9. HRMS (EI) *m/z* calcd for $C_{17}H_{14}ClI$ $[M]^+$ 379.9829, found 379.9809.

*1-chloro-2-(5-(2-iodophenyl)pent-1-yn-1-yl)benzene (**1g**)*. Eluent in chromatography: petroleum ether, **1g** was isolated as a light yellow liquid (1.37 g, 72%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.8 (d, J = 8.6 Hz, 1H), 7.5 – 7.4 (m, 1H), 7.4 – 7.3 (m, 1H), 7.31 – 7.25 (m, 2H), 7.2 – 7.1 (m, 2H), 6.91 – 6.85 (m, 1H), 3.0 – 2.9 (m, 2H), 2.5 (t, J = 6.8 Hz, 2H), 1.98 – 1.88 (m, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 144.1, 139.5, 135.8, 133.3, 129.7, 129.1, 128.6, 128.3, 127.8, 126.3, 123.7, 100.5, 95.3, 78.3, 39.6, 28.8, 19.1. HRMS (EI) *m/z* calcd for $C_{17}H_{14}ClI$ $[M]^+$ 379.9829, found 379.9849.

*1-(5-(2-iodophenyl)pent-1-yn-1-yl)-3,5-dimethoxybenzene (**1h**)*. Eluent in chromatography: petroleum ether, **1h** was isolated as a light yellow liquid (1.14 g, 56%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, J = 8.2 Hz, 1H), 7.32 – 7.18 (m, 2H), 6.94 – 6.82 (m, 1H), 6.60 – 6.53 (d, J = 2.2 Hz, 2H), 6.41 (t, J = 2.4 Hz, 1H), 3.77 (s, 6H), 2.96 – 2.82 (m, 2H), 2.47 (t, J = 6.8 Hz, 2H), 1.92 – 1.86 (m, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 160.5, 144.2, 139.5, 129.6, 128.3, 127.8, 125.2, 109.4, 101.1, 100.5, 89.3, 81.3, 55.4, 39.8, 29.0, 18.9. HRMS (EI) *m/z* calcd for $C_{19}H_{19}IO_2$ $[M]^+$ 406.0430, found 406.0412.

*1,3-difluoro-5-(5-(2-iodophenyl)pent-1-yn-1-yl)benzene (**1i**)*. Eluent in chromatography: petroleum ether, **1i** was isolated as a colorless oil (0.96 g, 50%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, J = 7.6 Hz, 1H), 7.32 – 7.25 (m, 1H), 7.24 – 7.17 (m, 1H), 6.95 – 6.83 (m, 3H), 6.79 – 6.67 (m, 1H), 2.91 – 2.83 (m, 2H), 2.46 (t, J = 6.8 Hz, 2H), 1.96 – 1.85 (m, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 162.6 (dd, J = 248.2, 13.6 Hz), 143.9, 139.6, 129.5, 128.3, 127.9, 114.6 (d, $J_{C\text{-}F}$ = 7.4 Hz), 114.4 (d, $J_{C\text{-}F}$ = 7.4 Hz), 103.8 (t, $J_{C\text{-}F}$ = 25.4 Hz), 100.5, 92.1, 79.4, 39.8, 28.7, 18.9. ^{19}F NMR (376 MHz, $CDCl_3$) δ -105.5 – -113.3 (m). HRMS (EI) *m/z* calcd for $C_{17}H_{13}F_2I$ $[M]^+$ 382.0030, found 382.0048.

*2-(5-(2-iodophenyl)pent-1-yn-1-yl)thiophene (**1j**)*. Eluent in chromatography: petroleum ether, **1j** was isolated as a light yellow liquid (1.14 g, 65%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, J = 8.2 Hz, 1H), 7.30 – 7.21 (m, 2H), 7.19 – 7.11 (m, 2H), 6.96 – 6.92 (m, 1H), 6.91 – 6.85 (m, 1H), 2.94 – 2.81 (m, 2H), 2.49 (t, J = 7.0 Hz, 2H), 1.94 – 1.85 (m, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 144.1, 139.5, 131.0, 129.6, 128.3, 127.9, 126.8, 126.0, 124.0, 100.5, 93.7, 74.4, 39.8, 28.9, 19.2. HRMS (ESI) *m/z* calcd for $C_{15}H_{14}IS$ $[M + H]^+$ 352.9855, found 352.9851.

*1-iodo-2-(6-methylhept-6-en-4-yn-1-yl)benzene (**1k**)*. Eluent in chromatography: petroleum ether, **1k** was isolated as a light yellow liquid (1.05 g, 68%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, J = 7.8 Hz, 1H), 7.30 – 7.26 (m, 1H), 7.24 – 7.21 (m, 1H), 6.91 – 6.85 (m, 1H), 5.24 (s, 1H), 5.16 (s, 1H), 2.89 – 2.77 (m, 2H), 2.37 (t, J = 7.0 Hz, 2H), 1.90 (s, 3H), 1.88 – 1.79 (m, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 144.2, 139.5, 129.5, 128.3, 127.8, 127.2, 120.5, 100.5, 88.6, 82.6, 39.7, 29.0, 23.9, 18.8. HRMS (EI) *m/z* calcd for $C_{14}H_{15}I$ $[M]^+$ 310.0218, found 310.0209.

*1-iodo-4-methyl-2-(5-phenylpent-4-yn-1-yl)benzene (**1l**)*. Eluent in chromatography: petroleum ether, **1l** was isolated as a yellow liquid (1.53 g, 85%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, J = 8.0 Hz, 1H), 7.45 –7.40 (m, 2H), 7.33 – 7.27 (m, 3H), 7.07 (s, 1H), 6.73 – 6.69 (m, 1H), 2.90 – 2.77 (m, 2H), 2.47 (t, J = 6.8 Hz, 2H), 2.27 (s, 3H), 1.93 – 1.83 (m, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 143.9,

139.2, 138.2, 131.6, 130.5, 128.8, 128.2, 127.5, 124.0, 96.4, 89.7, 81.3, 39.7, 29.2, 20.9, 19.0. HRMS (EI) *m/z* calcd for $C_{18}H_{17}I$ $[M]^+$ 360.0375, found 360.0366.

*1-iodo-4-methoxy-2-(5-phenylpent-4-yn-1-yl)benzene (**1m**)*. Eluent in chromatography: petroleum ether/ethyl acetate 100:1, **1m** was isolated as a yellow liquid (1.65 g, 88%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, *J* = 8.6 Hz, 1H), 7.46 – 7.37 (m, 2H), 7.32 – 7.25 (m, 3H), 6.84 (d, *J* = 3.0 Hz, 1H), 6.50 (dd, *J* = 8.6, 3.06 Hz, 1H), 3.76 (s, 3H), 2.90 – 2.79 (m, 2H), 2.48 (t, *J* = 6.8 Hz, 2H), 1.95 – 1.85 (m, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 159.9, 145.2, 139.9, 131.5, 128.2, 127.6, 123.9, 115.7, 113.8, 89.6, 89.0, 81.3, 55.3, 39.8, 28.9, 18.9. HRMS (ESI) *m/z* calcd for $C_{18}H_{17}INaO[M + Na]^+$ 399.0216, found 399.0193.

*4-fluoro-1-iodo-2-(5-phenylpent-4-yn-1-yl)benzene (**1n**)*. Eluent in chromatography: petroleum ether, **1n** was isolated as a yellow liquid (1.46 g, 80%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (dd, *J* = 8.6, 5.6 Hz, 1H), 7.44 – 7.40 (m, 2H), 7.33 – 7.25 (m, 3H), 7.00 (dd, *J* = 9.6, 2.98 Hz, 1H), 6.66 (td, *J* = 8.4, 2.8 Hz, 1H), 2.91 – 2.84 (m, 2H), 2.48 (t, *J* = 6.8 Hz, 2H), 1.94 – 1.83 (m, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 163.0 (d, $J_{C\text{-}F}$ = 247.2 Hz), 146.4 (d, $J_{C\text{-}F}$ = 7.2 Hz), 140.5 (d, $J_{C\text{-}F}$ = 7.8 Hz), 131.5, 128.2, 127.6, 123.8, 116.6 (d, $J_{C\text{-}F}$ = 21.8 Hz), 115.2 (d, $J_{C\text{-}F}$ = 21.6 Hz), 93.2, 89.2, 81.5, 39.8, 28.7, 18.9. ^{19}F NMR (376 MHz, $CDCl_3$) δ -114.35. HRMS (EI) *m/z* calcd for $C_{17}H_{14}FI$ $[M]^+$ 364.0124, found 364.0107.

*4-chloro-1-iodo-2-(5-phenylpent-4-yn-1-yl)benzene (**1o**)*. Eluent in chromatography: petroleum ether, **1o** was isolated as a yellow liquid (1.42 g, 75%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, *J* = 8.4 Hz, 1H), 7.45 – 7.40 (dd, *J* = 6.4, 3.2 Hz, 2H), 7.33 – 7.21 (m, 4H), 6.89 (dd, *J* = 8.4, 2.6 Hz, 1H), 2.98 – 2.74 (m, 2H), 2.48 (t, *J* = 6.8 Hz, 2H), 1.94 –1.84 (m, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 146.1, 140.4, 134.5, 131.6, 129.5, 128.2, 128.0, 127.6, 123.8, 97.5, 89.2, 81.5, 39.7, 28.7, 19.0. HRMS (EI) *m/z* calcd for $C_{17}H_{14}ClI$ $[M]^+$ 379.9829, found 379.9833.

