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Synthesis of Functionalized Indolizines via Gold(I)-Catalyzed Intramolecular Hydroarylation/aromatization of Pyrrole-Ynes

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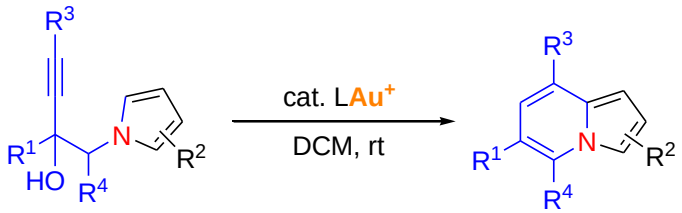

R^2 = H, alkyl, aryl, EWG *20 examples with up to 98% yield*

- *pyridine ring construction*
- *mild reaction conditions*
- *wide functional group compatibility*
- *high efficiency*

Abstract: A gold-catalyzed intramolecular hydroarylation/aromatization of pyrrole-ynes has been developed. The method provides a concise and straightforward route to functionalized indolizines through the construction of the pyridine ring of indolizines, and also allows elaboration of its pyrrole moiety with or without functional groups. In addition, a wide variety of the functional groups, such as aryl, alkenyl, alkynyl, pyridyl or thienyl groups can be easily incorporated into the pyridine unit of the indolizine products under mild conditions. The utility of the indolizine products was demonstrated by their efficient transformations into various C3-functionalized indolizine derivatives.

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INTRODUCTION

Indolizines are important *N*-fused aromatic heterocycles, which have attracted a lot of attention due to their pharmacological potential and unique photophysical properties. Many of the synthetic indolizines have displayed important biological activities,[1] such as antibacterial,[1b] antiproliferative activity,[1c] 15-lipoxygenase inhibitor,[1d] and H_3 receptor antagonist[1e] etc (Figure 1). They have also found utilities in the field of materials science[2]

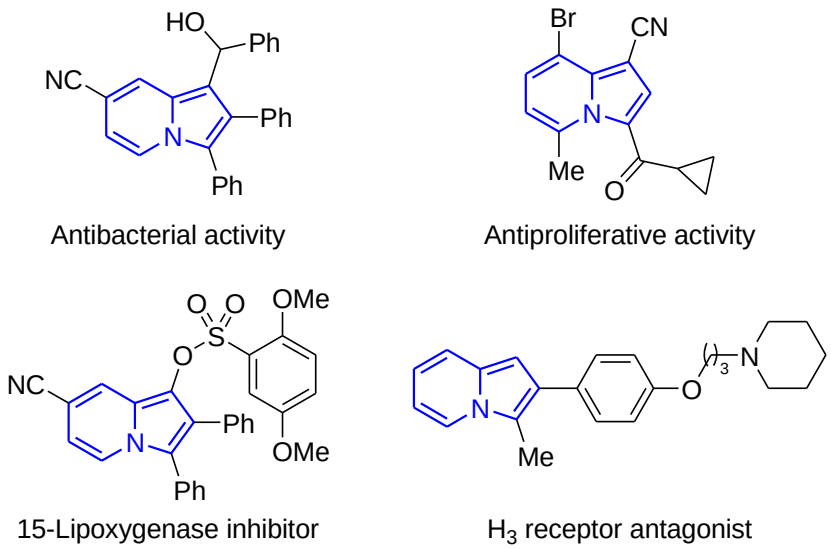

Figure 1. Representative biologically active indolizine derivatives

such as organic light emitting devices (OLEDs),[2a] fluorescent probes,[2b] and biological markers.[2c] Therefore, the development of efficient methods for the construction of functionalized indolizines has gained much attention.[3] Documented approaches to indolizines mainly involve Scholtz reaction,[4] Tschitschibabin reaction,[5] dipolar cycloadditions of pyridinium ylides with electron-deficient alkynes or alkenes,[6]

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transition-metal-catalyzed cycloisomerizations of alkynylpyridine or propargyl pyridine derivatives,[7] etc. These reactions generally focused on the construction of the pyrrole ring from pyridine derivatives. In contrast, few methods have allowed the formation of the pyridine ring from pyrrole derivatives,[8,9] and most of them limited to the synthesis of benzofused derivatives,[8e-g] or restricted to activated substrates[8h] (Scheme 1**a**). In line with the latter strategy, we recently developed an efficient route to highly substituted indolizines via gold-catalyzed[10] intermolecular hydroarylation/cycloaromatization of α-(*N*-pyrrolyl)ketones with alkynes (Scheme 1**b**).[9] However, in this method, the substrates bearing one or more substituents on the pyrrole ring were required in order to improve the regioselectivity of the intermolecular hydroarylation, leading to indolizines with limited substitution pattern on the pyrrole ring. For example, indolizines with a non-substituted pyrrole ring could not be constructed efficiently by this method.[11] To solve this problem, we envisioned that a gold-catalyzed intramolecular hydroarylation/aromatization of pyrrole-ynes might be utilized for the synthesis of indolizines with a wider diversity, especially, on their pyrrole rings (Scheme 1**c**). In this strtagy, both of the pyrrole-ynes with or without substituents on the pyrrole ring might be feasible due to the enhanced regioselectivity of the intramolecular hydroarylation[12] compared with that of intermolecular hydroarylation reactions, in which hydroarylation would occur predominantly at the C-2 position of the pyrrole moiety. Furthermore, the method would also allow for installing the C-5, C-6, and C-8 substituents on the resulting indolizines, which are not easily accessible with the existing methods. Herein, we report the facile synthesis of functionalized indolizines based on the above strategy.

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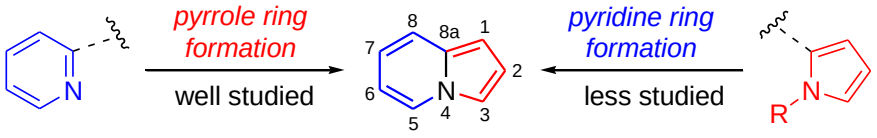
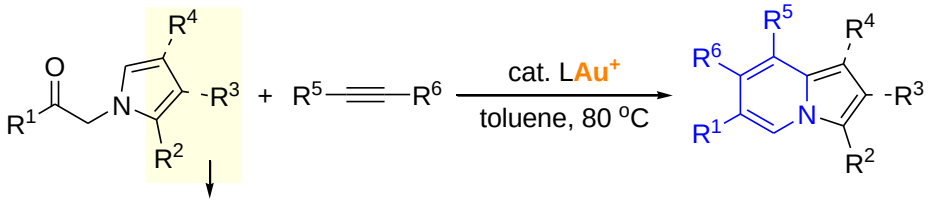
Scheme 1. Synthesis of Indolizines

a. Two complementary pathways towards the indolizine scaffold

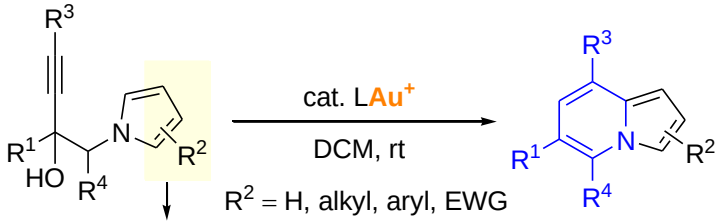


b. Intermolecular hydroarylation/cycloaromatization to indolizines (our previous work)



one or more substituents on the pyrrole ring are required

c. Intramolecular hydroarylation/aromatization to indolizines (this work)



with or without substituents on the pyrrole ring

RESULTS AND DISCUSSION

Pyrrole-ynes **2** employed in the present study could be prepared through addition of alkynylithium reagent to α-(*N*-pyrrolyl)ketones **1**. α-(*N*-pyrrolyl)ketones **1** are usually prepared by the reaction of *N*-H pyrrole with alkylating reagents in the presence of a base.[13] However, when free pyrrole was employed as the substrate, we failed to achieve satisfactory yields of the target products using α-bromoketones such as 2-bromo-1-phenylethanone as the alkylating reagent. After some trails, it was found that *N*-alkylation of pyrrole proceeded cleanly using 1-bromo-but-3-yn-2-ols as the alkylating reagent,[14] which also functioned as a synthetic equivalent of α-bromoketone through elimination of an alkynyl group in this reaction. Addition of alkynylithium reagent to the

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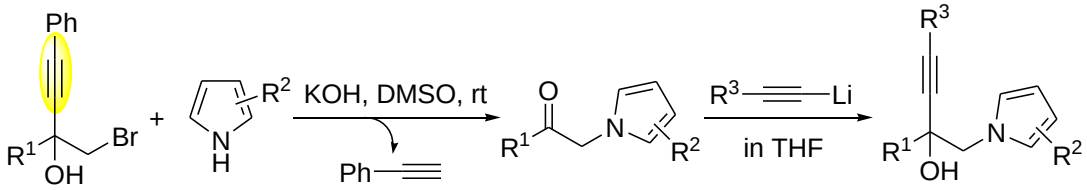
resulting *N*-substituted pyrroles **1** provided the substrate **2** (Scheme 2). The method allows for the convenient incorporation of various functional groups on either alkyne or pyrrole moiety in **2**, and was used for the synthesis of the most of the substrates.

Scheme 2. Synthesis of Pyrrole-ynes 2



masked α-bromoketones

For our initial experiments, we focused on the optimization of the gold-catalyzed cyclization of **2a** (Table 1). To our delight, the expected indolizine **3a** was obtained in 92% yield in the presence of 5 mol% Johnphos(MeCN)AuSbF$_6$ (catalyst **A**) in DCE at room temperature for 9 h (Table 1, entry 1). The reaction could also proceed in various solvents such as DCM, toluene, CH$_3$CN or THF, leading to **3a** in 93-94% yields (Table 1, entries 2-5). Further optimization indicated that *N*-heterocyclic carbene gold(I) complex of IPrAuCl/AgSbF$_6$ (IPr = 2,6-bis(diisopropylphenyl)imidazol-2-ylidene) displayed more efficient catalytic activity by shortening the reaction time dramatically to 2 h (Table 1, entry 6). However, the use of more electrophilic PPh$_3$AuCl/AgSbF$_6$ led to 91% yield of **3a** with a prolonged reaction time (Table 1, entry 7). With IPrAuCl as the gold catalyst, the effects of counter anions such as OTs$^-$, BF$_4^-$ or PF$_6^-$ were also examined (Table 1, entries 8-10). Gratifyingly, it was found that PF$_6^-$ was highly efficient for this transformation, leading to **3a** in 96% yield within 3 min, possibly due to the more weakly coordinating

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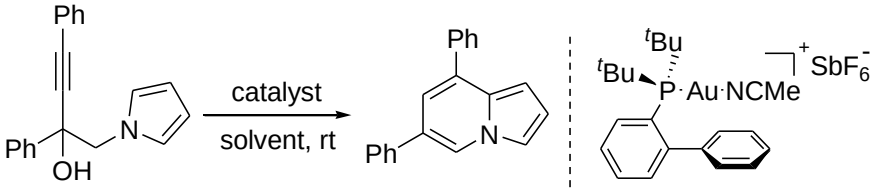
ability of this anion with gold (Table 1, entry 10). When the catalyst loading was lowered to 1-2 mol%, good results could also be obtained with a slightly prolonged reaction time (Table 1, entries 11-12). The use of $AgPF_6$ alone only provided little amounts of the desired product (Table 1, entry 13). Brønsted acid such as $HNTf_2$ or Lewis acid such as $Sc(OTf)_3$ failed to catalyze the reaction (Table 1, entries 14-15).

Table 1. Optimization of the Catalytic System



2a **3a** catalyst **A**

entry	catalyst (mol%)	solvent	time	yield (%)[a]
1	catalyst **A** (5)	DCE	9 h	92
2	catalyst **A** (5)	DCM	8 h	94
3	catalyst **A** (5)	toluene	8 h	93
4	catalyst **A** (5)	CH_3CN	32 h	93
5	catalyst **A** (5)	THF	19 h	93
6	IPrAuCl/$AgSbF_6$ (5)	DCM	2 h	94
7	PPh_3AuCl/$AgSbF_6$ (5)	DCM	36 h	91
8	IPrAuCl/AgOTs (5)	DCM	15 min	96
9	IPrAuCl/$AgBF_4$ (5)	DCM	0.5 h	95
10	IPrAuCl/$AgPF_6$ (5)	DCM	3 min	96
11	IPrAuCl/$AgPF_6$ (2)	DCM	10 min	97
12	IPrAuCl/$AgPF_6$ (1)	DCM	1 h	96
13	$AgPF_6$ (5)	DCM	42 h	7[b]
14	$HNTf_2$ (10)	DCM	24 h	0[c]
15	$Sc(OTf)_3$ (5)	DCM	24 h	0[d]

[a]Isolated yields. [b]**2a** was recovered in 82% yield. [c]**2a** was recovered in 67% yield. [d]**2a** was recovered in 93% yield.

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With an optimized set of conditions in hand (Table 1, entry 11), we focused our attention on the preparative scope of the reaction. Gratifyingly, this reaction proved to be quite general with respect to the substitution pattern on the pyrrole ring and the alkyne terminus. In most cases, the desired indolizine products were obtained in high to excellent yields (Table 2). We first investigated the effect of substituents on the alkyne terminus. In the cases of aryl-substituted alkynes, various functional groups on the aryl ring are compatible. For example, both electron-rich (*p*-OMe, *p*-NH_2) aryl alkynes and electron deficient (*p*-CF_3) underwent the reaction smoothly, providing the corresponding products **3b-3d** in high yields of 86-94%. 2-Pyridyl and 2-thienyl groups were also tolerated well in the reaction and afforded **3e-3f** in 85-97% yields. In the case of pyridine-substituted substrate, higher reaction temperature of 80 ^{o}C was required in order to achieve a better yield. Reaction of the cyclohexenyl-substituted **2g** gave **3g** in high yield of 94%. Interestingly, substrate bearing an alkynyl substituent on the alkyne terminus proved to be also suitable for the reaction, providing alkynyl indolizine **3h** in 54% yield. The reactions of alkyl-substituted alkynes such as n-butyl-, tert-butyl, or cyclopropyl-substituted ones were also satisfactory, leading to **3i-3k** in 80-96% yields. Terminal alkyne also worked but with a prolonged time, and the desired product **3l** was isolated in high yield of 90%. Silyl-substituted substrates, such as TMS-substituted one transformed to **3m** successfully in 84% yield. The substrate bearing a methyl substituent as R^1 gave 6-methylindolizine **3n** in 91% yield. The substrates bearing a methyl or a benzyl substituent as R^4 gave 5, 6, 8-tri-substituted indolizines **3o** and **3p** in 98% and 95% yields, respectively. Next, we

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anticipated that the use of substrates derived from functionalized pyrroles would enable the incorporation of substituents on the pyrrole ring of indolizine scaffold. As for the pyrrole moiety in pyrrole-yne **2**, substrates derived from 2,4-dimethyl pyrrole and 2,3-diphenyl pyrrole worked well to provide **3q-3r** in 66-97% yields. Substrate bearing an electron-withdrawing group such as a cyano group on the pyrrole moiety was also tolerated, and the corresponding product of **3s** was obtained in 93% yield. The reaction could also be extended efficiently to a substrate derived from indole, in which pyrido[1,2-*a*]indole **3t** was obtained in 55% yield.

Table 2. Substrate Scope of the Gold-Catalyzed Indolizine Synthesis[a]

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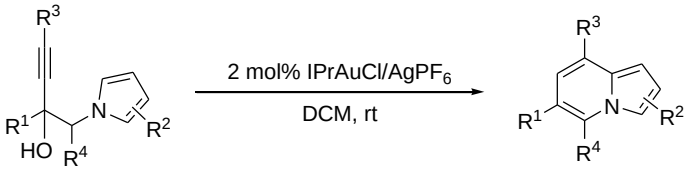
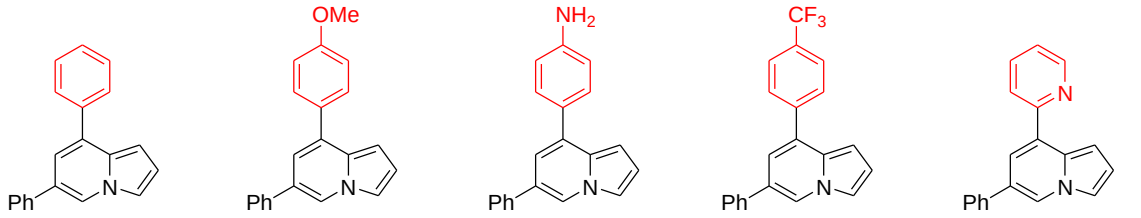


2 **3**



3a, 10 min, 97% **3b**, 10 min, 94% **3c**, 30 min, 91% **3d**, 10 min, 86% **3e**, 1 h, 85%[b]

3f, 10 min, 97% **3g**, 2 h, 94% **3h**, 1 h, 54% **3i**, 10 min, 90% **3j**, 24 h, 80%

3k, 10 min, 96% **3l**, 36 h, 90% **3m**, 24 h, 84%[c] **3n**, 0.5 h, 91%[b] **3o**, 1 h, 98%

3p, 16 h, 95% **3q**, 10 min, 66% **3r**, 30 min, 97% **3s**, 48 h, 93%[d] **3t**, 5 h, 55%[b]

[a]Isolated yields. [b]5 mol% IPrAuCl/$AgPF_6$, DCE, 80 °C. [c]5 mol% IPrAuCl/$AgSbF_6$. [d]5 mol% IPrAuCl/$AgPF_6$, 40 °C.

To explore the potential synthetic utility of the methodology, further derivatization of indolizine products **3** were carried out (Scheme 3). For examples, **3a** could be alkenylated at its C3-position regioselectively via gold-catalyzed hydroarylation of alkyne[15] to produce **4** in 65% yield. CuI-catalyzed C3 thioetherfication of **3a** using 1,2-diphenyldisulfane[16] as the reactant afforded **5** in 72% yield. Gold(I)-catalyzed alkynylation of **3a** with an alkynyl

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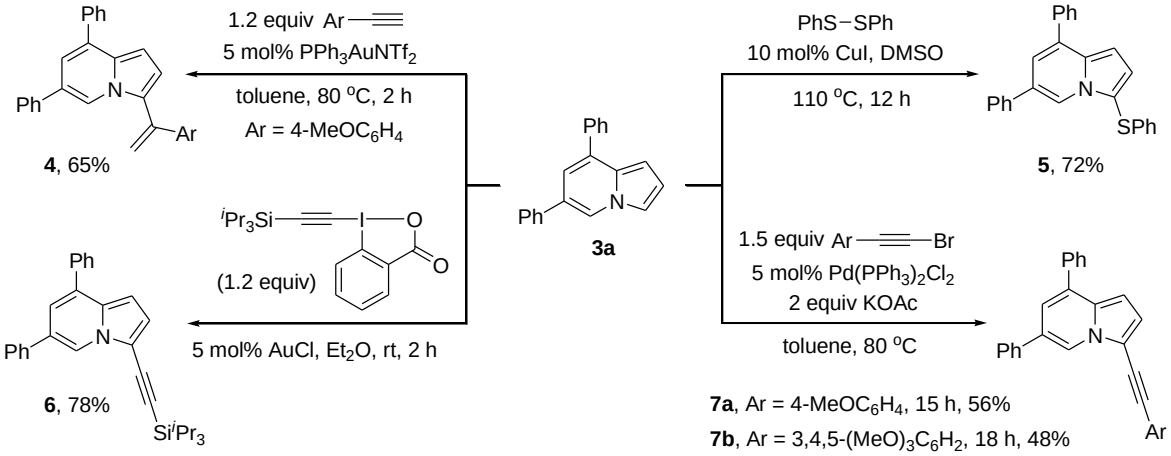
hypervalent iodine reagent[17] provided C3-alkynylated indolizine **6** in 78% yield. In addition, palladium-catalyzed alkynylation of **3a** with alkynyl bromide[18] afforded 3-alkynyl substituted indolizine **7a** and **7b** in 48-56% yields. The structure of **7b** was unambiguously confirmed by X-ray crystallographic analysis.[19]

Scheme 3. Functionalization of Indolizine 3a



A possible[20] reaction mechanism for the present Au(I)-catalyzed indolizine synthesis is illustrated in Scheme 4. Initially, the propargylic alcohol was activated by gold catalyst through coordination, this is followed by regioselective intramolecular hydroarylation of the alkyne with the pyrrole moiety to afford the vinylgold intermediate **9**. Protodeauration of **9** followed by elimination of water[21] leads to the final product **3**.

Scheme 4. Proposed Reaction Mechanism

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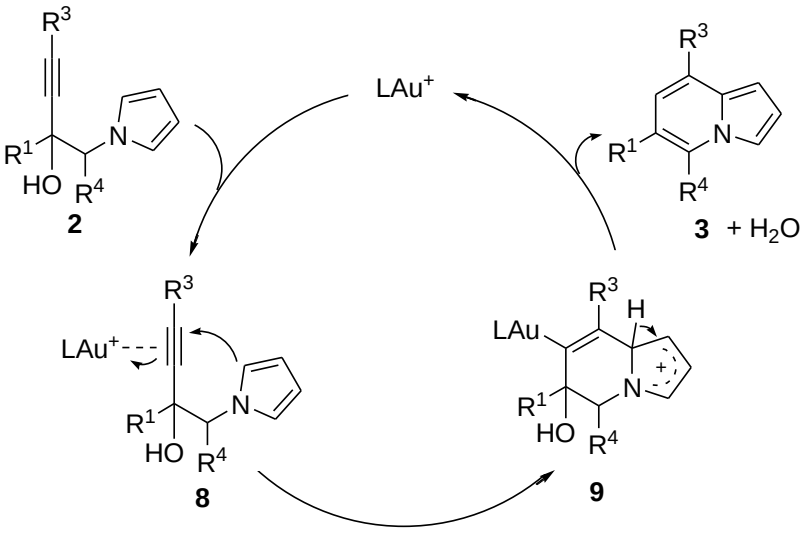

CONCLUSION

In summary, we have developed an efficient method for the synthesis of multi-substituted indolizines based on gold-catalyzed intramolecular hydroarylation/aromatization of pyrrole-ynes. The method allows for accessing indolizines with or without functional groups on its pyrrole ring. In addition, a wide variety of the functional groups, such as aryl, alkenyl, alkynyl, pyridyl or thienyl groups can also be easily incorporated into the pyridine unit of the indolizine products. The utility of indolizine products was demonstrated by their efficient transformations into various 3-functionalized indolizine derivatives.

EXPERIMENTAL SECTION

General Methods. All reactions were carried out using standard Schlenk technique under Argon unless noted. DCM and DCE were distilled from CaH_2. Toluene and THF were distilled from sodium and benzophenone. MeCN and THF (for the synthesis of starting materials) were dried using Innovative Technology Solvent Purifier. Unless noted, all

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commercial reagents were used without further purification. Ph_3PAuCl[22] was prepared according to the published method. (Acetonitrile)[(2-biphenyl)di-*tert*-butylphosphine]gold(I) hexafluoroantimonate (catalyst **A**), 1,3-Bis(2,6-di-isopropylphenyl)-imidazole-2-ylidenegold(I) chloride and $AgSbF_6$ were purchased from Chemical Company. ^1H and ^{13}C NMR spectra were recorded on 400 MHz NMR spectrometer. ^1H NMR spectra was recorded with tetramethylsilane (δ = 0.00 ppm) as an internal reference; ^{13}C NMR spectra was recorded with $CDCl_3$ (δ = 77.00 ppm) or C_6D_6 (δ = 128.06 ppm) as an internal reference. High-resolution mass spectra was performed on a mass spectrometer with a TOF analyzer. Melting points were measured using a SGW-4 microscopic melting point apparatus.

Synthesis of α-(*N*-pyrrolyl)ketones 1a-1d.