*1-iodo-2-((5-phenylpent-4-yn-1-yl)oxy)benzene (**1p**)*. Eluent in chromatography: petroleum ether/ethyl acetate 100:1, **1p** was isolated as a light yellow liquid (1.23 g, 70%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.40 – 7.35 (m, 2H), 7.31 – 7.18 (m, 4H), 6.83 (dd, *J* = 8.2, 1.2 Hz, 1H), 6.70 (td, *J* = 7.6, 1.2 Hz, 1H), 4.15 (t, *J* = 5.8 Hz, 2H), 2.71 (t, *J* = 6.8 Hz, 2H), 2.17 – 2.08 (m, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 157.3, 139.4, 131.5, 129.4, 128.2, 127.6, 123.7, 122.5, 112.1, 89.1, 86.7, 81.2, 67.5, 28.5, 16.3. HRMS (ESI) *m/z* calcd for $C_{17}H_{15}INaO$ $[M + Na]^+$ 385.0060, found 385.0061.

*diethyl 2-(2-iodobenzyl)-2-(4-phenylbut-3-yn-1-yl)malonate (**1q**)*. Eluent in chromatography: petroleum ether/ethyl acetate 20:1, **1q** was isolated as a colorless oil (1.69 g, 67%); ^{1}H NMR (400 MHz, Benzene-d_6) δ 7.64 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.46 – 7.40 (m, 2H), 7.34 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.08 – 6.80 (m, 4H), 6.46 (td, *J* = 7.6, 1.60 Hz, 1H), 3.94 (q, *J* = 7.0 Hz, 4H), 3.73 (s, 2H), 2.71 – 2.62 (m, 2H), 2.62 – 2.51 (m, 2H), 0.85 (t, *J* = 7.2 Hz, 6H). ^{13}C{^{1}H} NMR (100 MHz, Benzene-d_6) δ 170.6, 140.3, 140.2, 131.9, 130.5, 128.7, 128.4, 124.5, 103.4, 89.5, 81.8, 61.4, 58.8, 43.3, 33.4, 16.2, 13.8. HRMS (ESI) *m/z* calcd for $C_{24}H_{26}IO_4$ $[M + H]^+$ 505.0870, found 505.0866.

*diethyl 2-(2-iodobenzyl)-2-(3-phenylprop-2-yn-1-yl)malonate (**1r**)*. Eluent in chromatography: petroleum ether/ethyl acetate 20:1, **1r** was isolated as a colorless oil (2.08 g, 85%); ^{1}H NMR (400 MHz, Benzene-d_6) δ 7.68 (dd, J = 7.8, 1.22 Hz, 1H), 7.54 (dd, J = 7.6, 1.6 Hz, 1H), 7.47 – 7.44 (m, 2H), 7.04 – 6.96 (m, 3H), 6.91 (td, J = 7.6, 1.2 Hz, 1H), 6.48 (td, J = 7.6, 1.6 Hz, 1H), 4.09 – 4.01 (m, 4H), 4.00 – 3.92 (m, 2H), 3.31 (s, 2H), 0.92 (t, J = 7.2 Hz, 6H). ^{13}C{^{1}H} NMR (100 MHz, Benzene-d_6) δ 169.8, 140.4, 140.1, 132.0, 131.1, 128.8, 128.5, 128.2, 123.9, 102.8, 85.9, 85.0, 61.7, 58.7, 42.1, 25.0, 13.9. HRMS (ESI) *m/z* calcd for $C_{23}H_{23}INaO_4$ [M + Na]$^+$ 513.0533, found 513.0514.

*diethyl 2-(2-iodo-5-methoxybenzyl)-2-(3-phenylprop-2-yn-1-yl)malonate (**1s**)*. Eluent in chromatography: petroleum ether/ethyl acetate 30:1, **1s** was isolated as a light yellow liquid (1.98 g, 76%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, J = 8.6 Hz, 1H), 7.42 – 7.36 (m, 2H), 7.31 – 7.26 (m, 3H), 7.06 (d, J = 3.0 Hz, 1H), 6.53 (dd, J = 7.8, 1.6 Hz, 1H), 4.32 – 4.13 (m, 4H), 3.74 (s, 3H), 3.64 (s, 2H), 3.03 (s, 2H), 1.3 (t, J = 7.2 Hz, 1H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 169.7, 159.6, 140.3, 140.3, 131.6, 128.2, 128.0, 123.2, 116.6, 115.2, 90.6, 85.1, 84.4, 61.8, 58.1, 55.2, 41.4, 24.3, 13.9. HRMS (ESI) *m/z* calcd for $C_{24}H_{25}INaO_5$ [M + Na]$^+$ 543.0639, found 543.0631.

*diethyl 2-(5-chloro-2-iodobenzyl)-2-(3-phenylprop-2-yn-1-yl)malonate (**1t**)*. Eluent in chromatography: petroleum ether/ethyl acetate 20:1, **1t** was isolated as a yellow liquid (2.02 g, 77%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, J = 8.6 Hz, 1H), 7.45 (d, J = 2.4 Hz, 1H), 7.42 – 7.38 (m, 2H), 7.32 – 7.28 (m, 3H), 6.91 (dd, J = 8.4, 2.54 Hz, 1H), 4.37 – 4.09 (m, 4H), 3.64 (s, 2H), 3.03 (s, 2H), 1.28 – 1.22 (m, 6H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 169.5, 141.4, 140.8, 134.3, 131.6, 130.8, 128.9, 128.2, 128.1, 123.1, 99.3, 84.7, 84.6, 62.0, 58.2, 41.4, 24.5, 13.9. HRMS (ESI) *m/z* calcd for $C_{23}H_{22}ClINaO_4$ [M + Na]$^+$ 547.0144, found 547.0131.

*diethyl 2-(4-chloro-2-iodobenzyl)-2-(3-phenylprop-2-yn-1-yl)malonate (**1u**)*. Eluent in chromatography: petroleum ether/ethyl acetate 20:1, **1u** was isolated as a light yellow liquid (2.17 g, 83%); ^{1}H NMR (400 MHz, Benzene-d_6) δ 7.70 (d, J = 2.2 Hz, 1H), 7.48 – 7.40 (m, 2H), 7.31 (d, J = 8.4 Hz, 1H), 7.02 – 6.91 (m, 3H), 6.84 (dd, J = 8.2, 2.2 Hz, 1H), 4.04 – 3.89 (m, 4H), 3.87 (s, 2H), 3.24 (s, 2H), 0.95 – 0.86 (m, 6H). ^{13}C{^{1}H} NMR (100 MHz, Benzene-d_6) δ 169.3, 139.0, 138.4, 133.2, 131.7, 131.3, 128.3, 127.7, 127.5, 123.4, 102.3, 85.3, 84.8, 61.5, 58.3, 41.1, 24.7, 13.6. HRMS (ESI) *m/z* calcd for $C_{23}H_{22}ClINaO_4$ [M + Na]$^+$ 547.0144, found 547.0138.

*1-iodo-2-(oct-4-yn-1-yl)benzene (**1v**)*. Eluent in chromatography: petroleum ether, **1v** was isolated as a colorless oil (1.09 g, 70%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, J = 7.6 Hz, 1H), 7.30 – 7.17 (m, 2H), 6.90 – 6.82 (m, 1H), 2.87 – 2.72 (m, 2H), 2.27 – 2.19 (m, 2H), 2.19 – 2.09 (m, 2H), 1.82 – 1.73 (m, 2H), 1.58 – 1.46 (m, 2H), 0.99 (t, J = 7.4 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 144.4, 139.5, 129.5, 128.2, 127.7, 100.5, 80.9, 79.6, 39.7, 29.4, 22.5, 20.8, 18.3, 13.6. HRMS (EI) *m/z* calcd for $C_{14}H_{17}I$ [M]$^+$ 312.0375, found 312.0381.

*1-iodo-2-(tridec-4-yn-1-yl)benzene (**1w**)*. Eluent in chromatography: petroleum ether, **1w** was isolated as a colorless oil (1.18 g, 62%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 –7.78 (m, 1H), 7.30 – 7.17 (m, 2H), 6.90 – 6.84 (m, 1H), 2.92 – 2.74 (m, 2H), 2.31 – 2.11 (m, 4H), 1.88 – 1.70 (m, 2H), 1.55 – 1.46 (m, 2H), 1.42 – 1.35 (m, , 2H), 1.27 (s, 8H), 0.90 – 0.84 (m, 3H). ^{13}C{^{1}H} NMR (100 MHz,

$CDCl_3$) δ 144.4, 139.5, 129.5, 128.2, 127.7, 100.5, 81.1, 79.4, 39.7, 31.9, 30.3, 29.4, 29.2, 29.2, 28.9, 22.7, 18.8, 18.3, 14.1. HRMS (EI) *m/z* calcd for $C_{19}H_{27}I$ $[M]^+$ 382.1157, found 382.1165.

*4-chloro-1-iodo-2-(pent-4-yn-1-yl)benzene (**1x**)*. Eluent in chromatography: petroleum ether/ethyl acetate 100:1, **1x** was isolated as a yellow liquid (1.67 g, 55%); ^1H NMR (400 MHz, $CDCl_3$) δ 7.71 (dd, *J* = 8.4, 2.2 Hz, 1H), 7.23 – 7.15 (m, 1H), 6.92 – 6.86 (m, 1H), 2.90 – 2.69 (m, 2H), 2.26 (td, *J* = 6.8, 2.6 Hz, 2H), 2.05 – 2.00 (m, 1H), 1.86 – 1.76 (m, 2H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 145.9, 140.4, 134.5, 129.4, 128.0, 97.5, 83.6, 69.2, 39.4, 28.4, 18.0. HRMS (EI) *m/z* calcd for $C_{11}H_{10}ClI$ $[M]^+$ 303.9516, found 303.9525.

*1-(but-3-yn-1-yloxy)-2-iodobenzene (**1y**)*. Eluent in chromatography: petroleum ether/ethyl acetate 100:1, **1y** was isolated as a colorless oil (1.77 g, 65%); ^1H NMR (400 MHz, $CDCl_3$) δ 7.77 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.31 – 7.26 (m, 1H), 6.82 (dd, *J* = 8.2, 1.2 Hz, 1H), 6.72 (td, *J* = 7.6, 1.2 Hz, 1H), 4.14 (t, *J* = 7.2 Hz, 2H), 2.75 (td, *J* = 7.2, 2.6 Hz, 2H), 2.08 – 2.04 (m, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 157.0, 139.6, 129.4, 123.0, 112.6, 86.8, 80.1, 70.1, 67.3, 19.5. HRMS (EI) *m/z* calcd for $C_9H_{10}IO$ $[M]^+$ 271.9698, found 271.9707.

*1-iodo-2-(pent-4-yn-1-yloxy)benzene (**1z**)*. Eluent in chromatography: petroleum ether/ethyl acetate 100:1, **1z** was isolated as a colorless oil (1.94 g, 68%); ^1H NMR (400 MHz, $CDCl_3$) δ 7.76 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.31 – 7.26 (m, 1H), 6.82 (dd, *J* = 8.2, 1.2 Hz, 1H), 6.70 (td, *J* = 7.6, 1.2 Hz, 1H), 4.11 (t, *J* = 5.8 Hz, 2H), 2.51 (td, *J* = 6.8, 2.6 Hz, 2H), 2.12 – 2.01 (m, 2H), 2.00 – 1.95 (m, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 157.3, 139.4, 129.4, 122.5, 112.1, 86.7, 83.5, 68.9, 67.2, 28.1, 15.3. HRMS (ESI) *m/z* calcd for $C_{11}H_{11}INaO$ $[M + Na]^+$ 308.9747, found 308.9735.

*1,2-di-tert-butyldiaziridin-3-one (**2a**)*. Distilled under reduced pressure (56 ºC/ 4 mmHg) to give **2a** as a colorless liquid (4.40 g, 75% yield). ^1H NMR (400 MHz, $CDCl_3$) δ 1.22 (s, 18H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 159.3, 59.2, 26.9.

General procedure for the synthesis of compounds 3,4-Fused tricyclic indoles. Synthesis of **3a** is representative. 1-iodo-2-(5-phenylpent-4-yn-1-yl)benzene **1a** (0.2 mmol), diaziridinone **2a** (0.4 mmol), $Pd(OAc)_2$ (0.02 mmol), Cs_2CO_3 (0.2 mmol) and PPh_3 (0.2 mmol) were dissolved in DMF (2.0 mL). The mixture was placed in a preheated metal block and stirred at 130 °C (temperature of the metal block) under argon atmosphere for 4 hours. Then the resulting mixture was cooled to room temperature and then diluted with ethyl acetate. The combined organic layer was washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography (petroleum ether/ethyl acetate = 100 : 1) to give **3a** (48 mg, 83% yield) as a white solid.

Gram-scale synthesis of 3a. To a three-neck flask was added 1-iodo-2-(5-phenylpent-4-yn-1-yl)benzene **1a** (1.500 g, 4.34 mmol), diaziridinone **2a** (1.480 g, 8.68 mmol), $Pd(OAc)_2$ (0.098 g, 10 mol %), Cs_2CO_3 (1.415 g, 1 equiv.), PPh_3 (1.142 g, 1 equiv.) and DMF (40.0 mL). After stirring at 130 °C (temperature of the oil bath) under argon atmosphere for 4 hours, the resulting mixture was cooled to room temperature and then diluted with ethyl acetate. The combined organic layer was washed with brine, dried over anhydrous Na_2SO_4, filtered, and

concentrated under reduced pressure. The residue was purified by flash chromatography (petroleum ether/ ethyl acetate = 100 : 1) to give **3a** as a white solid (1.067 g, 85% yield).

*1-(tert-butyl)-2-phenyl-1,3,4,5-tetrahydrobenzo[cd]indole (**3a**)*. Following the general procedure (eluent in chromatography: petroleum ether/ethyl acetate 100:1), **3a** was isolated as a white solid (48 mg, 83%); m.p. 157 – 159 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, J = 8.4 Hz, 1H), 7.38 – 7.31 (m, 5H), 7.12 – 7.04 (m, 1H), 6.82 (d, J = 7.0 Hz, 1H), 2.95 – 2.87 (m, 2H), 2.51 – 2.43 (m, 2H), 1.98 – 1.92 (m, 2H), 1.57 (s, 9H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 137.2, 135.2, 134.6, 132.2, 130.6, 127.7, 127.6, 127.2, 121.4, 115.7, 114.4, 112.2, 58.6, 32.0, 28.0, 24.2, 21.7. HRMS (ESI) *m/z* calcd for $C_{21}H_{24}N$ $[M + H]^+$ 290.1903, found 290.1889.

*1-(tert-butyl)-2-(p-tolyl)-1,3,4,5-tetrahydrobenzo[cd]indole (**3b**)*. Following the general procedure (eluent in chromatography: petroleum ether/ethyl acetate 100:1), **3b** was isolated as a white solid (51 mg, 84%); m.p. 144 – 146 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, J = 8.4 Hz, 1H), 7.24 – 7.19 (m, 2H), 7.19 – 7.14 (m, 2H), 7.11 – 7.04 (m, 1H), 6.82 (d, J = 7.0 Hz, 1H), 2.95 – 2.86 (m, 2H), 2.51 – 2.43 (m, 2H), 2.41 (s, 3H), 1.99 – 1.89 (m, 2H), 1.59 –1.56 (m, 9H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 136.8, 135.1, 134.7, 134.1, 132.1, 130.5, 128.3, 127.7, 121.2, 115.6, 114.1, 112.2, 58.5, 32.0, 28.0, 24.2, 21.8, 21.3. HRMS (ESI) *m/z* calcd for $C_{22}H_{26}N$ $[M + H]^+$ 304.2060, found 304.2065.

1-(*tert*-butyl)-2-(4-chlorophenyl)-1,3,4,5-tetrahydrobenzo[*cd*]indole *(**3c**)*. Following the general procedure (eluent in chromatography: petroleum ether/ethyl acetate 100:1), **3c** was isolated as a white solid (50 mg, 77%); m.p. 205 – 207 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, J = 8.4 Hz, 1H), 7.38 – 7.32 (m, 2H), 7.30 – 7.25 (m, 2H), 7.10 (t, J = 7.8 Hz, 1H), 6.83 (d, J = 7.0 Hz, 1H), 2.95 – 2.88 (m, 2H), 2.52 – 2.43 (m, 2H), 2.00 – 1.89 (m, 2H), 1.57 (s, 9H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 135.7, 135.4, 133.2, 133.1, 132.3, 131.8, 127.9, 127.6, 121.7, 115.9, 114.9, 112.3, 58.6, 32.1, 27.9, 24.2, 21.7. HRMS (ESI) *m/z* calcd for $C_{21}H_{23}ClN$ $[M + H]^+$ 324.1514, found 324.1496.

*1-(tert-butyl)-2-(4-(trifluoromethyl)phenyl)-1,3,4,5-tetrahydrobenzo[cd]indole (**3d**)*. Following the general procedure (eluent in chromatography: petroleum ether/ethyl acetate 100:1), **3d** was isolated as a white solid (51 mg, 71%); m.p. 160 – 162 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, J = 8.0 Hz, 2H), 7.51 – 7.43 (m, 3H), 7.15 – 7.08 (m, 1H), 6.85 (d, J = 6.8 Hz, 1H), 2.95 – 2.86 (m, 2H), 2.53 – 2.38 (m, 2H), 2.00 – 1.88 (m, 2H), 1.57 (s, 9H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 141.0, 135.8, 132.9, 132.5, 130.6, 129.1 (q, $J_{C\text{-}F}$ = 32.6 Hz), 127.7, 125.6, 124.6 (q, $J_{C\text{-}F}$ = 3.8 Hz), 122.0, 116.0, 115.5, 112.4, 58.7, 32.1, 27.9, 24.2, 21.7. ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.34. HRMS (ESI) *m/z* calcd for $C_{22}H_{23}F_3N$ $[M + H]^+$ 358.1777, found 358.1774.