Typical procedure for the synthesis of 1-phenyl-2-(1*H*-pyrrol-1-yl)ethan-1-one (1a). Under argon, to a Schlenk tube were added DMSO (60 mL), pyrrole (4.04 mL, 58.2 mmol) and KOH (4.35 g, 77.6 mmol). The resulting mixture was stirred at room temperature for 1 h. Then, 1-bromo-2,4-diphenylbut-3-yn-2-ol (5.84 g, 19.4 mmol) in DMSO (10 mL) was added dropwise. The reaction mixture was stirred at room temperature for another 10 h. Then the mixture was quenched with water, extracted with ethyl acetate, washed with brine and dried over anhydrous Na_2SO_4. The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: petroleum ether: dichloromethane = 2:1) to afford **1a** (3.11 g, 87% yield) as a light yellow solid. ^1H NMR (400 MHz, $CDCl_3$) δ 7.96-7.93 (m, 2H), 7.64-7.59 (m, 1H), 7.51-7.47 (m, 2H), 6.66

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(t, J = 2.4 Hz, 2H), 6.24 (t, J = 2.4 Hz, 2H), 5.29 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.3, 134.6, 133.9, 128.9, 127.9, 121.9, 109.0, 55.3. The spectroscopic data is in agreement with that previously reported.[12a] In another experiment, phenylacetylene was detected as a by-product through analyzing the crude reaction mixture by NMR, which revealed that the alkynyl group was eliminated to furnish a ketone functionality in the reaction.

2-(2,4-Dimethyl-1*H*-pyrrol-1-yl)-1-phenylethan-1-one (1b). 8 mmol scale. 3.0 equiv of 2,4-dimethyl-1*H*-pyrrole (24.0 mmol, 2.28 g) and 4.0 equiv of KOH were used. Column chromatography on silica gel (eluent: petroleum ether: ethyl acetate: dichloromethane = 30:1:3) afforded the title product in 65% yield (1.11 g) as a light yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96-7.94 (m, 2H), 7.63-7.59 (m, 1H), 7.51-7.47 (m, 2H), 6.31 (s, 1H), 5.82 (s, 1H), 5.14 (s, 2H), 2.08 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.7, 134.6, 133.8, 128.9, 128.8, 127.8, 118.7, 118.1, 109.0, 52.6, 11.8, 11.7. The spectroscopic data is in agreement with that previously reported.[9]

2-(2,3-Diphenyl-1*H*-pyrrol-1-yl)-1-phenylethan-1-one (1c). 6 mmol scale. 1.5 equiv of of 2,3-diphenyl-1*H*-pyrrole and 2 equiv of KOH (12 mmol, 673 mg) were used. Column chromatography on silica gel (eluent: petroleum ether: dichloromethane = 4:1 to 3:1) afforded the title product in 81% yield (1.64 g) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78-7.76 (m, 2H), 7.55-7.51 (m, 1H), 7.40-7.37 (m, 2H), 7.27-7.17 (m, 7H), 7.15-7.12 (m, 2H), 7.07-7.03 (m, 1H), 6.74 (d, J = 2.8 Hz, 1H), 6.54 (d, J = 2.8 Hz, 1H),

5.14 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.9, 136.3, 134.5, 133.7, 132.3, 130.9, 130.8, 128.7, 128.6, 127.9, 127.81, 127.77, 127.6, 125.0, 122.8, 122.3, 108.9, 53.1. The spectroscopic data is in agreement with that previously reported.[9]

2-(1*H*-Indol-1-yl)-1-phenylethan-1-one (1d). 8 mmol scale. 1.0 equiv of indole and 2 equiv of KOH were used. Column chromatography on silica gel (eluent: petroleum ether: ethyl acetate: dichloromethane = 30:1:10) afforded the title product in 78% yield (1.47 g) as a white solid. M.p. 124-125 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88-7.86 (m, 2H), 7.65-7.62 (m, 1H), 7.57-7.53 (m, 1H), 7.43-7.39 (m, 2H), 7.16-7.07 (m, 3H), 6.97 (d, *J* = 3.2 Hz, 1H), 6.56 (d, *J* = 3.2 Hz, 1H), 5.27 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.1, 136.5, 134.5, 133.8, 128.8, 128.7, 128.5, 127.9, 121.8, 121.0, 119.6, 108.9, 102.2, 52.0; IR (neat): 3048, 2920, 1692, 1512, 1483, 1464, 1449, 1324, 1224, 1002, 983, 755, 740, 724, 688, 660 cm^{-1}; HRMS (ESI) calcd for $C_{16}H_{14}NO$ $[M+H]^+$: 236.1070, found 236.1069.

Synthesis of α-(*N*-pyrrolyl)ketones 1e and 1f.

Typical procedure for the synthesis of 1-phenyl-2-(1*H*-pyrrol-1-yl)propan-1-one (1e). Under argon, **1a** (1.11 g, 6.0 mmol) was added to a stirred and cooled (0 ^{o}C) suspension of sodium hydride (60% w/w in mineral oil, 360 mg, 9.0 mmol) in THF (25 mL). After 30 min, the iodomethane (560 μL, 9.0 mmol) was added slowly and the reaction mixture was kept at 0 ^{o}C for 1 h. Thereafter, the reaction mixture was quenched with saturated NH_4Cl aqueous solution. The product was extracted with ethyl acetate, washed with brine, dried over anhydrous Na_2SO_4. The solvent was evaporated under the reduced pressure and the

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residue was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 30:1) to afford **1e** in 77% yield (0.918 g) as a light yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90-7.88 (m, 2H), 7.55 (t, *J* = 7.6 Hz, 1H), 7.43 (t, *J* = 8.0 Hz, 2H), 6.75 (t, *J* = 2.0 Hz, 2H), 6.18 (t, *J* = 2.0 Hz, 2H), 5.64 (q, *J* = 6.8 Hz, 1H), 1.73 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.1, 134.9, 133.5, 128.8, 128.4, 119.7, 108.9, 58.2, 18.6; IR (neat): 3099, 3064, 2989, 2935, 1678, 1595, 1490, 1446, 1391, 1374, 1341, 1306, 1293, 1272, 1240, 1214, 1183, 1159, 1114, 1096, 1069, 1050, 1014, 1001, 983, 963, 934, 809, 760, 723, 683, 659, 626 cm^{-1}; HRMS (ESI) calcd for $C_{13}H_{14}NO$ $[M+H]^+$: 200.1070, found 200.1071.

1,3-Diphenyl-2-(1*H*-pyrrol-1-yl)propan-1-one (1f). 6 mmol scale. Benzyl bromide was used. Column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 40:1) afforded the title product in 87% yield (1.43 g) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85-7.83 (m, 2H), 7.48-7.44 (m, 1H), 7.36-7.32 (m, 2H), 7.21-7.13 (m, 3H), 6.98-6.95 (m, 2H), 6.65-6.63 (m, 2H), 6.11-6.09 (m, 2H), 5.57-5.54 (m, 1H), 3.46-3.41 (m, 1H), 3.29-3.23 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.9, 137.1, 135.2, 133.5, 128.9, 128.6, 128.4, 128.3, 126.7, 119.8, 109.0, 64.0, 39.0; IR (neat): 3082, 3062, 3026, 2961, 2927, 1681, 1597, 1580, 1538, 1486, 1450, 1402, 1349, 1304, 1288, 1274, 1256, 1203, 1173, 1094, 1069, 1029, 1003, 989, 969, 930, 869, 801, 769, 756, 715, 696, 683, 665, 627 cm^{-1}; HRMS (ESI) calcd for $C_{19}H_{18}NO$ $[M+H]^+$: 276.1383, found 276.1384.

Synthesis of 1-(2-oxo-2-phenylethyl)-1*H*-pyrrole-2-carbonitrile (1g). Under argon, to a

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Schlenk tube were added 1*H*-pyrrole-2-carbonitrile (461 mg, 5 mmol), 2-bromo-1-phenylethan-1-one (1.19 g, 6 mmol), K_2CO_3 (1.04 g, 7.5 mmol) and CH_3CN (25 mL) sequentially. The resulting mixture was stirred at room temperature for 20.5 h. Then, the mixture was filtered through a pad of celite, concentrated under reduced pressure, diluted with ethyl acetate, washed with brine and dried over anhydrous Na_2SO_4. The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: petroleum ether: dichloromethane = 3:2) to afford **1g** (0.933 g, 89% yield) as a yellow solid. M.p. 97-98 ^oC. ^1H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, *J* = 8.4 Hz, 2H), 7.63 (t, *J* = 7.6 Hz, 1H), 7.50 (t, *J* = 7.6 Hz, 2H), 6.85 (d, *J* = 3.2 Hz, 2H), 6.26 (t, *J* = 3.2 Hz, 1H), 5.46 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.4, 134.3, 133.8, 128.9, 128.0, 127.9, 120.3, 113.4, 110.0, 104.7, 54.0; IR (neat): 3132, 3119, 2928, 2853, 2216, 2163, 1698, 1595, 1581, 1528, 1468, 1448, 1433, 1406, 1352, 1322, 1224, 1155, 1077, 1024, 994, 923, 881, 833, 812, 755, 731, 688, 655, 631 cm^{-1}; HRMS (ESI) calcd for $C_{13}H_{11}N_2O$ $[M+H]^+$: 211.0866, found 211.0866.

Synthesis of pyrrole-ynes 2a-2b, 2g, 2i-2k, 2m and 2o-2t.

Typical procedure for the synthesis of 2,4-diphenyl-1-(1*H*-pyrrol-1-yl)but-3-yn-2-ol (2a). Under argon, to a solution of phenylacetylene (1.81 mL, 16.5 mmol) in THF (30 mL) was added *n*-BuLi (6 mL, 15 mmol, 2.5 M in hexane) at 0 ^oC. After stirring at the same temperature for 1 h, **1a** (926 mg, 5 mmol) was added, and the reaction mixture was warmed up to room temperature and stirred for 1 h. Then, the resulting mixture was quenched with saturated NH_4Cl solution, extracted with ethyl acetate, washed with brine,

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and dried over anhydrous Na_2SO_4. The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: petroleum ether: dichloromethane= 4:1 to 1:1) to afford **2a** in 81% isolated yield (1.16 g) as a light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65-7.62 (m, 2H), 7.46-7.43 (m, 2H), 7.40-7.28 (m, 6H), 6.71 (t, *J* = 2.0 Hz, 2H), 6.14 (t, *J* = 2.0 Hz, 2H), 4.24-4.15 (m, 2H), 2.76 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.3, 131.7, 128.8, 128.4, 128.32, 128.31, 125.6, 122.4, 121.9, 108.1, 89.2, 87.4, 73.4, 61.9; IR (neat): 3534, 3451, 3060, 2940, 2230, 1956, 1683, 1598, 1573, 1491, 1448, 1396, 1287, 1265, 1172, 1090, 1072, 1027, 998, 971, 916, 815, 756, 723, 689 cm^{-1}; HRMS (ESI) calcd for $C_{20}H_{18}NO$ $[M+H]^+$: 288.1383, found 288.1381.

4-(4-Methoxyphenyl)-2-phenyl-1-(1*H*-pyrrol-1-yl)but-3-yn-2-ol (2b). 4 mmol scale. Column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 30:1 to 10:1) afforded the title product in 93% yield (1.18 g) as a light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, *J* = 6.8 Hz, 2 H), 7.40-7.34 (m, 5 H), 6.84 (d, *J* = 8.8 Hz, 2 H), 6.72 (t, *J* = 2.0 Hz, 2 H), 6.14 (t, *J* = 2.0 Hz, 2 H), 4.24-4.16 (m, 2 H), 3.80 (s, 3 H), 2.77 (s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.9, 141.5, 133.2, 128.3, 128.2, 125.7, 122.4, 114.0, 113.9, 108.0, 87.9, 87.4, 73.5, 62.0, 55.3; IR (neat): 3458, 2937, 2837, 2227, 1605, 1570, 1508, 1495, 1448, 1288, 1246, 1172, 1107, 1090, 1072, 1057, 1027, 972, 917, 831, 773, 723, 697 cm^{-1}; HRMS (ESI) calcd for $C_{21}H_{20}NO_2$ $[M+H]^+$: 318.1489, found 318.1487.

4-(Cyclohex-1-en-1-yl)-2-phenyl-1-(1*H*-pyrrol-1-yl)but-3-yn-2-ol (2g). 4 mmol scale. Column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 20:1)

afforded the title product in 91% yield (1.06 g) as a light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57-7.55 (m, 2H), 7.37-7.28 (m, 3H), 6.64 (t, *J* = 2.4 Hz, 2H), 6.16-6.14 (m, 1H), 6.10 (t, *J* = 2.4 Hz, 2H), 4.15-4.07 (m, 2H), 2.61 (s, 1H), 2.14-2.08 (m, 4H), 1.66-1.56 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.6, 136.1, 128.2, 128.1, 125.6, 122.4, 119.7, 107.8, 89.3, 86.5, 73.3, 62.0, 28.8, 25.6, 22.1, 21.3; IR (neat): 3454, 3060, 3028, 2929, 2858, 2832, 2217, 1678, 1601, 1547, 1494, 1448, 1435, 1397, 1346, 1288, 1240, 1172, 1137, 1090, 1072, 1057, 1016, 971, 918, 842, 800, 786, 766, 722, 697, 643, 631, 614 cm^{-1}; HRMS (ESI) calcd for $C_{20}H_{22}NO$ $[M+H]^+$: 292.1696, found 292.1697.