*1-(tert-butyl)-2-(m-tolyl)-1,3,4,5-tetrahydrobenzo[cd]indole (**3e**)*. Following the general procedure (eluent in chromatography: petroleum ether/ethyl acetate 100:1), **3e** was isolated as a white solid (52 mg, 86%); m.p. 118 – 120 °C; ^{1}H NMR (400 MHz, Benzene-d_6) δ 7.45 (d, J = 8.4 Hz, 1H), 7.27 – 7.20 (m, 1H), 7.19 – 7.16 (m, 2H), 7.14 – 7.07 (m, 1H), 7.01 – 6.93 (m, 2H), 2.90 – 2.80 (m, 2H), 2.58 – 2.50 (m, 2H), 2.15 (s, 3H), 1.90 – 1.79 (m, 2H), 1.44 (s, 9H). ^{13}C{^{1}H} NMR (100 MHz, Benzene-d_6) δ 137.9, 137.2, 136.2, 134.8, 132.5, 131.6, 128.7, 128.1, 128.2, 127.8, 122.0, 116.3, 114.8, 112.8, 58.4, 32.1, 28.5, 24.8, 22.4, 21.3. HRMS (ESI) *m/z* calcd for $C_{22}H_{26}N$ $[M + H]^+$ 304.2060, found 304.2049.

*1-(tert-butyl)-2-(3-chlorophenyl)-1,3,4,5-tetrahydrobenzo[cd]indole (**3f**)*. Following the general procedure (eluent in chromatography: petroleum ether/ethyl acetate 100:1), **3f** was isolated as a white solid (60 mg, 93%); m.p. 139 – 141 °C; ^{1}H NMR (400 MHz, Benzene-d_6) δ 7.40 – 7.35 (m, 2H), 7.25 – 7.18 (m, 1H), 7.11 – 7.05 (m, 1H), 7.04 – 6.97 (m, 1H), 6.95 (d, J = 6.8 Hz, 1H), 6.82 (t, J = 7.8 Hz, 1H), 2.84 – 2.76 (m, 2H), 2.46 – 2.33 (m, 2H), 1.83 – 1.73 (m, 2H), 1.33 (s, 9H). ^{13}C{^{1}H} NMR (100 MHz, Benzene-d_6) δ 139.8, 136.5, 133.9, 132.8, 132.7, 130.8, 129.0, 129.0, 128.5, 127.4, 122.5, 116.5, 115.7, 112.8, 58.4, 32.0, 28.3, 24.7, 22.2. HRMS (ESI) *m/z* calcd for $C_{21}H_{23}ClN$ $[M + H]^+$ 324.1514, found 324.1495.

*1-(tert-butyl)-2-(2-chlorophenyl)-1,3,4,5-tetrahydrobenzo[cd]indole (**3g**)*. Following the general procedure (eluent in chromatography: petroleum ether/ethyl acetate 100:1), **3g** was isolated as a white solid (62 mg, 96%); m.p. 168 – 170 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (t, J = 8.6 Hz, 2H), 7.36 – 7.25 (m, 3H), 7.15 – 7.07 (m, 1H), 6.83 (d, J = 7.0 Hz, 1H), 2.98 – 2.88 (m, 2H), 2.49 – 2.29 (m, 2H), 2.06 – 1.88 (m, 2H), 1.57 (s, 9H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 136.4, 135.2, 134.6, 132.8, 132.4, 130.8, 129.1, 129.1, 127.6, 126.0, 121.6, 115.5, 114.3, 112.1, 58.5, 31.0, 27.9, 24.2, 21.3. HRMS (ESI) *m/z* calcd for $C_{21}H_{23}ClN$ $[M + H]^+$ 324.1514, found 324.1511.

*1-(tert-butyl)-2-(3,5-dimethoxyphenyl)-1,3,4,5-tetrahydrobenzo[cd]indole (**3h**)*. Following the general procedure (eluent in chromatography: petroleum ether/ethyl acetate 100:1), **3h** was isolated as a white solid (65 mg, 93%); m.p. 104 – 106 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, J = 8.4 Hz, 1H), 7.08 (t, J = 7.8 Hz, 1H), 6.82 (d, J = 7.0 Hz, 1H), 6.55 – 6.49 (m, 2H), 6.48 – 6.40 (m, 1H), 3.81 (s, 6H), 2.95 – 2.87 (m, 2H), 2.58 – 2.48 (m, 2H), 2.00 – 1.90 (m, 2H), 1.62 (s, 9H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 160.0, 139.0, 135.3, 134.5, 132.3, 127.6, 121.5, 115.7, 114.2, 112.3, 109.1, 99.2, 58.6, 55.4, 31.8, 28.0, 24.2, 21.8. HRMS (ESI) *m/z* calcd for $C_{23}H_{28}NO_2$ $[M + H]^+$ 350.2115, found 350.2099.

*1-(tert-butyl)-2-(3,5-difluorophenyl)-1,3,4,5-tetrahydrobenzo[cd]indole (**3i**)*. Following the general procedure (eluent in chromatography: petroleum ether/ethyl acetate 100:1), **3i** was isolated as a white solid (46 mg, 70%); m.p. 113 – 115 °C; ^{1}H NMR (400 MHz, Benzene-d_6) δ 7.35 (d, J = 8.2 Hz, 1H), 7.25 – 7.17 (m, 1H), 6.94 (d, J = 7.0 Hz, 1H), 6.79 – 6.67 (m, 2H), 6.54 – 6.43 (m, 1H), 2.85 – 2.75 (m, 2H), 2.38 – 2.30 (m, 2H), 1.82 – 1.70 (m, 2H), 1.29 (s, 9H). ^{13}C{^{1}H} NMR (100 MHz, Benzene-d_6) δ 162.7 (dd, J = 248.8, 13.2 Hz), 141.1 (t, J = 10.0 Hz), 136.8, 132.8, 131.8 (t, J = 2.2 Hz), 122.8, 116.7, 116.0, 113.8 (d, J = 6.8 Hz), 113.6 (d, J = 6.8 Hz), 112.9, 102.6 (t, J = 25.2 Hz), 58.4, 31.8, 28.3, 24.7, 22.1. ^{19}F NMR (376 MHz, Benzene-d_6) δ -110.45. HRMS (ESI) *m/z* calcd for $C_{21}H_{22}F_2N$ $[M + H]^+$ 326.1715, found 326.1712.

*1-(tert-butyl)-2-(thiophen-2-yl)-1,3,4,5-tetrahydrobenzo[cd]indole (**3j**)*. Following the general procedure (eluent in chromatography: petroleum ether/ethyl acetate 100:1), **3j** was isolated as a white solid (31 mg, 53%); m.p. 140 – 142 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (d, J = 8.6 Hz, 1H), 7.43 (d, J = 5.2 Hz, 1H), 7.17 – 7.07 (m, 2H), 7.06 – 7.02 (m, 1H), 6.86 (d, J = 7.0 Hz, 1H), 3.00 – 2.90 (m, 2H), 2.63 – 2.55 (m, 2H), 2.07 – 1.95 (m, 2H), 1.70 (s, 9H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 137.4, 135.4, 132.5, 129.2, 127.1, 126.4, 126.4, 125.7, 122.1, 117.4, 115.6, 112.2, 58.9, 31.5, 27.9, 24.1, 21.8. HRMS (ESI) *m/z* calcd for $C_{19}H_{22}NS$ $[M + H]^+$ 296.1467, found 296.1454.

*1-(tert-butyl)-7-methyl-2-phenyl-1,3,4,5-tetrahydrobenzo[cd]indole (**3l**)*. Following the general procedure (eluent in chromatography: petroleum ether/ethyl acetate 100:1), **3l** was isolated as a yellow solid (53 mg, 87%); m.p. 124 – 126 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.30 (m, 5H), 7.29 – 7.25 (m, 1H), 6.85 – 6.50 (m, 1H), 3.06 – 2.75 (m, 2H), 2.65 – 2.34 (m, 5H), 2.12 – 1.80 (m, 2H), 1.57 (s, 9H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 137.4, 135.7, 134.0, 131.9, 131.1, 130.6, 127.5, 127.0, 125.7, 117.4, 114.3, 112.3, 58.4, 32.0, 27.9, 24.4, 22.6, 21.8. HRMS (ESI) *m/z* calcd for $C_{22}H_{26}N$ $[M + H]^+$ 304.2060, found 304.2048.

*1-(tert-butyl)-7-methoxy-2-phenyl-1,3,4,5-tetrahydrobenzo[cd]indole (**3m**)*. Following the general procedure (eluent in chromatography: petroleum ether/ethyl acetate 100:1), **3m** was isolated as a light yellow solid (50 mg, 78%); m.p. 130 – 132 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 – 7.32 (m, 5H), 7.05 – 7.03 (m, 1H), 6.61 – 6.59 (m, 1H), 3.92 (s, 3H), 2.95 – 2.87 (m, 2H), 2.63 – 2.40 (m, 2H), 2.07 – 1.82 (m, 2H), 1.60 (s, 9H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 156.1, 137.3, 135.6, 133.6, 132.6, 130.6, 127.5, 127.0, 122.5, 114.2, 105.1, 97.7, 58.4, 56.3, 31.8, 28.0, 24.3, 21.6. HRMS (ESI) *m/z* calcd for $C_{22}H_{26}NO$ $[M + H]^+$ 320.2009, found 320.2005.

*1-(tert-butyl)-7-fluoro-2-phenyl-1,3,4,5-tetrahydrobenzo[cd]indole (**3n**)*. Following the general procedure (eluent in chromatography: petroleum ether/ethyl acetate 100:1), **3n** was isolated as a white solid (59 mg, 96%); m.p. 137 – 139 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 – 7.32 (m, 5H), 7.20 (dd, J = 12.2, 1.8 Hz, 1H), 6.67 (d, J = 11.4 Hz, 1H), 2.95 – 2.87 (m, 2H), 2.58 – 2.40 (m, 2H), 2.02 – 1.90 (m, 2H), 1.59 (s, 9H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 159.7 (d, $J_{C\text{-}F}$ = 234.6 Hz), 136.8, 134.7 (d, $J_{C\text{-}F}$ = 3.8 Hz), 134.5 (d, $J_{C\text{-}F}$ = 12.8 Hz), 133.0 (d, $J_{C\text{-}F}$ = 10.2 Hz), 130.6, 127.6, 127.3, 123.9, 114.2 (d, $J_{C\text{-}F}$ = 1.4 Hz), 104.7 (d, $J_{C\text{-}F}$ = 25.0 Hz), 98.8 (d, $J_{C\text{-}F}$ = 28.8 Hz), 58.7, 31.9, 27.9, 24.1, 21.5. ^{19}F NMR (376 MHz, $CDCl_3$) δ -120.71. HRMS (ESI) *m/z* calcd for $C_{21}H_{23}FN$ $[M + H]^+$ 308.1809, found 308.1801.

*1-(tert-butyl)-7-chloro-2-phenyl-1,3,4,5-tetrahydrobenzo[cd]indole (**3o**)*. Following the general procedure (eluent in chromatography: petroleum ether/ethyl acetate 100:1), **3o** was isolated as a white solid (63 mg, 98%); m.p. 142 – 144 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 – 7.44 (m, 1H), 7.41 – 7.29 (m, 5H), 6.86 – 6.80 (m, 1H), 2.90 – 2.83 (m, 2H), 2.48 – 2.40 (m, 2H), 1.97 – 1.87 (m, 2H), 1.55 (s, 9H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 136.6, 135.2, 135.2, 133.1, 130.5, 127.7, 127.4, 127.1, 126.1, 116.5, 114.3, 112.1, 58.8, 32.0, 27.8, 24.1, 21.5. HRMS (ESI) *m/z* calcd for $C_{21}H_{23}ClN$ $[M + H]^+$ 324.1514, found 324.1503.

*6-(tert-butyl)-5-phenyl-2,3,4,6-tetrahydrooxepino[4,3,2-cd]indole (**3p**)*. Following the general procedure (eluent in chromatography: petroleum ether/ethyl acetate 30:1), **3p** was isolated as a white solid (46 mg, 75%); m.p. 170 – 172 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 – 7.35 (m, 3H), 7.35 – 7.28 (m, 3H), 7.07 (t, J = 7.4 Hz, 1H), 6.64 (d, J = 7.8 Hz, 1H), 4.34 – 4.24 (m, 2H), 2.53 – 2.41 (m, 2H), 2.11 – 2.01 (m, 2H), 1.57 (s, 9H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 153.0, 138.6, 137.6, 136.0, 130.9, 127.9, 127.6, 121.2, 118.1, 113.2, 107.7, 106.1, 72.5, 58.8, 31.9, 30.3, 27.3. HRMS (ESI) *m/z* calcd for $C_{21}H_{24}NO$ $[M + H]^+$ 306.1852, found 306.1843.

*diethyl 2-(tert-butyl)-1-phenyl-2,6,8,9-tetrahydro-7H-cyclohepta[cd]indole-7,7-dicarboxylate (**3q**)*. Following the general procedure (eluent in chromatography: petroleum ether/ethyl acetate 50:1), **3q**

was isolated as a white solid (81 mg, 91%); m.p. 135 – 137 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, *J* = 8.6 Hz, 1H), 7.43 – 7.36 (m, 3H), 7.35 – 7.30 (m, 2H), 7.10 – 7.02 (m, 1H), 6.89 (d, *J* = 7.2 Hz, 1H), 4.23 – 4.11 (m, 4H), 3.67 (s, 2H), 2.64 – 2.54 (m, 2H), 2.41 – 2.27 (m, 2H), 1.56 (s, 9H), 1.24 (t, *J* = 7.2 Hz, 6H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 172.1, 136.8, 136.5, 136.2, 131.1, 130.3, 128.9, 127.6, 127.5, 120.9, 119.6, 117.8, 113.4, 61.2, 58.9, 58.5, 37.2, 34.2, 31.9, 21.3, 14.0. HRMS (ESI) *m/z* calcd for $C_{28}H_{34}NO_4$ $[M + H]^+$ 448.2482, found 448.2479.

*diethyl 1-(tert-butyl)-2-phenyl-1,5-dihydrobenzo[cd]indole-4,4(3H)-dicarboxylate (**3r**)*. Following the general procedure (eluent in chromatography: petroleum ether/ethyl acetate 50:1), **3r** was isolated as a white solid (82 mg, 95%); m.p. 85 – 87 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, *J* = 8.4 Hz, 1H), 7.42 – 7.30 (m, 5H), 7.12 – 7.05 (m, 1H), 6.88 (d, *J* = 7.8 Hz, 1H), 4.06 (q, *J* = 7.2 Hz, 4H), 3.49 (s, 2H), 3.06 (s, 2H), 1.55 (s, 9H), 1.10 (t, *J* = 7.2 Hz, 6H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 171.2, 136.5, 135.5, 134.8, 130.6, 128.0, 127.7, 127.4, 126.2, 121.8, 116.1, 112.7, 110.7, 61.3, 58.8, 56.0, 34.3, 32.0, 28.4, 13.9. HRMS (ESI) *m/z* calcd for $C_{27}H_{32}NO_4$ $[M + H]^+$ 434.2326, found 434.2325.

*diethyl 1-(tert-butyl)-7-methoxy-2-phenyl-1,5-dihydrobenzo[cd]indole-4,4(3H)-dicarboxylate (**3s**)*. Following the general procedure (eluent in chromatography: petroleum ether/ethyl acetate 50:1), **3s** was isolated as a light yellow liquid (89 mg, 96%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.30 (m, 5H), 6.97 (s, 1H), 6.61 (s, 1H), 4.07 (q, *J* = 7.2 Hz, 4H), 3.87 (s, 3H), 3.44 (s, 2H), 3.04 (s, 2H), 1.53 (s, 9H), 1.11 (t, *J* = 7.2 Hz, 6H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 171.1, 156.4, 136.7, 135.4, 134.5, 130.6, 128.4, 127.7, 127.3, 121.2, 110.6, 105.4, 98.3, 61.3, 58.6, 56.2, 56.2, 34.4, 31.9, 28.4, 13.9. HRMS (ESI) *m/z* calcd for $C_{28}H_{34}NO_5$ $[M + H]^+$ 464.2431, found 464.2417.

*diethyl 1-(tert-butyl)-7-chloro-2-phenyl-1,5-dihydrobenzo[cd]indole-4,4(3H)-dicarboxylate (**3t**)*. Following the general procedure (eluent in chromatography: petroleum ether/ethyl acetate 50:1), **3t** was isolated as a light yellow solid (70 mg, 75%); m.p. 80 – 82 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (s, 1H), 7.41 – 7.29 (m, 5H), 6.89 (s, 1H), 4.07 (q, *J* = 7.2 Hz, 4H), 3.44 (s, 2H), 3.03 (s, 2H), 1.53 (s, 9H), 1.10 (t, *J* = 6.8 Hz, 6H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 170.9, 136.2, 136.0, 134.9, 130.5, 129.0, 127.8, 127.7, 127.5, 124.8, 116.9, 112.7, 110.8, 61.4, 59.1, 55.9, 34.0, 32.0, 28.2, 13.9. HRMS (ESI) *m/z* calcd for $C_{27}H_{31}ClNO_4$ $[M + H]^+$ 468.1936, found 468.1939.

*diethyl 1-(tert-butyl)-8-chloro-2-phenyl-1,5-dihydrobenzo[cd]indole-4,4(3H)-dicarboxylate (**3u**)*. Following the general procedure (eluent in chromatography: petroleum ether/ethyl acetate 50:1), **3u** was isolated as a light yellow liquid (64 mg, 69%); ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.54 – 7.33 (m, 5H), 7.13 (d, *J* = 7.6 Hz, 1H), 6.90 (d, *J* = 7.6 Hz, 1H), 3.99 – 3.93 (m, 4H), 3.36 (s, 2H), 3.04 (s, 2H), 1.54 (s, 9H), 1.02 – 0.94 (m, 6H). ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ 170.4, 140.3, 136.4, 135.4, 130.4, 129.4, 128.8, 127.9, 127.6, 125.7, 119.8, 116.1, 112.8, 61.6, 59.5, 55.3, 33.9, 33.9, 28.7, 14.2. HRMS (ESI) *m/z* calcd for $C_{27}H_{31}ClNO_4$ $[M + H]^+$ 468.1936, found 468.1926.

Removal of the *tert*-butyl group of product 3a. To an oven-dried 10 mL pressure tube was added 1-(*tert*-butyl)-2-phenyl-1,3,4,5-tetrahydrobenzo[*cd*]indole **1a** (0.2 mmol) , 1 M HCl (0.3 mL) and MeCN (0.7 mL). After stirring at room temperature for overnight, the resulting mixture was diluted with ethyl acetate. The combined organic layer was washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography

(petroleum ether/ethyl acetate = 10 : 1) to give **3a**, (35 mg, 75% yield) as a white solid, m.p. 117 – 119 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.00 (s, 1H), 7.72 – 7.70 (m, 2H), 7.47 (t, J = 7.8 Hz, 2H), 7.28 (t, J = 7.4 Hz, 1H), 7.13 – 7.11 (m, 1H), 7.04 – 6.94 (m, 1H), 6.71 (d, J = 6.8 Hz, 1H), 3.01 (t, J = 6.0 Hz, 2H), 2.87 (t, J = 5.8 Hz, 2H), 2.00 (p, J = 6.4 Hz, 2H). ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ 134.7, 133.7, 131.9, 130.5, 129.3, 128.6, 126.8, 126.3, 122.8, 115.7, 110.5, 108.6, 27.4, 24.9, 23.5. HRMS (ESI) *m/z* calcd for $C_{17}H_{16}N$ $[M + H]^+$ 234.1277, found 234.1274.