2-Phenyl-1-(1*H*-pyrrol-1-yl)oct-3-yn-2-ol (2i). 4 mmol scale. Column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 25:1) afforded the title product in 91% yield (0.972 g) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57-7.55 (m, 2H), 7.37-7.30 (m, 3H), 6.63 (t, *J* = 2.4 Hz, 2H), 6.10 (t, *J* = 2.4 Hz, 2H), 4.13-4.05 (m, 2H), 2.54 (s, 1H), 2.26 (t, *J* = 6.8 Hz, 2H), 1.55-1.49 (m, 2H), 1.44-1.38 (m, 2H), 0.92 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.9, 128.2, 128.1, 125.6, 122.3, 107.8, 88.5, 80.5, 73.0, 62.0, 30.4, 22.0, 18.4, 13.5; IR (neat): 3459, 3061, 2957, 2932, 2861, 2237, 1683, 1601, 1548, 1495, 1449, 1430, 1379, 1327, 1288, 1235, 1173, 1142, 1090, 1071, 1050, 1031, 1003, 971, 927, 887, 820, 769, 722, 698, 671 cm^{-1}; HRMS (ESI) calcd for $C_{18}H_{22}NO$ $[M+H]^+$: 268.1696, found 268.1695.

5,5-Dimethyl-2-phenyl-1-(1*H*-pyrrol-1-yl)hex-3-yn-2-ol (2j). 4 mmol scale. Column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 20:1) afforded the

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title product in 88% yield (0.941 g) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57-7.54 (m, 2H), 7.37-7.30 (m, 3H), 6.63 (t, *J* = 2.0 Hz, 2H), 6.09 (t, *J* = 2.0 Hz, 2H), 4.06 (s, 2H), 2.53 (s, 1H), 1.25 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.9, 128.2, 128.0, 125.7, 122.4, 107.7, 96.4, 79.1, 72.9, 62.1, 30.7, 27.4; IR (neat): 3464, 3062, 2968, 2867, 2247, 1686, 1602, 1548, 1495, 1475, 1448, 1393, 1362, 1288, 1265, 1205, 1172, 1118, 1090, 1070, 1030, 1003, 973, 923, 873, 840, 778, 721, 697 cm^{-1}; HRMS (ESI) calcd for $C_{18}H_{22}NO$ $[M+H]^+$: 268.1696, found 268.1699.

4-Cyclopropyl-2-phenyl-1-(1*H*-pyrrol-1-yl)but-3-yn-2-ol (2k). 4 mmol scale. Column chromatography on silica gel (eluent: petroleum ether: dichloromethane = 3:1 to 1:1) afforded the title product in 92% yield (0.923 g) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57-7.54 (m, 2H), 7.38-7.29 (m, 3H), 6.63 (t, *J* = 2.0 Hz, 2H), 6.12-6.11 (m, 2H), 4.12-4.04 (m, 2H), 2.49 (s, 1H), 1.33-1.26 (m, 1H), 0.84-0.77 (m, 2H), 0.77-0.68 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.8, 128.2, 128.1, 125.6, 122.3, 107.9, 91.5, 75.6, 73.0, 62.1, 8.22, 8.19, -0.6; IR (neat): 3455, 3089, 3010, 2939, 2239, 1955, 1891, 1810, 1682, 1601, 1546, 1495, 1449, 1429, 1397, 1361, 1287, 1174, 1090, 1072, 1056, 1029, 1003, 968, 930, 890, 868, 813, 768, 723, 697, 665 cm^{-1}; HRMS (ESI) calcd for $C_{17}H_{18}NO$ $[M+H]^+$: 252.1383, found 252.1383.

2-Phenyl-1-(1*H*-pyrrol-1-yl)-4-(trimethylsilyl)but-3-yn-2-ol (2m). 4 mmol scale. Column chromatography on silica gel (eluent: petroleum ether: dichloromethane = 40:1 to 20:1) afforded the title product in 89% yield (1.01 g) as a colorless oil. ^{1}H NMR (400 MHz,

$CDCl_3$) δ 7.57-7.54 (m, 2H), 7.39-7.32 (m, 3H), 6.64 (t, *J* = 2.0 Hz, 2H), 6.10 (t, *J* = 2.0 Hz, 2H), 4.16-4.06 (m, 2H), 2.57 (s, 1H), 0.21 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.0, 128.32, 128.28, 125.6, 122.4, 108.0, 105.4, 92.7, 73.2, 61.9, -0.3; IR (neat): 3450, 2959, 2899, 2169, 1495, 1449, 1288, 1250, 1174, 1090, 1073, 1028, 973, 918, 902, 840, 789, 760, 720, 697, 645, 632, 612 cm^{-1}; HRMS (ESI) calcd for $C_{17}H_{22}NOSi$ $[M+H]^+$: 284.1465, found 284.1467.

1,3-Diphenyl-4-(1*H*-pyrrol-1-yl)pent-1-yn-3-ol (2o). 4.605 mmol scale. Column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 30:1) afforded the title product in 95% yield (1.32 g) as a mixture of two diastereoisomers in a ratio of 3.9:1 as a light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) two isomers: δ 7.66-7.63 (m), 7.50-7.46 (m), 7.43-7.40 (m), 7.34-7.22 (m), 6.84 (t, *J* = 2.0 Hz, major isomer), 6.56 (t, *J* = 2.0 Hz, minor isomer), 6.14 (t, *J* = 2.0 Hz, major isomer), 6.01 (t, *J* = 2.0 Hz, minor isomer), 4.28-4.22 (m), 2.78 (s, major isomer), 2.73 (s, minor isomer), 1.55 (d, *J* = 6.8 Hz, minor isomer), 1.44 (d, *J* = 6.8 Hz, major isomer); ^{13}C NMR (100 MHz, $CDCl_3$) two isomers: δ 141.6, 141.1, 131.59, 131.56, 128.7, 128.6, 128.3, 128.2, 128.1, 128.0, 127.8, 126.2, 125.7, 121.98, 121.96, 120.7, 120.3, 107.6, 107.0, 89.5, 88.33, 88.28, 87.2, 76.8, 76.2, 65.1, 64.3, 16.5, 15.8; IR (neat): 3543, 3451, 3060, 3031, 2985, 2940, 2225, 1598, 1487, 1447, 1408, 1376, 1341, 1302, 1272, 1174, 1092, 1070, 1028, 971, 944, 927, 756, 722, 690, 647, 627 cm^{-1}; HRMS (ESI) calcd for $C_{21}H_{20}NO$ $[M+H]^+$: 302.1539, found 302.1540.

1,3,5-Triphenyl-4-(1*H*-pyrrol-1-yl)pent-1-yn-3-ol (2p). 4.82 mmol scale. Column

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chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 30:1) afforded the title product in 94% yield (1.71 g) as a mixture of two diastereoisomers in a ratio of 10:1 as a yellow oil. Major isomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.72-7.70 (m, 2H), 7.57-7.52 (m, 2H), 7.37-7.28 (m, 6H), 7.09-7.04 (m, 3H), 6.78 (t, *J* = 2.0 Hz, 2H), 6.75-6.72 (m, 2H), 6.07 (t, *J* = 2.0 Hz, 2H), 4.28-4.24 (m, 1H), 3.34-3.28 (m, 1H), 3.16-3.12 (m, 1H), 2.81 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.2, 138.0, 131.65, 128.9, 128.4, 128.3, 128.25, 128.18, 128.1, 126.31, 126.26, 121.9, 121.1, 108.0, 88.8, 88.7, 76.4, 72.3, 36.7; Minor isomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51-7.49 (m, 2H), 7.46-7.44 (m, 2H), 7.25-7.23 (m, 3H), 6.88-6.86 (m, 2H), 6.55 (t, *J* = 2.0 Hz, 2H), 5.95 (t, *J* = 2.0 Hz, 2H), 4.23-4.20 (m, 1H), 3.46-3.41 (m, 1H), 2.85 (s, 3H), other peaks are overlapped with the signals of the major isomer; ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.9, 138.4, 131.71, 128.8, 128.5, 128.0, 127.9, 126.2, 125.6, 120.5, 107.4, 89.3, 87.6, 76.1, 71.5, 36.1, other peaks are overlapped with the signals of the major isomer; IR (neat), two isomers: 3541, 3442, 3061, 3028, 2936, 2227, 1952, 1885, 1806, 1600, 1487, 1448, 1409, 1306, 1278, 1173, 1091, 1070, 1030, 920, 846, 754, 724, 690, 648, 628 cm^{-1}; HRMS (ESI) calcd for $C_{27}H_{24}NO$ $[M+H]^+$: 378.1852, found 378.1852.

1-(2,4-Dimethyl-1*H*-pyrrol-1-yl)-2,4-diphenylbut-3-yn-2-ol (2q). 4 mmol scale. Column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 20:1) afforded the title product in 88% yield (1.11 g) as a light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66-7.64 (m, 2H), 7.47-7.44 (m, 2H), 7.41-7.29 (m, 6H), 6.57 (s, 1H), 5.71 (s, 1H), 4.13-4.02 (m, 2H), 2.82 (s, 1H), 2.06 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.7, 131.7,

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129.7, 128.8, 128.4, 128.33, 128.27, 125.7, 122.1, 119.3, 117.6, 108.5, 89.8, 87.3, 73.7, 58.0, 12.0, 11.9; IR (neat): 3414, 3060, 3031, 2933, 2861, 2230, 1683, 1598, 1517, 1490, 1446, 1410, 1386, 1337, 1277, 1202, 1176, 1145, 1092, 1061, 1026, 1000, 917, 846, 821, 755, 690, 627 cm^{-1}; HRMS (ESI) calcd for $C_{22}H_{22}NO$ $[M+H]^+$: 316.1696, found 316.1698.

1-(2,3-Diphenyl-1*H*-pyrrol-1-yl)-2,4-diphenylbut-3-yn-2-ol (2r). 4 mmol scale. Column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 20:1) afforded the title product in 75% yield (1.32 g) as a light yellow oil. ^1H NMR (400 MHz, $CDCl_3$) δ 7.44-7.40 (m, 4H), 7.33-7.17 (m, 10H), 7.12-7.09 (m, 4H), 7.06-7.00 (m, 3H), 6.48 (d, *J* = 2.8 Hz, 1H), 4.26-4.17 (m, 2H), 2.70 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.6, 136.5, 132.4, 131.8, 131.6, 131.5, 128.8, 128.3, 128.24, 128.22, 127.9, 127.7, 127.4, 125.6, 124.9, 122.5, 122.3, 121.9, 108.3, 89.7, 87.5, 73.7, 57.5; IR (neat): 3527, 3453, 3057, 3030, 2932, 2226, 1885, 1810, 1677, 1600, 1574, 1503, 1490, 1472, 1446, 1421, 1390, 1344, 1270, 1206, 1176, 1094, 1068, 1025, 916, 843, 782, 756, 731, 690, 640 cm^{-1}; HRMS (ESI) calcd for $C_{32}H_{26}NO$ $[M+H]^+$: 440.2009, found 440.2009.

1-(2-Hydroxy-2,4-diphenylbut-3-yn-1-yl)-1*H*-pyrrole-2-carbonitrile (2s). 4 mmol scale. Column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 10:1) afforded the title product in 81% yield (1.01 g) as a light yellow oil. ^1H NMR (400 MHz, $CDCl_3$) δ 7.67-7.64 (m, 2H), 7.50-7.47 (m, 2H), 7.43-7.31 (m, 6H), 6.96-6.95 (m, 1H), 6.77-6.76 (m, 1H), 6.17-6.16 (m, 1H), 4.42-4.33 (m, 2H), 2.76 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.8, 131.8, 129.0, 128.8, 128.6, 128.4, 128.0, 125.7, 121.5, 119.7, 113.8,

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109.3, 105.6, 88.2, 88.0, 73.4, 59.9; IR (neat): 3375, 3051, 3032, 2953, 2227, 1599, 1528, 1489, 1464, 1442, 1406, 1332, 1308, 1263, 1244, 1218, 1190, 1147, 1098, 1072, 1062, 1041, 1004, 917, 896, 885, 813, 799, 756, 732, 706, 690, 665, 642, 613 cm^{-1}; HRMS (ESI) calcd for $C_{21}H_{20}N_3O$ $[M+NH_4]^+$: 330.1601, found 330.1602.