Competition experiments. (a) To an oven-dried 10 mL pressure tube was added substrate **1b** (36 mg, 0.1 mmol), substrate **1c** (38 mg, 0.1 mmol), $Pd(OAc)_2$ (5 mg, 10 mol %), PPh_3 (0.2 mmol), Cs_2CO_3 (0.2 mmol), diaziridinone **2a** (68 mg, 0.4 mmol) and DMF (2.0 mL) under Ar. After stirring at 130 °C (temperature of the metal block) under argon atmosphere for 4 hours, the resulting mixture was diluted with ethyl acetate. The combined organic layer was washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography (petroleum ether/ethyl acetate = 100 : 1). The ratio of product **3c**/**3b** was analyzed by ^{1}H NMR.

(b) To an oven-dried 10 mL pressure tube was added substrate **1l** (36 mg, 0.1 mmol), substrate **1o** (38 mg, 0.1 mmol), $Pd(OAc)_2$ (5 mg, 10 mol %), PPh_3 (0.2 mmol), Cs_2CO_3 (0.2 mmol), diaziridinone **2a** (68 mg, 0.4 mmol) and DMF (2.0 mL) under Ar. After stirring at 130 °C (temperature of the metal block) under argon atmosphere for 4 hours, the resulting mixture was diluted with ethyl acetate. The combined organic layer was washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography (petroleum ether/ethyl acetate = 100 : 1). The ratio of product **3o**/**3l** was analyzed by ^{1}H NMR.

ASSOCIATED CONTENT

Supporting Information

The supporting information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.xxxxxxx

Copies of NMR spectra of products.

AUTHOR INFORMATION

Corresponding Author

Chuanming Yu − *College of Pharmaceutical Sciences, Zhejiang University of Technology, Hangzhou 310014, P. R. China; Email: ycm@zjut.edu.cn*

Xinpeng Jiang− *College of Pharmaceutical Sciences, Zhejiang University of Technology, Hangzhou 310014, P. R. China; Email: xjiang@zjut.edu.cn*

Authors

Lei Zhang − *College of Pharmaceutical Sciences, Zhejiang University of Technology, Hangzhou 310014, P. R. China*

Junyu Chen − *College of Pharmaceutical Sciences, Zhejiang University of Technology, Hangzhou 310014, P. R. China*

Tianshuo Zhong − *College of Pharmaceutical Sciences, Zhejiang University of Technology, Hangzhou 310014, P. R. China*

Xiangyun Zheng − *College of Pharmaceutical Sciences, Zhejiang University of Technology,*

Hangzhou 310014, P. R. China

Jian Zhou − *College of Pharmaceutical Sciences, Zhejiang University of Technology, Hangzhou 310014, P. R. China*

Complete contact information is available at:

https://pubs.acs.org/10.1021/

Notes

The authors declare no competing financial interest.

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(1) (a) Van Zandt, M. C.; Jones, M. L.; Gunn, D. E.; Geraci, L. S.; Jones, J. H.; Sawicki, D. R.; Sredy, J.; Jacot, J. L.; DiCioccio, A. T.; Petrova, T.; Mitschler, A.; Podjarny, A. D. Discovery of 3-[(4,5,7-Trifluorobenzothiazol-2-yl)methyl]indole-N-acetic Acid (Lidorestat) and Congeners as Highly Potent and Selective Inhibitors of Aldose Reductase for Treatment of Chronic Diabetic Complications. *J. Med. Chem.* **2005**, *48*, 3141-3152. (b) Kuo, Y.-Y.; Haddow, M. F.; Pérez-Redondo, A.; Owen, G. R. Rhodium and iridium complexes containing diphenyl-2-(3-methyl)indolylphosphine: synthesis, structure and application in the catalytic transfer hydrogenation of ketones. *Dalton Trans.* **2010**, *39*, 6239-6248. (c) Kochanowska-Karamyan, A. J.; Hamann, M. T. Marine Indole Alkaloids: Potential New Drug Leads for the Control of Depression and Anxiety. *Chem. Rev.* **2010**, *110*, 4489-4497. (d) Ishikura, M.; Abe, T.; Choshi, T.; Hibino, S. Simple indole alkaloids and those with a non-rearranged monoterpenoid unit. *Nat. Prod. Rep.* **2013**, *30*, 694-752. (e) Taylor, R. D.; MacCoss, M.; Lawson, A. D. G. Rings in Drugs. *J. Med. Chem.* **2014**, *57*, 5845-5859. (f) Zhang, M.-Z.; Chen, Q.; Yang, G.-F. A review on recent developments of indole-containing antiviral agents. *Eur. J. Med. Chem.* **2015**, *89*, 421-441. (g) Chadha, N.; Silakari, O. Indoles as therapeutics of interest in medicinal chemistry: Bird's eye view. *Eur. J. Med. Chem.* **2017**, *134*, 159-184. (h) Goyal, D.; Kaur, A.; Goyal, B. Benzofuran and Indole: Promising Scaffolds for Drug Development in Alzheimer's Disease. *ChemMedChem.* **2018**, *13*, 1275-1299.

(2) (a) Peat, A. J.; Buchwald, S. L. Novel Syntheses of Tetrahydropyrroloquinolines: Applications to Alkaloid Synthesis. *J. Am. Chem. Soc.* **1996**, *118*, 1028-1030. (b) Liu, P.; Seo, J. H.; Weinreb, S. M. Total Synthesis of the Polycyclic Fungal Metabolite (±)-Communesin F. *Angew. Chem., Int. Ed.* **2010**, *49*, 2000-2003. (c) Bhat, V.; Allan, K. M.; Rawal, V. H. Total Synthesis of N-Methylwelwitindolinone D Isonitrile. *J. Am. Chem. Soc.* **2011**, *133*, 5798-5801.

(3) Iwata, A.; Inuki, S.; Oishi, S.; Fujii, N.; Ohno, H. Formal Total Synthesis of (+)-Lysergic Acid via Zinc(II)-Mediated Regioselective Ring-Opening Reduction of 2-Alkynyl-3-indolyloxirane. *J. Org. Chem.* **2011**, *76*, 5506-5512.

(4) Xu, Z.; Zhang, F.; Zhang, L.; Jia, Y. Total synthesis of (-)-indolactam V. *Org. Biomol. Chem.*

2011, *9*, 2512-2517.

(5) Feldman, K. S.; Ngernmeesri, P. Total Synthesis of (±)-Dragmacidin E. *Org. Lett.* **2011**, *13*, 5704-5707.

(6) Gillmore, A. T.; Badland, M.; Crook, C. L.; Castro, N. M.; Critcher, D. J.; Fussell, S. J.; Jones, K. J.; Jones, M. C.; Kougoulos, E.; Mathew, J. S.; McMillan, L.; Pearce, J. E.; Rawlinson, F. L.; Sherlock, A. E.; Walton, R. Multkilogram Scale-Up of a Reductive Alkylation Route to a Novel PARP Inhibitor. *Org. Process Res. Dev.* **2012**, *16*, 1897-1904.

(7) (a) Minami, Y.; Hiyama, T. Synthetic Transformations through Alkynoxy-Palladium Interactions and C-H Activation. *Acc. Chem. Res.* **2016**, *49*, 67-77. (b) Park, Y.; Kim, Y.; Chang, S. Transition Metal-Catalyzed C-H Amination: Scope, Mechanism, and Applications. *Chem. Rev.* **2017**, *117*, 9247-9301. (c) Hu, Y.; Zhou, B.; Wang, C. Inert C-H Bond Transformations Enabled by Organometallic Manganese Catalysis. *Acc. Chem. Res.* **2018**, *51*, 816-827. (d) Danopoulos, A. A.; Simler, T.; Braunstein, P. N-Heterocyclic Carbene Complexes of Copper, Nickel, and Cobalt. *Chem. Rev.* **2019**, *119*, 3730-3961.

(8) (a) Piou, T.; Bunescu, A.; Wang, Q.; Neuville, L.; Zhu, J. Palladium-Catalyzed Through-Space C(sp3)-H and C(sp^2)-H Bond Activation by 1,4-Palladium Migration: Efficient Synthesis of [3,4]-Fused Oxindoles. *Angew. Chem., Int. Ed.* **2013**, *52*, 12385-12389. (b) Chernyak, N.; Tilly, D.; Li, Z.; Gevorgyan, V. Pd-catalyzed cascade carbopalladation-annulation reaction of 3-(2-iodobenzyl)-indoles into fused 6/5/7/6- and 6/5/5/6- heterocyclic systems. *Chem. Commun.* **2010**, *46*, 150-152. (c) Sickert, M.; Weinstabl, H.; Peters, B.; Hou, X.; Lautens, M. Intermolecular domino reaction of two aryl iodides involving two C-H functionalizations. *Angew. Chem., Int. Ed.* **2014**, *53*, 5147-5151. (d) Hu, T.-J.; Zhang, G.; Chen, Y.-H.; Feng, C.-G.; Lin, G.-Q. Borylation of olefin C-H bond via aryl to vinyl palladium 1,4-migration. *J. Am. Chem. Soc.* **2016**, *138*, 2897-2900. (e) Perez-Gomez, M.; Hernandez-Ponte, S.; Bautista, D.; Garcia-Lopez, J.-A. Synthesis of spiro-oxoindoles through Pd-catalyzed remote C-H alkylation using α-diazocarbonyl compounds. *Chem. Commun.* **2017**, *53*, 2842-2845. (f) Yang, L.; Melot, R.; Neuburger, M.; Baudoin, O. Palladium(0)-catalyzed asymmetric C(sp3)-H arylation using a chiral binol-derived phosphate and an achiral ligand. *Chem. Sci.* **2017**, *8*, 1344-1349. (g) Yao, T.; He, D. Palladium-Catalyzed Domino Heck/Aryne Carbopalladation/C-H Functionalization: Synthesis of Heterocycle-Fused 9,10-Dihydrophenanthrenes. *Org. Lett.* **2017**, *19*, 842-845. (h) Lu, A.; Ji, X.; Zhou, B.; Wu, Z.; Zhang, Y. Palladium-Catalyzed C-H Silylation through Palladacycles Generated from Aryl Halides. *Angew. Chem., Int. Ed.* **2018**, *57*, 3233-3237.

(9) Ramirez, T. A.; Wang, Q.; Zhu, Y.; Zheng, H.; Peng, X.; Cornwall, R. G.; Shi, Y. Pd(0)-Catalyzed Sequential C-N Bond Formation via Allylic and Aromatic C-H Amination of α-Methylstyrenes with Diaziridinone. *Org. Lett.* **2013**, *15*, 4210-4213.

(10) (a) Du, H.; Yuan, W.; Zhao, B.; Shi, Y. Catalytic asymmetric diamination of conjugated dienes and triene. *J. Am. Chem. Soc.* **2007**, *129*, 11688-11689. (b) Zhao, B.; Du, H.; Cui, S.; Shi, Y. Synthetic and Mechanistic Studies on Pd(0)-Catalyzed Diamination of Conjugated Dienes. *J. Am. Chem. Soc.* **2010**, *132*, 3523-3532. (c) Zhao, B.; Peng, X.; Cui, S.; Shi, Y. Cu(I)-Catalyzed Regioselective Diamination of Conjugated Dienes via Dual Mechanistic Pathways. *J. Am. Chem. Soc.* **2010**, *132*, 11009-11011. (d) Zhao, B.; Peng, X.; Zhu, Y.; Ramirez, T. A.; Cornwall, R. G.; Shi, Y. Cu(I)-Catalyzed Diamination of Conjugated Dienes. Complementary Regioselectivity from Two Distinct Mechanistic Pathways Involving Cu(II)

and Cu(III) Species. *J. Am. Chem. Soc.* **2011**, *133*, 20890-20900. (e) Gou, X.-Y.; Li, Y.; Wang, X.-G.; Liu, H.-C.; Zhang, B.-S.; Zhao, J.-H.; Zhou, Z.-Z.; Liang, Y.-M. Ruthenium-catalyzed ortho-selective CAr-H amination of heteroaryl arenes with di-tert-butyldiaziridinone. *Chem. Commun.* **2019**, *55*, 5487-5490. (f) Dai, Q.; Zhao, B.; Yang, Y.; Shi, Y. Pd-Catalyzed Oxidative Heck Reaction of Grignard Reagents with Diaziridinone as Oxidant. *Org. Lett.* **2019**, *21*, 5157-5161.

(11) Zheng, H.; Zhu, Y.; Shi, Y. Palladium(0)-Catalyzed Heck Reaction/C-H Activation/Amination Sequence with Diaziridinone: A Facile Approach to Indolines. *Angew. Chem., Int. Ed.* **2014**, *53*, 11280-11284.

(12) Shao, C.; Zhou, B.; Wu, Z.; Ji, X.; Zhang, Y. Synthesis of Carbazoles from 2-Iodobiphenyls by Palladium-Catalyzed C-H Activation and Amination with Diaziridinone. *Adv. Synth. Catal.* **2018**, *360*, 887-892.

(13) Ma, D.; Ji, X.; Wu, Z.; Cheng, C.; Zhou, B.; Zhang, Y. Synthesis of Benzimidazoles through Palladium-Catalyzed Amination of 2-Iodobenzimines with Diaziridinone. *Adv. Synth. Catal.* **2019**, *361*, 739-746.

(14) Zhou, B.; Wu, Z.; Ma, D.; Ji, X.; Zhang, Y. Synthesis of Indoles through Palladium-Catalyzed Three-Component Reaction of Aryl Iodides, Alkynes, and Diaziridinone. *Org. Lett.* **2018**, *20*, 6440-6443.

(15) Sun, X.; Wu, Z.; Qi, W.; Ji, X.; Cheng, C.; Zhang, Y. Synthesis of Indolines by Palladium-Catalyzed Intermolecular Amination of Unactivated C(sp3)-H Bonds. *Org. Lett.* **2019**, *21*, 6508-6512.

(16) Cheng, C.; Zuo, X.; Tu, D.; Wan, B.; Zhang, Y. Synthesis of 3,4-Fused Tricyclic Indoles through Cascade Carbopalladation and C-H Amination: Development and Total Synthesis of Rucaparib. *Org. Lett.* **2020**, *22*, 4985-4989.

(17) (a) Liang, Y.; Yu, K.; Li, B.; Xu, S.; Song, H.; Wang, B. Rh(III)-catalyzed synthesis of 1-aminoindole derivatives from 2-acetyl-1-arylhydrazines and diazo compounds in water. *Chem. Commun.* **2014**, *50*, 6130-6133. (b) Li, D. Y.; Chen, H. J.; Liu, P. N. Rhodium-Catalyzed Oxidative Annulation of Hydrazines with Alkynes Using a Nitrobenzene Oxidant. *Org. Lett.* **2014**, *16*, 6176-6179. (c) Li, Y.; Qi, Z.; Wang, H.; Yang, X.; Li, X. Ruthenium(II)-Catalyzed C-H Activation of Imidamides and Divergent Couplings with Diazo Compounds: Substrate-Controlled Synthesis of Indoles and 3H-Indoles. *Angew. Chem., Int. Ed.* **2016**, *55*, 11877-11881. (d) Yang, Z.; Lin, X.; Wang, L.; Cui, X. Facile synthesis of 1-aminoindoles via Rh(III)-catalyzed intramolecular three-component annulation. *Org. Chem. Front.* **2017**, *4*, 2179-2183. (e) Shi, P.; Wang, L.; Guo, S.; Chen, K.; Wang, J.; Zhu, J. A C-H Activation-Based Strategy for N-Amino Azaheterocycle Synthesis. *Org. Lett.* **2017**, *19*, 4359-4362. (f) Xie, W.; Chen, X.; Shi, J.; Li, J.; Liu, R. Synthesis of 1-aminoindole derivatives via Rh(III)-catalyzed annulation reactions of hydrazines with sulfoxonium ylides. *Org. Chem. Front.* **2019**, *6*, 2662-2666. (g) Thombal, R. S.; Lee, Y. R. Palladium-Catalyzed Direct Oxidative C-H Activation/Annulation for Regioselective Construction of N-Acylindoles. *Org. Lett.* **2020**, *22*, 3397-3401.

(18) (a) Qin, H.; Xu, Z.; Cui, Y.; Jia, Y. Total Synthesis of (±)-Decursivine and (±)-Serotobenine: A Witkop Photocyclization/Elimination/O-Michael Addition Cascade Approach. *Angew. Chem., Int. Ed.* **2011**, *50*, 4447-4449. (b) Breazzano, S. P.; Poudel, Y. B.; Boger, D. L. A Pd(0)-Mediated Indole (Macro)cyclization Reaction. *J. Am. Chem. Soc.* **2013**, *135*, 1600-1606.

(c) Liu, Q.; Zhang, Y.-A.; Xu, P.; Jia, Y. Total Synthesis of (+)-Lysergic Acid. *J. Org. Chem.* **2013**, *78*, 10885-10893. (d) Guo, L.; Zhang, F.; Hu, W.; Li, L.; Jia, Y. Palladium-catalyzed synthesis of benzofurans via C-H activation/oxidation tandem reaction and its application to the synthesis of decursivine and serotobenine. *Chem. Commun.* **2014**, *50*, 3299-3302. (e) Zhou, B.; Yang, Y.; Tang, H.; Du, J.; Feng, H.; Li, Y. Rh(III)-Catalyzed Intramolecular Redox-Neutral or Oxidative Cyclization of Alkynes: Short, Efficient Synthesis of 3,4-Fused Indole Skeletons. *Org. Lett.* **2014**, *16*, 3900-3903.

(19) Shan, D.; Gao, Y.; Jia, Y. Intramolecular Larock Indole Synthesis: Preparation of 3,4-Fused Tricyclic Indoles and Total Synthesis of Fargesine. *Angew. Chem., Int. Ed.* **2013**, *52*, 4902-4905.

(20) Tao, P.; Jia, Y. Rhodium-catalyzed intramolecular annulation via C-H activation leading to fused tricyclic indole scaffolds. *Chem. Commun.* **2014**, *50*, 7367-7370.