1-(1*H*-Indol-1-yl)-2,4-diphenylbut-3-yn-2-ol (2t). 4 mmol scale. Column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 50:1 to 30:1) afforded the title product in 82% yield (1.11 g) as a light yellow oil. ^1H NMR (400 MHz, $CDCl_3$) δ 7.69-7.66 (m, 2H), 7.60 (d, *J* = 8.0 Hz, 1H), 7.42-7.21 (m, 9H), 7.17-7.05 (m, 3H), 6.49 (d, *J* = 3.6 Hz, 1H), 4.45 (s, 2H), 2.72 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.5, 137.2, 131.7, 129.4, 128.8, 128.44, 128.40, 128.23, 128.21, 125.7, 121.8, 121.5, 120.6, 119.4, 110.2, 101.7, 89.3, 87.6, 74.2, 58.5; IR (neat): 3520, 3055, 3031, 2935, 2230, 2199, 1953, 1885, 1674, 1611, 1598, 1514, 1488, 1461, 1447, 1397, 1335, 1313, 1254, 1205, 1173, 1128, 1100, 1088, 1068, 1012, 917, 882, 844, 818, 756, 737, 690, 658, 637, 618 cm^{-1}; HRMS (ESI) calcd for $C_{24}H_{20}NO$ $[M+H]^+$: 338.1539, found 338.1540.

Synthesis of 2-phenyl-1-(1*H*-pyrrol-1-yl)but-3-yn-2-ol (2l). Under argon, to a solution of ethynyltrimethylsilane (4.66 mL, 33 mmol) in THF (30 mL) was added *n*-BuLi (12 mL, 30 mmol, 2.5 M in hexane) at 0 ^oC. After stirring at the same temperature for 1 h, **1a** (1.85 g, 10 mmol) was added, and the reaction mixture was warmed up to room temperature and stirred for 1 h. Then, the resulting mixture was quenched with saturated NH_4Cl solution, extracted with ethyl acetate, washed with brine, and dried over anhydrous Na_2SO_4. The

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solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 10:1) to afford **2m** as a crude product.

Under air, to a solution of the above crude **2m** in MeOH (30 mL) was added K_2CO_3 (829 mg, 6 mmol). The resulting suspension was stirred under room temperature for 11 h. Then, the mixture was quenched with saturated NH_4Cl solution, extracted with ethyl acetate, washed with brine and dried over anhydrous Na_2SO_4. The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 20:1 to 10:1) to afford **2l** (1.825 g, 86% yield) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56-7.52 (m, 2H), 7.37-7.29 (m, 3H), 6.62 (t, *J* = 2.0 Hz, 2H), 6.09 (t, *J* = 2.0 Hz, 2H), 4.16-4.06 (m, 2H), 2.70 (s, 1H), 2.67 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.7, 128.4, 128.3, 125.5, 122.4, 108.1, 84.1, 75.9, 72.8, 61.5; IR (neat): 3305, 3267, 2114, 1499, 1439, 1387, 1345, 1288, 1250, 1178, 1098, 1076, 1017, 973, 916, 873, 774, 752, 730, 704, 694, 665, 631 cm^{-1}; HRMS (EI) calcd for $C_{14}H_{13}NO$ $[M]^+$: 211.0997, found 211.1006.

Synthesis of pyrrole-ynes 2c-2f.

Typical procedure for the synthesis of 4-(4-aminophenyl)-2-phenyl-1-(1*H*-pyrrol-1-yl)but-3-yn-2-ol (2c). Under argon, to a solution of **2l** (845 mg, 4 mmol) and 4-iodoaniline (1.05 g, 4.8 mmol) in triethylamine (20 mL) were added CuI (38.1 mg, 0.2 mmol) and $Pd(PPh_3)_2Cl_2$ (56.2 mg, 0.08 mmol). The resulting suspension was stirred under 50 ^{o}C for 3 h. Then, the mixture was filtered through

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a pad of celite, diluted with ethyl acetate, washed with brine, and dried over anhydrous Na_2SO_4. The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 3:1 to 2:1) to afford **2c** (0.898 g, 74% yield) as a light yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, *J* = 7.6 Hz, 2H), 7.38-7.30 (m, 3H), 7.16 (d, *J* = 8.4 Hz, 2H), 6.73 (s, 2H), 6.52 (d, *J* = 8.4 Hz, 2H), 6.14 (s, 2H), 4.21-4.11 (m, 2H), 3.56 (bs, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.8, 141.8, 133.0, 128.3, 128.1, 125.7, 122.5, 114.9, 111.4, 107.9, 88.0, 87.2, 73.3, 62.1; IR (neat): 3462, 3372, 3216, 3059, 3033, 2940, 2222, 1891, 1619, 1606, 1513, 1494, 1448, 1431, 1397, 1286, 1215, 1175, 1128, 1090, 1072, 1057, 1027, 972, 938, 912, 829, 768, 723, 697, 657, 642, 628, 609 cm^{-1}; HRMS (ESI) calcd for $C_{20}H_{19}N_2O$ $[M+H]^+$: 303.1492, found 303.1494.

2-Phenyl-1-(1*H*-pyrrol-1-yl)-4-(4-(trifluoromethyl)phenyl)but-3-yn-2-ol (2d). 4 mmol scale. Column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 10:1) afforded the title product in 92% yield (1.31 g) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62-7.59 (m, 2H), 7.55-7.48 (m, 4H), 7.39-7.31 (m, 3H), 6.68 (t, *J* = 2.0 Hz, 2H), 6.13 (t, *J* = 2.0 Hz, 2H), 4.22-4.13 (m, 2H), 2.94 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.8, 131.9, 130.4 (q, $^2J_{C\text{-}F}$ = 32.1 Hz), 128.5, 128.4, 125.7 (q, $^5J_{C\text{-}F}$ = 1.5 Hz), 125.5, 125.2 (q, $^3J_{C\text{-}F}$ = 3.8 Hz), 123.7 (q, $^1J_{C\text{-}F}$ = 271.6 Hz), 122.4, 108.2, 91.6, 86.0, 73.5, 61.8; IR (neat): 3443, 3062, 2941, 1614, 1494, 1450, 1404, 1320, 1288, 1166, 1124, 1105, 1090, 1066, 1015, 972, 917, 842, 771, 724, 697, 644, 630, 613 cm^{-1}; HRMS (ESI) calcd for $C_{21}H_{17}F_3NO$ $[M+H]^+$: 356.1257, found 356.1257.

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2-Phenyl-4-(pyridin-2-yl)-1-(1*H*-pyrrol-1-yl)but-3-yn-2-ol (2e). 4 mmol scale. Column chromatography on silica gel (eluent: petroleum ether: dichloromethane: ethyl acetate = 1:4:1 to dichloromethane: ethyl acetate = 4:1) afforded the title product in 93% yield (1.07 g) as a white solid. M.p. 145-146 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.41 (d, *J* = 4.4 Hz, 1H), 7.64-7.57 (m, 3H), 7.36-7.28 (m, 4H), 7.20-7.16 (m, 1H), 6.64 (t, *J* = 2.0 Hz, 2H), 6.06 (t, *J* = 2.0 Hz, 2H), 4.89 (bs, 1H), 4.31-4.23 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.7, 142.1, 141.2, 136.3, 128.3, 128.2, 127.4, 125.7, 123.3, 122.4, 107.9, 90.2, 85.9, 73.1, 61.7; IR (neat): 3063, 2940, 2774, 2232, 1703, 1679, 1586, 1562, 1494, 1467, 1431, 1341, 1289, 1195, 1155, 1095, 1070, 999, 972, 942, 916, 828, 778, 735, 696, 646, 610 cm^{-1}; HRMS (ESI) calcd for $C_{19}H_{17}N_2O$ $[M+H]^+$: 289.1335, found 289.1337.

2-Phenyl-1-(1*H*-pyrrol-1-yl)-4-(thiophen-2-yl)but-3-yn-2-ol (2f). 4 mmol scale. Column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 10:1) afforded the title product in 90% yield (1.052 g) as a light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63-7.60 (m, 2H), 7.41-7.33 (m, 3H), 7.29-7.27 (m, 1H), 7.24-7.23 (m, 1H), 6.99-6.97 (m, 1H), 6.71 (t, *J* = 2.4 Hz, 2H), 6.14 (t, *J* = 2.4 Hz, 2H), 4.26-4.16 (m, 2H), 2.69 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.9, 132.7, 128.44, 128.41, 127.8, 127.0, 125.6, 122.4, 121.7, 108.2, 93.0, 81.0, 73.7, 61.9; IR (neat): 3441, 3101, 3061, 3029, 2939, 2220, 1493, 1448, 1426, 1287, 1221, 1181, 1090, 1072, 1035, 971, 916, 851, 833, 775, 721, 695, 659, 643, 628, 611 cm^{-1}; HRMS (ESI) calcd for $C_{18}H_{16}NOS$ $[M+H]^+$: 294.0947, found 294.0949.

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Synthesis of 2,6-diphenyl-1-(1*H*-pyrrol-1-yl)hexa-3,5-diyn-2-ol (2h). Under argon, to a solution of **2l** (845 mg, 4 mmol), CuCl (59.4 mg, 0.6 mmol) and hydroxylamine hydrochloride (83.4 mg, 1.2 mmol) in toluene (25 mL) were added (bromoethynyl)benzene (941 mg, 5.2 mmol) and butan-1-amine (439 mg, 6.0 mmol) at 0 ^{o}C. The resulting suspension was stirred under room temperature for 12 h. Then, the mixture was quenched with saturated NH_4Cl solution, extracted with ethyl acetate, washed with brine and dried over anhydrous Na_2SO_4. The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 50:1 to 40:1) to afford **2h** (1.06 g, 85% yield) as a light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57-7.55 (m, 2H), 7.51-7.49 (m, 2H), 7.40-7.30 (m, 6H), 6.67 (t, *J* = 2.0 Hz, 2H), 6.14 (t, *J* = 2.0 Hz, 2H), 4.25-4.12 (m, 2H), 2.73 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.5, 132.6, 129.5, 128.54, 128.47, 128.4, 125.5, 122.4, 121.1, 108.4, 82.1, 79.7, 73.6, 72.9, 72.1, 61.6; IR (neat): 3436, 3060, 3031, 2940, 2338, 2233, 1678, 1599, 1570, 1493, 1443, 1396, 1324, 1288, 1235, 1177, 1121, 1090, 1071, 1055, 1027, 1001, 970, 917, 885, 841, 755, 722, 697, 687, 642, 628 cm^{-1}; HRMS (ESI) calcd for $C_{22}H_{18}NO$ $[M+H]^+$: 312.1383, found 312.1383.

Synthesis of 2-methyl-4-phenyl-1-(1*H*-pyrrol-1-yl)but-3-yn-2-ol (2n).

1) Synthesis of the precursor of 1-bromo-2-methyl-4-phenylbut-3-yn-2-ol.

To a solution of *N*-bromosuccinimide (4.27 g, 24 mmol) and *p*-TsOH H_2O (0.380 g, 2.0 mmol) in dichloromethane (32 mL) was added a solution of acetone (1.16 g, 20 mmol) in dichloromethane (8 mL) at 0 ^{o}C. The resulting mixture was refluxed under 60 ^{o}C for 5 h.

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Then, the mixture was quenched with water, extracted with dichloromethane, washed with saturated $NaHCO_3$ solution and brine, dried over anhydrous Na_2SO_4, and reduced to afford crude product of 1-bromopropan-2-one which was used without further purification.

Under argon, to a solution of phenylacetylene (2.86 mL, 26 mmol) in THF (40 mL) was added ethylmagnesium bromide (8 mL, 24 mmol, 3.0 M in diethyl ether) dropwise at 0 ^oC. Then the resulting mixture was stirred at the same temperature for 1 h. Then, the above crude product of 1-bromopropan-2-one was added. The reaction mixture was stirred at 0 ^oC for another 0.5 h. Then, the reaction was quenched with saturated NH_4Cl solution, extracted with ethyl acetate, washed with brine and dried over anhydrous Na_2SO_4. The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 30:1) to afford 1-bromo-2-methyl-4-phenylbut-3-yn-2-ol (3.07 g, 64% yield) as a colorless liquid. ^1H NMR (400 MHz, $CDCl_3$) δ 7.45-7.42 (m, 2H), 7.33-7.26 (m, 3H), 3.69-3.58 (m, 2H), 3.01 (s, 1H), 1.70 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 131.7, 128.6, 128.2, 121.9, 89.6, 84.3, 67.2, 43.9, 27.4; IR (neat): 3533, 3384, 3056, 2986, 2231, 1598, 1489, 1444, 1416, 1371, 1331, 1281, 1235, 1203, 1159, 1107, 1049, 950, 930, 864, 812, 755, 689, 661 cm^{-1}; HRMS (EI) calcd for $C_{11}H_{11}OBr$ $[M]^+$: 237.9993, found 237.9986.

2) Synthesis of 2n.

Under argon, to a Schlenk tube were added KOH (1.34 g, 23.8 mmol), DMSO (30 mL) and pyrrole (1.20 g, 17.85 mmol). The resulting mixture was stirred at room temperature for 1 h. Then, 1-bromo-2-methyl-4-phenylbut-3-yn-2-ol (2.85 g, 11.9 mmol) in DMSO (10

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mL) was added dropwise. The reaction mixture was stirred at room temperature for another 3 h. Then the mixture was quenched with water, extracted with ethyl acetate, washed with brine and dried over anhydrous Na_2SO_4. The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 10:1) to afford an inseparable mixture of **2n** and 1-(1*H*-pyrrol-1-yl)propan-2-one as a light yellow oil.

In order to obtain the pure **2n**, further reduction reaction was performed. Under air, to a solution of the above mixture in MeOH (20 mL) was added $NaBH_4$ (151 mg, 4 mmol). The resulting suspension was stirred under room temperature for 1 h. Then, the mixture was quenched with water, extracted with ethyl acetate, washed with brine and dried over anhydrous Na_2SO_4. The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 10:1) to afford **2n** (0.824 g, 31% yield) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40-7.38 (m, 2H), 7.31-7.27 (m, 3H), 6.81 (t, *J* = 2.0 Hz, 2H), 6.18 (t, *J* = 2.0 Hz, 2H), 4.14-3.98 (m, 2H), 2.45 (bs, 1H), 1.55 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 131.6, 128.6, 128.3, 122.3, 122.1, 108.3, 90.4, 85.0, 68.3, 60.3, 26.9; IR (neat): 3447, 2982, 2933, 2232, 1679, 1598, 1573, 1494, 1443, 1374, 1317, 1287, 1215, 1121, 1087, 1067, 1027, 969, 944, 925, 899, 816, 755, 723, 690, 616 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{16}NO$ $[M+H]^+$: 226.1226, found 226.1228.

Synthesis of indolizines 3.

Typical procedure for the synthesis of 6,8-diphenylindolizine (3a). A Schlenk tube

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containing a stirring bar was introduced into a nitrogen-filled glovebox, and $AgPF_6$ (2.5 mg, 0.01 mmol) was added. The tube with the silver catalyst was taken out of the glovebox. Then, to this tube were added IPrAuCl (6.2 mg, 0.01 mmol) and dichloromethane (2 mL) under argon. The resulting suspension was stirred at room temperature for 10 min. Then, **2a** (144 mg, 0.5 mmol) in dichloromethane (3 mL) was added. The reaction mixture was stirred at room temperature for another 10 min. The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 100:1) to afford **3a** (131 mg, 97% yield) as a light yellow oil. ^{1}H NMR (400 MHz, C_6D_6) δ 7.67-7.64 (m, 2H), 7.48 (t, *J* = 1.2 Hz, 1H), 7.28-7.10 (m, 8H), 6.98 (dd, *J* = 2.6, 1.2 Hz, 1H), 6.86 (d, *J* = 1.2 Hz, 1H), 6.79 (dd, *J* = 4.0, 2.4 Hz, 1H), 6.72 (dt, *J* = 4.0, 1.2 Hz, 1H); ^{13}C NMR (100 MHz, C_6D_6) δ 139.7, 138.8, 133.3, 131.7, 129.0, 128.9, 128.7, 128.2, 127.3, 127.0, 124.9, 122.1, 117.5, 114.7, 114.2, 100.1; IR (neat): 3055, 3031, 1955, 1889, 1705, 1645, 1598, 1492, 1450, 1390, 1348, 1312, 1264, 1146, 1084, 1042, 1027, 912, 889, 840, 756, 734, 695, 611 cm^{-1}; HRMS (ESI) calcd for $C_{20}H_{16}N$ $[M+H]^+$: 270.1277, found 270.1278.

8-(4-Methoxyphenyl)-6-phenylindolizine (3b). A mixture of $AgPF_6$ (2.5 mg, 0.01 mmol), IPrAuCl (6.2 mg, 0.01 mmol), **2b** (159 mg, 0.5 mmol) and dichloromethane (5 mL) were stirred at room temperature for 10 min. Column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 100:1) afforded the title product in 94% yield (140 mg) as a light yellow oil. ^{1}H NMR (400 MHz, C_6D_6) δ 7.63-7.60 (m, 2H), 7.54 (t, *J* = 1.2 Hz, 1H), 7.33-7.30 (m, 2H), 7.22-7.19 (m, 2H), 7.16-7.12 (m, 1H), 7.03 (dd, *J* = 2.6, 1.2 Hz, 1H),

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6.90 (d, *J* = 1.2 Hz, 1H), 6.87-6.82 (m, 3H), 6.78 (dt, J = 3.6, 1.2 Hz, 1H), 3.34 (s, 3H); ^{13}C NMR (100 MHz, C_6D_6) δ 160.1, 139.0, 133.1, 132.0, 131.9, 129.8, 129.1, 127.3, 127.1, 125.0, 121.8, 117.1, 114.6, 114.4, 114.2, 100.1, 54.9; IR (neat): 3057, 3033, 3000, 2960, 2932, 2908, 2836, 1894, 1698, 1645, 1608, 1574, 1506, 1463, 1420, 1389, 1349, 1307, 1290, 1246, 1177, 1147, 1109, 1084, 1028, 889, 832, 791, 760, 732, 720, 697, 670, 665, 626, 612 cm^{-1}; HRMS (EI) calcd for $C_{21}H_{17}NO$ $[M]^+$: 299.1310, found 299.1316.

4-(6-Phenylindolizin-8-yl)aniline (3c). A mixture of $AgPF_6$ (2.5 mg, 0.01 mmol), IPrAuCl (6.2 mg, 0.01 mmol), **2c** (151 mg, 0.5 mmol) and dichloromethane (5 mL) were stirred at room temperature for 30 min. Column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 3:1) afforded the title product in 91% yield (129 mg) as a light yellow oil. ^{1}H NMR (400 MHz, C_6D_6) δ 7.59-7.54 (m, 3H), 7.33-7.30 (m, 2H), 7.21-7.17 (m, 2H), 7.15-7.10 (m, 1H), 7.04 (dd, *J* = 2.4, 1.2 Hz, 1H), 6.94 (d, *J* = 1.6 Hz, 1H), 6.85-6.82 (m, 2H), 6.40-6.36 (m, 2H), 2.93 (bs, 2H); ^{13}C NMR (100 MHz, C_6D_6) δ 147.2, 139.1, 133.6, 132.0, 129.6, 129.3, 129.0, 127.2, 127.1, 125.0, 121.5, 116.6, 115.1, 114.5, 114.1, 100.2; IR (neat): 3451, 3364, 3216, 3054, 3028, 2278, 1892, 1619, 1505, 1488, 1466, 1449, 1431, 1379, 1349, 1337, 1310, 1280, 1256, 1180, 1146, 1126, 1083, 1027, 913, 888, 829, 758, 719, 693, 627, 612 cm^{-1}; HRMS (ESI) calcd for $C_{20}H_{17}N_2$ $[M+H]^+$: 285.1386, found 285.1387.

6-Phenyl-8-(4-(trifluoromethyl)phenyl)indolizine (3d). A mixture of $AgPF_6$ (2.5 mg, 0.01 mmol), IPrAuCl (6.2 mg, 0.01 mmol), **2d** (178 mg, 0.5 mmol) and dichloromethane

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(5 mL) were stirred at room temperature for 10 min. Column chromatography on silica gel (eluent: petroleum ether: dichloromethane = 10:1) afforded the title product in 86% yield (145 mg) as a yellow oil. ^{1}H NMR (400 MHz, C_6D_6) δ 7.46 (s, 1H), 7.43-7.38 (m, 4H), 7.28-7.20 (m, 4H), 7.17-7.14 (m, 1H), 6.97 (dd, *J* = 2.2, 1.2 Hz, 1H), 6.77 (dd, *J* = 4.0, 2.8 Hz, 1H), 6.70 (d, *J* = 0.8 Hz, 1H), 6.52 (d, *J* = 4.0 Hz, 1H); ^{13}C NMR (100 MHz, C_6D_6) δ 143.1 (q, $^{5}J_{C\text{-}F}$ = 1.5 Hz), 138.5, 131.7, 131.0, 130.0 (q, $^{2}J_{C\text{-}F}$ = 32.2 Hz), 129.1, 128.9, 127.6, 127.0, 125.8 (q, $^{3}J_{C\text{-}F}$ = 3.8 Hz), 125.1 (q, $^{1}J_{C\text{-}F}$ = 270.6 Hz), 124.8, 122.7, 118.0, 114.9, 114.4, 99.9; IR (neat): 3066, 3029, 1746, 1696, 1612, 1493, 1468, 1448, 1421, 1380, 1323, 1259, 1192, 1166, 1146, 1121, 1106, 1086, 1063, 1041, 1027, 1016, 978, 948, 914, 890, 867, 840, 778, 762, 744, 723, 697, 677, 632, 614cm^{-1}; HRMS (EI) calcd for $C_{21}H_{14}NF_3$ $[M]^+$: 337.1078, found 337.1075.

6-Phenyl-8-(pyridin-2-yl)indolizine (3e). A mixture of $AgPF_6$ (3.8 mg, 0.015 mmol), IPrAuCl (9.3 mg, 0.015 mmol), **2e** (86.5 mg, 0.3 mmol) and 1,2-dichloroethane (3 mL) were stirred at 80 ^{o}C for 1 h. Column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 20:1) afforded the title product in 85% yield (68.9 mg) as a yellow oil. ^{1}H NMR (400 MHz, C_6D_6) δ 8.62 (d, *J* = 4.4 Hz, 1H), 7.61-7.56 (m, 3H), 7.32 (d, *J* = 7.6 Hz, 2H), 7.20-7.10 (m, 5H), 7.03 (d, *J* = 0.8 Hz, 1H), 6.88 (s, 1H), 6.70 (t, *J* = 5.6 Hz, 1H); ^{13}C NMR (100 MHz, C_6D_6) δ 157.1, 150.0, 138.8, 136.1, 131.4, 130.7, 129.0, 127.3, 127.1, 124.5, 123.4, 122.5, 122.4, 119.1, 114.9, 114.1, 100.9; IR (neat): 3054, 3029, 1712, 1642, 1585, 1566, 1464, 1449, 1430, 1386, 1350, 1311, 1260, 1151, 1081, 1027, 991, 888, 843, 790, 757, 718, 694 cm^{-1}; HRMS (ESI) calcd for $C_{19}H_{15}N_2$ $[M+H]^+$: 271.1230, found

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271.1232.

6-Phenyl-8-(thiophen-2-yl)indolizine (3f). A mixture of $AgPF_6$ (2.5 mg, 0.01 mmol), IPrAuCl (6.2 mg, 0.01 mmol), **2f** (147 mg, 0.5 mmol) and dichloromethane (5 mL) were stirred at room temperature for 10 min. Column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 250:1) afforded the title product in 97% yield (134 mg) as a yellow oil. ^{1}H NMR (400 MHz, C_6D_6) δ 7.40-7.38 (m, 2H), 7.24-7.21 (m, 2H), 7.18-7.14 (m, 2H), 7.12-7.08 (m, 2H), 7.01-7.00 (m, 1H), 6.93 (dd, *J* = 2.4, 1.2 Hz, 1H), 6.91 (dd, *J* = 5.2, 0.8 Hz, 1H), 6.83 (dd, *J* = 4.8, 3.6 Hz, 1H), 6.80 (dd, *J* = 4.0, 2.8 Hz, 1H); ^{13}C NMR (100 MHz, C_6D_6) δ 141.4, 138.5, 130.5, 129.0, 127.7, 127.4, 127.0, 126.1, 125.9, 125.2, 124.5, 122.4, 117.3, 114.8, 114.5, 100.7; IR (neat): 3101, 3058, 3028, 1642, 1599, 1547, 1478, 1448, 1433, 1412, 1388, 1363, 1339, 1308, 1256, 1213, 1182, 1156, 1131, 1084, 1027, 909, 886, 854, 832, 812, 801, 757, 689, 633 cm^{-1}; HRMS (ESI) calcd for $C_{18}H_{14}NS$ $[M+H]^+$: 276.0841, found 276.0842.