(21) Fan, L.; Hao, J.; Yu, J.; Ma, X.; Liu, J.; Luan, X. Hydroxylamines As Bifunctional Single-Nitrogen Sources for the Rapid Assembly of Diverse Tricyclic Indole Scaffolds. *J. Am. Chem. Soc.* **2020**, *142*, 6698-6707.

(22) (a) Zuo, Z.; Liu, J.; Nan, J.; Fan, L.; Sun, W.; Wang, Y.; Luan, X. Highly Stereoselective Synthesis of Imine-Containing Dibenzo[b,d]azepines by a Palladium(II)-Catalyzed [5+2] Oxidative Annulation of o-Arylanilines with Alkynes. *Angew. Chem., Int. Ed.* **2015**, *54*, 15385-15389. (b) Yang, L.; Zheng, H.; Luo, L.; Nan, J.; Liu, J.; Wang, Y.; Luan, X. Palladium-Catalyzed Dynamic Kinetic Asymmetric Transformation of Racemic Biaryls: Axial-to-Central Chirality Transfer. *J. Am. Chem. Soc.* **2015**, *137*, 4876-4879. (c) Zuo, Z.; Wang, H.; Fan, L.; Liu, J.; Wang, Y.; Luan, X. Modular Assembly of Spirocarbocyclic Scaffolds through Pd0-Catalyzed Intermolecular Dearomatizing [2+2+1] Annulation of Bromonaphthols with Aryl Iodides and Alkynes. *Angew. Chem., Int. Ed.* **2017**, *56*, 2767-2771. (d) Fan, L.; Liu, J.; Bai, L.; Wang, Y.; Luan, X. Rapid Assembly of Diversely Functionalized Spiroindenes by a Three-Component Palladium-Catalyzed C-H Amination/Phenol Dearomatization Domino Reaction. *Angew. Chem., Int. Ed.* **2017**, *56*, 14257-14261. (e) Bai, L.; Liu, J.; Hu, W.; Li, K.; Wang, Y.; Luan, X. Palladium/Norbornene-Catalyzed C-H Alkylation/Alkyne Insertion/Indole Dearomatization Domino Reaction: Assembly of Spiroindolenine-Containing Pentacyclic Frameworks. *Angew. Chem., Int. Ed.* **2018**, *57*, 5151-5155. (f) Tan, B.; Bai, L.; Ding, P.; Liu, J.; Wang, Y.; Luan, X. Palladium-Catalyzed Intermolecular [4+1] Spiroannulation by C(sp3)-H Activation and Naphthol Dearomatization. *Angew. Chem., Int. Ed.* **2019**, *58*, 1474-1478.

(23) (a) Jiang, X.; Chen, J.; Zhu, W.; Cheng, K.; Liu, Y.; Su, W.-K.; Yu, C. Cobalt(III)-Catalyzed Fast and Solvent-Free C-H Allylation of Indoles Using Mechanochemistry. *J. Org. Chem.* **2017**, *82*, 10665-10672. (b) Zhang, L.; Zheng, X.; Chen, J.; Cheng, K.; Jin, L.; Jiang, X.; Yu, C. Ru(II)-Catalyzed C6-Selective C-H Amidation Of 2-Pyridones. *Org. Chem. Front.* **2018**, *5*, 2969-2973. (c) Zhang, L.; Chen, J.; Chen, J.; Jin, L.; Zheng, X.; Jiang, X.; Yu, C. Synthesis of 2-substituted indoles by iridium (III)-catalyzed C-H functionalization of N-phenylpyridin-2-amines. *Tetrahedron Lett.* **2019**, *60*, 1053-1056. (d) Chen, J.; Jin, L.; Zhou, J.; Jiang, X.; Yu, C. Cobalt-catalyzed electrochemical C-H/N-H functionalization of N-(quinolin-8-yl)benzamide with isocyanides. *Tetrahedron Lett.* **2019**, *60*, 2054-2058. (e) Zhang, L.; Chen, J.; Chen, X.; Zheng, X.; Zhou, J.; Zhong, T.; Chen, Z.; Yang, Y.-F.; Jiang, X.; She, Y.-B.; Yu, C. Rh(III)-catalyzed, hydrazine-directed C-H functionalization with

1-alkynylcyclobutanols: a new strategy for 1H-indazoles. *Chem. Commun.* **2020**, *56*, 7415-7418.

(24) (a) Jiang, X.; Li, G.; Yu, C. Synthesis of N-aryl-3-(arylimino)-3H-indo1-2-amines via hypervalent iodine promoted oxidative diamination of indoles. *Tetrahedron Lett.* **2018**, *59*, 1506-1510. (b) Jiang, X.; Zheng, C.; Lei, L.; Lin, K.; Yu, C. Synthesis of 2-Oxindoles from Substituted Indoles by Hypervalent-Iodine Oxidation. *Eur. J. Org. Chem.* **2018**, 1437-1442. (c) Jiang, X.; Zhu, B.; Lin, K.; Wang, G.; Su, W.-K.; Yu, C. Metal-free synthesis of 2,2-disubstituted indolin-3-ones. *Org. Biomol. Chem.* **2019**, *17*, 2199-2203. (d) Jiang, X.; Zhu, W.; Yang, L.; Zheng, Z.; Yu, C. Hypervalent Iodine-Mediated Cyclization of Homotryptamine Derivatives. *Eur. J. Org. Chem.* **2019**, 2268-2274.

(25) Zlatopolskiy, B. D.; Zischler, J.; Schaefer, D.; Urusova, E. A.; Guliyev, M.; Bannykh, O.; Endepols, H.; Neumaier, B. Discovery of 7-[18F]Fluorotryptophan as a Novel Positron Emission Tomography (PET) Probe for the Visualization of Tryptophan Metabolism in Vivo. *J. Med. Chem.* **2018**, *61*, 189-206.

(26) (a) Zhang, X.; Liu, H.; Jia, Y. A palladium-catalyzed intramolecular carbonylative annulation reaction for the synthesis of 4,5-fused tricyclic 2-quinolones. *Chem. Commun.* **2016**, *52*, 7665-7667. (b) Bai, L.; Yuan, Y.; Liu, J.; Wu, J.; Han, L.; Wang, H.; Wang, Y.; Luan, X. Palladium(0)-Catalyzed Intermolecular Carbocyclization of (1,n)-Diynes and Bromophenols: An Efficient Route to Tricyclic Scaffolds. *Angew. Chem., Int. Ed.* **2016**, *55*, 6946-6950. (c) Nan, J.; Yuan, Y.; Bai, L.; Liu, J.; Luan, X. Highly Chemoselective Construction of Spiro[4,5]decane-Embedded Polycyclic Scaffolds by a Palladium/Norbornene-Catalyzed C-H Activation/Arene Dearomatization Reaction. *Org. Lett.* **2018**, *20*, 7731-7734. (d) Zuo, Z.; Wang, J.; Liu, J.; Wang, Y.; Luan, X. Palladium-Catalyzed [2+2+1] Spiroannulation via Alkyne-Directed Remote C-H Arylation and Subsequent Arene Dearomatization. *Angew. Chem., Int. Ed.* **2020**, *59*, 653-657.

(27) (a) Fillion, E.; Trepanier, V. E.; Heikkinen, J. J.; Remorova, A. A.; Carson, R. J.; Goll, J. M.; Seed, A. Palladium-catalyzed intramolecular reactions of (E)-2,2-disubstituted 1-alkenyldimethylalanes with aryl triflates. *Organometallics.* **2009**, *28*, 3518-3531. (b) Willand-Charnley, R.; Puffer, B. W.; Dussault, P. H. Oxacycle Synthesis via Intramolecular Reaction of Carbanions and Peroxides. *J. Am. Chem. Soc.* **2014**, *136*, 5821-5823.

(28) Wagner, M.; Schepmann, D.; Ametamey, S. M.; Wuensch, B. Modification of the 4-phenylbutyl side chain of potent 3-benzazepine-based GluN2B receptor antagonists. *Bioorg. Med. Chem.* **2019**, *27*, 3559-3567.

(29) (a) Sylvester, K. T.; Chirik, P. J. Iron-Catalyzed, Hydrogen-Mediated Reductive Cyclization of 1,6-Enynes and Diynes: Evidence for Bis(imino)pyridine Ligand Participation. *J. Am. Chem. Soc.* **2009**, *131*, 8772-8774. (b) Kinoshita, H.; Miyama, C.; Miura, K. Cyclization of alk-5-ynyl ketones promoted by Tf2NH and In(OTf)3: selective synthesis of 5- and 7-membered carbocycles. *Tetrahedron Lett.* **2016**, *57*, 5065-5069.

(30) Nagarjuna Reddy, M.; Kumara Swamy, K. C. Facile Construction of [6,6]-, [6,7]-, [6,8]-, and [6,9]Ring-Fused Triazole Frameworks by Copper-Catalyzed, Tandem, One-Pot, Click and Intramolecular Arylation Reactions: Elaboration to Fused Pentacyclic Derivatives. *Eur. J. Org. Chem.* **2012**, 2013-2022.

(31) Du, H.; Zhao, B.; Shi, Y. Catalytic asymmetric allylic and homoallylic diamination of terminal olefins via Formal C-H Activation. *J. Am. Chem. Soc.* **2008**, *130*, 8590-8591.