8-(Cyclohex-1-en-1-yl)-6-phenylindolizine (3g). A mixture of $AgPF_6$ (2.5 mg, 0.01 mmol), IPrAuCl (6.2 mg, 0.01 mmol), **2g** (146 mg, 0.5 mmol) and dichloromethane (5 mL) were stirred at room temperature for 2 h. Column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 100:1) afforded the title product in 94% yield (129 mg) as a light yellow oil. ^{1}H NMR (400 MHz, C_6D_6) δ 7.47 (s, 1H), 7.33-7.30 (m, 2H), 7.22-7.18 (m, 2H), 7.15-7.11 (m, 1H), 6.98 (dd, *J* = 2.6, 1.2 Hz, 1H), 6.83-6.81 (m, 2H), 6.74-6.73 (m, 1H), 6.28-6.25 (m, 1H), 2.42-2.38 (m, 2H), 2.11-2.05 (m, 2H), 1.67-1.61 (m, 2H),

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1.59-1.53 (m, 2H); ^{13}C NMR (100 MHz, C_6D_6) δ 139.2, 136.2, 135.5, 131.5, 129.0, 127.2, 127.09, 127.07, 124.7, 121.6, 115.2, 114.1, 113.8, 100.3, 28.9, 25.9, 23.4, 22.6; IR (neat): 3054, 2933, 2860, 1714, 1640, 1598, 1541, 1447, 1392, 1338, 1264, 1077, 1027, 905, 844, 802, 762, 733, 699, 612 cm^{-1}; HRMS (EI) calcd for $C_{20}H_{19}N$ $[M]^+$: 273.1517, found 273.1523.

6-Phenyl-8-(phenylethynyl)indolizine (3h). A mixture of $AgPF_6$ (2.5 mg, 0.01 mmol), IPrAuCl (6.2 mg, 0.01 mmol), **2h** (156 mg, 0.5 mmol) and dichloromethane (5 mL) were stirred at room temperature for 1 h. Column chromatography on silica gel (eluent: petroleum ether: dichloromethane = 10:1) afforded the title product in 54% yield (78.5 mg) as a light yellow oil. ^{1}H NMR (400 MHz, C_6D_6) δ 7.58-7.55 (m, 2H), 7.38 (s, 1H), 7.20-7.09 (m, 6H), 7.06-6.98 (m, 4H), 6.93 (dd, *J* = 2.4, 1.6 Hz, 1H), 6.85 (dd, *J* = 3.8, 2.4 Hz, 1H); ^{13}C NMR (100 MHz, C_6D_6) δ 138.1, 132.13, 132.09, 129.0, 128.74, 128.71, 127.4, 126.9, 124.3, 123.7, 123.3, 122.6, 114.8, 114.6, 114.4, 100.3, 94.1, 87.2; IR (neat): 3128, 3076, 3041, 2919, 2850, 2210, 1747, 1667, 1596, 1548, 1514, 1487, 1463, 1452, 1440, 1412, 1386, 1357, 1340, 1320, 1268, 1187, 1159, 1083, 1068, 1028, 1010, 913, 904, 883, 858, 839, 775, 714, 685, 629, 609 cm^{-1}; HRMS (ESI) calcd for $C_{22}H_{16}N$ $[M+H]^+$: 294.1277, found 294.1278.

8-Butyl-6-phenylindolizine (3i). A mixture of $AgPF_6$ (2.5 mg, 0.01 mmol), IPrAuCl (6.2 mg, 0.01 mmol), **2i** (134 mg, 0.5 mmol) and dichloromethane (5 mL) were stirred at room temperature for 10 min. Column chromatography on silica gel (eluent: petroleum ether:

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ethyl acetate = 100:1) afforded the title product in 90% yield (112 mg) as a light yellow solid. ^{1}H NMR (400 MHz, C_6D_6) δ 7.47 (s, 1H), 7.35-7.33 (m, 2H), 7.23-7.19 (m, 2H), 7.15-7.12 (m, 1H), 6.97 (dd, *J* = 2.6, 1.2 Hz, 1H), 6.82 (dd, *J* = 4.0, 2.8 Hz, 1H), 6.68 (s, 1H), 6.54 (d, *J* = 4.0 Hz, 1H), 2.69 (t, *J* = 7.6 Hz, 2H), 1.70-1.62 (m, 2H), 1.35-1.25 (m, 2H), 0.86 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, C_6D_6) δ 139.4, 133.1, 132.9, 129.0, 127.2, 127.1, 124.7, 121.2, 116.1, 114.0, 113.8, 98.1, 32.7, 31.4, 23.1, 14.2; IR (neat): 2951, 2922, 2889, 2856, 1598, 1464, 1417, 1380, 1348, 1321, 1308, 1256, 1197, 1079, 1026, 984, 901, 839, 792, 762, 735, 691, 633, 611 cm^{-1}; HRMS (ESI) calcd for $C_{18}H_{20}N$ $[M+H]^+$: 250.1590, found 250.1591.

8-(*tert*-Butyl)-6-phenylindolizine (3j). A mixture of $AgPF_6$ (2.5 mg, 0.01 mmol), IPrAuCl (6.2 mg, 0.01 mmol), **2j** (134 mg, 0.5 mmol) and dichloromethane (5 mL) were stirred at room temperature for 24 h. Column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 200:1) afforded the title product in 80% yield (99.8 mg) as a light yellow oil. ^{1}H NMR (400 MHz, C_6D_6) δ 7.49-7.48 (m, 1H), 7.39-7.36 (m, 2H), 7.24-7.20 (m, 2H), 7.16-7.12 (m, 1H), 6.95 (dd, *J* = 2.8, 1.2 Hz, 1H), 6.87 (d, *J* = 1.6 Hz, 1H), 6.81 (dd, *J* = 4.0, 2.4 Hz, 1H), 6.67 (d, *J* = 4.0 Hz, 1H), 1.43 (s, 9H); ^{13}C NMR (100 MHz, C_6D_6) δ 140.9, 139.6, 130.9, 129.1, 127.2, 127.1, 124.2, 121.7, 114.1, 113.5, 113.3, 101.9, 35.4, 29.8; IR (neat): 3105, 2961, 2868, 1718, 1599, 1492, 1457, 1381, 1366, 1340, 1313, 1255, 1215, 1182, 1093, 1076, 1029, 976, 912, 896, 859, 845, 798, 772, 758, 732, 713, 694, 649, 625 cm^{-1}; HRMS (ESI) calcd for $C_{18}H_{20}N$ $[M+H]^+$: 250.1590, found 250.1590.

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8-Cyclopropyl-6-phenylindolizine (3k). A mixture of $AgPF_6$ (2.5 mg, 0.01 mmol), IPrAuCl (6.2 mg, 0.01 mmol), **2k** (126 mg, 0.5 mmol) and dichloromethane (5 mL) were stirred at room temperature for 10 min. Column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 100:1) afforded the title product in 96% yield (112 mg) as a light yellow oil. ^{1}H NMR (400 MHz, C_6D_6) δ 7.45 (s, 1H), 7.30-7.27 (m, 2H), 7.21-7.17 (m, 2H), 7.15-7.10 (m, 1H), 6.99 (dd, *J* = 2.6, 1.2 Hz, 1H), 6.86 (dd, *J* = 4.0, 2.4 Hz, 1H), 6.73 (dt, *J* = 4.0, 0.8 Hz, 1H), 6.53 (t, *J* = 1.2 Hz, 1H), 1.96-1.89 (m, 1H), 0.72-0.62 (m, 4H); ^{13}C NMR (100 MHz, C_6D_6) δ 139.4, 134.1, 133.6, 129.0, 127.2, 127.1, 124.6, 121.1, 114.1, 113.8, 112.8, 98.3, 12.9, 6.7; IR (neat): 3081, 3058, 3003, 2963, 2363, 2338, 2308, 1707, 1673, 1599, 1553, 1480, 1418, 1342, 1320, 1303, 1261, 1080, 1021, 907, 886, 819, 757, 693, 667, 630, 612 cm^{-1}; HRMS (EI) calcd for $C_{17}H_{15}N$ $[M]^+$: 233.1204, found 233.1201.

6-Phenylindolizine (3l). A mixture of $AgPF_6$ (2.5 mg, 0.01 mmol), IPrAuCl (6.2 mg, 0.01 mmol), **2l** (106 mg, 0.5 mmol) and dichloromethane (5 mL) were stirred at room temperature for 36 h. Column chromatography on silica gel (eluent: petroleum ether) afforded the title product in 90% yield (86.5 mg) as a light yellow solid. ^{1}H NMR (400 MHz, C_6D_6) δ 7.474-7.470 (m, 1H), 7.26-7.23 (m, 2H), 7.20-7.10 (m, 4H), 6.92-6.91 (m, 1H), 6.80 (dd, *J* = 3.8, 2.8 Hz, 1H), 6.67 (dd, *J* = 9.2, 1.6 Hz, 1H), 6.48 (d, *J* = 3.6 Hz, 1H); ^{13}C NMR (100 MHz, C_6D_6) δ 138.9, 132.3, 129.0, 127.2, 127.0, 124.5, 123.0, 119.4, 117.6, 114.5, 113.4, 99.6; IR (neat): 3131, 3115, 3104, 3059, 3035, 2921, 2852, 2660, 1953, 1897, 1806, 1748, 1682, 1625, 1597, 1577, 1527, 1480, 1467, 1450, 1421, 1391, 1342, 1318,

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1274, 1262, 1234, 1187, 1145, 1105, 1079, 1026, 969, 951, 912, 879, 843, 802, 785, 768, 749, 726, 710, 692, 623, 611 cm^{-1}; HRMS (EI) calcd for $C_{14}H_{11}N$ $[M]^+$: 193.0891, found 193.0892.

6-Phenyl-8-(trimethylsilyl)indolizine (3m). A mixture of $AgSbF_6$ (5.2 mg, 0.015 mmol), IPrAuCl (9.3 mg, 0.015 mmol), **2m** (85.0 mg, 0.3 mmol) and dichloromethane (3 mL) were stirred at room temperature for 24 h. Column chromatography on silica gel (eluent: petroleum ether to petroleum ether: ethyl acetate = 200:1) afforded the title product in 84% yield (66.9 mg) as a light yellow oil. ^{1}H NMR (400 MHz, C_6D_6) δ 7.544-7.538 (m, 1H), 7.38-7.35 (m, 2H), 7.24-7.20 (m, 2H), 7.16-7.12 (m, 2H), 6.96 (dd, *J* = 2.6, 1.6 Hz, 1H), 6.85 (dd, *J* = 3.8, 2.4 Hz, 1H), 6.64 (d, *J* = 4.0 Hz, 1H), 0.36 (s, 9H); ^{13}C NMR (100 MHz, C_6D_6) δ 139.4, 134.6, 130.2, 129.1, 127.2, 127.1, 124.6, 124.3, 124.1, 114.4, 113.1, 101.0, -1.2; IR (neat): 3450, 2959, 2899, 2169, 1495, 1449, 1288, 1250, 1174, 1090, 1073, 1028, 973, 918 902, 840, 789, 760, 720, 697, 645, 632, 612 cm^{-1}; HRMS (EI) calcd for $C_{17}H_{19}NSi$ $[M]^+$: 265.1287, found 265.1292.

6-Methyl-8-phenylindolizine (3n). A mixture of $AgPF_6$ (3.8 mg, 0.015 mmol), IPrAuCl (9.3 mg, 0.015 mmol), **2n** (67.6 mg, 0.3 mmol) and 1,2-dichloroethane (3 mL) were stirred at 80 ^{o}C for 0.5 h. Column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 100:1) afforded the title product in 91% yield (56.3 mg) as a light yellow oil. ^{1}H NMR (400 MHz, C_6D_6) δ 7.67-7.65 (m, 2H), 7.24-7.21 (m, 2H), 7.18-7.14 (m, 1H), 6.97 (s, 2H), 6.79-6.78 (m, 1H), 6.71 (d, *J* = 4.0 Hz, 1H), 6.35 (s, 1H), 1.86 (s, 3H); ^{13}C NMR (100

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MHz, C_6D_6) δ 139.9, 132.8, 131.4, 128.8, 128.6, 128.0, 122.2, 119.9, 119.3, 113.7, 113.1, 99.8, 18.0; IR (neat): 3055, 3029, 2920, 2859, 1952, 1888, 1716, 1642, 1599, 1546, 1493, 1442, 1384, 1347, 1304, 1258, 1144, 1080, 1041, 918, 894, 863, 819, 772, 760, 719, 695, 653, 633, 612 cm^{-1}; HRMS (EI) calcd for $C_{15}H_{13}N$ $[M]^+$: 207.1048, found 207.1049.

5-Methyl-6,8-diphenylindolizine (3o). A mixture of $AgPF_6$ (2.5 mg, 0.01 mmol), IPrAuCl (6.2 mg, 0.01 mmol), **2o** (151 mg, 0.5 mmol) and dichloromethane (5 mL) were stirred at room temperature for 1 h. Column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 100:1) afforded the title product in 98% yield (139 mg) as a light yellow oil. ^1H NMR (400 MHz, C_6D_6) δ 7.68 (d, *J* = 7.6 Hz, 2H), 7.24-7.10 (m, 8H), 6.998-6.995 (m, 1H), 6.93-6.91 (m, 2H), 6.77 (s, 1H), 2.00 (s, 3H); ^{13}C NMR (100 MHz, C_6D_6) δ 140.7, 139.9, 132.4, 130.7, 130.3, 129.0, 128.9, 128.5, 127.9, 127.1, 124.0, 120.5, 114.8, 111.3, 100.9, 16.0; IR (neat): 3054, 3025, 1955, 1699, 1599, 1486, 1443, 1376, 1357, 1328, 1265, 1188, 1109, 1072, 1061, 1030, 981, 930, 875, 809, 770, 755, 723, 698, 685, 637, 619 cm^{-1}; HRMS (ESI) calcd for $C_{21}H_{18}N$ $[M+H]^+$: 284.1434, found 284.1434.

5-Benzyl-6,8-diphenylindolizine (3p). A mixture of $AgPF_6$ (2.5 mg, 0.01 mmol), IPrAuCl (6.2 mg, 0.01 mmol), **2p** (189 mg, 0.5 mmol) and dichloromethane (5 mL) were stirred at room temperature for 16 h. Column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 100:1) afforded the title product in 95% yield (170 mg) as a light yellow oil. ^1H NMR (400 MHz, C_6D_6) δ 7.74 (d, *J* = 7.2 Hz, 2H), 7.35-7.33 (m, 2H), 7.23 (t, *J* = 7.2 Hz, 2H), 7.18-7.14 (m, 1H), 7.09-7.05 (m, 4H), 7.00-6.91 (m, 6H), 6.88-6.87 (m, 1H),

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6.74-6.73 (m, 1H), 4.06 (s, 2H); ^{13}C NMR (100 MHz, C_6D_6) δ 140.5, 139.8, 137.3, 132.4, 131.8, 130.0, 129.7, 129.2, 128.94, 128.93, 128.7, 128.1, 127.9, 127.5, 126.8, 126.0, 120.2, 114.9, 113.1, 101.0, 36.0; IR (neat): 3136, 3056, 3024, 2349, 1711, 1600, 1493, 1449, 1388, 1362, 1336, 1282, 1215, 1179, 1124, 1105, 1075, 1050, 1029, 958, 930, 876, 863, 781, 772, 745, 721, 696, 665, 656, 638, 619 cm^{-1}; HRMS (ESI) calcd for $C_{27}H_{22}N$ $[M+H]^+$: 360.1747, found 360.1746.

1,3-Dimethyl-6,8-diphenylindolizine (3q). A mixture of $AgPF_6$ (2.5 mg, 0.01 mmol), IPrAuCl (6.2 mg, 0.01 mmol), **2q** (158 mg, 0.5 mmol) and dichloromethane (5 mL) were stirred at room temperature for 10 min. Column chromatography on silica gel (eluent: petroleum ether: dichloromethane = 30:1) afforded the title product in 66% yield (97.4 mg) as a light yellow oil. ^{1}H NMR (400 MHz, C_6D_6) δ 7.53 (d, *J* = 0.8 Hz, 1H), 7.44-7.41 (m, 4H), 7.24-7.12 (m, 6H), 6.75 (s, 1H), 6.38 (s, 1H), 2.07 (s, 3H), 2.04 (s, 3H); ^{13}C NMR (100 MHz, C_6D_6) δ 140.6, 139.5, 134.7, 129.9, 129.1, 128.1, 127.7, 127.2, 127.1, 127.0, 123.9, 119.4, 118.6, 117.0, 116.7, 109.2, 14.1, 11.5; IR (neat): 3056, 3029, 2920, 2349, 2323, 1694, 1627, 1599, 1539, 1491, 1444, 1347, 1314, 1271, 1244, 1211, 1174, 1156, 1074, 1045, 1026, 906, 845, 791, 756, 696, 670, 665, 641, 623 cm^{-1}; HRMS (ESI) calcd for $C_{22}H_{20}NO$ $[M+H]^+$: 314.1539, found 314.1542.

2,3,6,8-Tetraphenylindolizine (3r). A mixture of $AgPF_6$ (2.5 mg, 0.01 mmol), IPrAuCl (6.2 mg, 0.01 mmol), **2r** (220 mg, 0.5 mmol) and dichloromethane (5 mL) were stirred at room temperature for 30 min. Column chromatography on silica gel (eluent: petroleum

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ether: ethyl acetate= 50:1) afforded the title product in 97% yield (205 mg) as a yellow solid. M.p. 198-200 ^{o}C. ^{1}H NMR (400 MHz, C_6D_6) δ 8.18 (s, 1H), 7.77 (d, *J* = 7.6 Hz, 2H), 7.41 (d, *J* = 7.2 Hz, 2H), 7.33-7.22 (m, 7H), 7.15-7.00 (m, 11H); ^{13}C NMR (100 MHz, C_6D_6) δ 139.8, 139.1, 136.7, 133.5, 132.3, 131.8, 131.3, 129.51, 129.48, 129.4, 129.2, 129.1, 128.9, 128.7, 128.4, 128.1, 127.3, 127.0, 126.5, 125.7, 123.1, 119.1, 118.4, 101.1; IR (neat): 3056, 3028, 1669, 1600, 1489, 1448, 1402, 1340, 1325, 1261, 1207, 1135, 1068, 1027, 914, 866, 836, 774, 763, 734, 695, 652, 608 cm^{-1}; HRMS (ESI) calcd for $C_{32}H_{24}N$ $[M+H]^+$: 422.1903, found 422.1902.

6,8-Diphenylindolizine-3-carbonitrile (3s). A mixture of $AgPF_6$ (3.8 mg, 0.015 mmol), IPrAuCl (9.3 mg, 0.015 mmol), **2s** (93.7 mg, 0.3 mmol) and dichloromethane (3 mL) were stirred at 40 ^{o}C for 48 h. Column chromatography on silica gel (eluent: petroleum ether: ethyl acetate= 20:1) afforded the title product in 93% yield (81.7 mg) as a colorless oil. ^{1}H NMR (400 MHz, C_6D_6) δ 8.02 (s, 1H), 7.39-7.36 (m, 2H), 7.26-7.11 (m, 8H), 6.87 (d, *J* = 1.2 Hz, 1H), 6.80 (d, *J* = 4.4 Hz, 1H), 6.24 (d, *J* = 4.4 Hz, 1H); ^{13}C NMR (100 MHz, C_6D_6) δ 138.0, 137.1, 134.8, 133.3, 129.3, 129.1, 128.8, 128.6, 128.1, 127.8, 127.1, 122.7, 121.8, 121.5, 114.1, 101.5, 97.2; IR (neat): 3056, 2973, 2901, 2206, 1732, 1595, 1557, 1493, 1471, 1438, 1389, 1336, 1311, 1247, 1173, 1075, 1034, 916, 854, 779, 769, 751, 719, 699, 678, 626 cm^{-1}; HRMS (ESI) calcd for $C_{21}H_{15}N_2$ $[M+H]^+$: 295.1230, found 295.1230.

7,9-Diphenylpyrido[1,2-*a*]indole (3t). A mixture of $AgPF_6$ (3.8 mg, 0.015 mmol), IPrAuCl (9.3 mg, 0.015 mmol), **2t** (101 mg, 0.3 mmol) and 1,2-dichloroethane (3 mL)

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were stirred at 80 ^{o}C for 5 h. Column chromatography on silica gel (eluent: petroleum ether) afforded the title product in 55% yield (52.7 mg) as a yellow oil. ^{1}H NMR (400 MHz, C_6D_6) δ 7.99 (s, 1H), 7.77 (d, *J* = 8.4 Hz, 1H), 7.65-7.63 (m, 2H), 7.45 (d, *J* = 8.4 Hz, 1H), 7.38-7.13 (m, 10H), 7.02 (s, 1H), 6.85 (s, 1H); ^{13}C NMR (100 MHz, C_6D_6) δ 139.5, 138.7, 135.4, 133.1, 130.7, 130.3, 129.1, 129.0, 128.7, 128.4, 127.3, 126.9, 123.4, 122.4, 122.3, 121.2, 120.8, 120.3, 110.9, 92.9; IR (neat): 3054, 3031, 2919, 2851, 1914, 1731, 1627, 1599, 1575, 1517, 1494, 1478, 1458, 1440, 1401, 1336, 1316, 1249, 1209, 1131, 1076, 1028, 1012, 919, 897, 866, 831, 771, 753, 746, 727, 694, 652, 626 cm^{-1}; HRMS (ESI) calcd for $C_{24}H_{18}N$ $[M+H]^+$: 320.1434, found 320.1433.

Synthesis of 3-(1-(4-methoxyphenyl)vinyl)-6,8-diphenylindolizine (4). To a dry Schlenk tube was added **3a** (53.9 mg, 0.2 mmol). The Schlenk tube was evacuated and back-filled with argon for three times. Then, PPh_3AuNTf_2 (7.4 mg, 0.01 mmol), toluene (2 mL) and 1-ethynyl-4-methoxybenzene (31.7 mg, 0.24 mmol) were added. The resulting solution was stirred at 80 ^{o}C for 2 h. Then, the solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 100:1) to afford **4** (51.8 mg, 65% yield) as a light yellow oil. ^{1}H NMR (400 MHz, C_6D_6) δ 7.97 (s, 1H), 7.73-7.71 (m, 2H), 7.29-7.20 (m, 7H), 7.11-7.08 (m, 2H), 7.05-7.01 (m, 2H), 6.96 (d, *J* = 1.6 Hz, 1H), 6.84 (d, *J* = 4.0 Hz, 1H), 6.68-6.66 (m, 2H), 5.54 (d, *J* = 1.6 Hz, 1H), 5.45 (d, *J* = 1.2 Hz, 1H), 3.22 (s, 3H); ^{13}C NMR (100 MHz, C_6D_6) δ 160.3, 140.5, 139.8, 139.0, 133.7, 133.1, 132.4, 129.1, 128.98, 128.95, 128.91, 128.88, 128.3, 127.3, 126.9, 126.7, 125.0, 121.4, 117.7, 117.1, 114.5, 114.3, 100.6, 54.8;

IR (neat): 3048, 2923, 2840, 1718, 1602, 1509, 1438, 1248, 1159, 1028, 836, 757, 697 cm^{-1}; HRMS (ESI) calcd for $C_{29}H_{24}NO$ $[M+H]^+$: 402.1852, found 402.1850.

Synthesis of 6,8-diphenyl-3-(phenylthio)indolizine (5). To a dry Schlenk tube was added **3a** (53.9 mg, 0.2 mmol). The Schlenk tube was evacuated and back-filled with argon for three times. Then, 1,2-diphenyldisulfane (43.7 mg, 0.2 mmol), CuI (3.8 mg, 0.02 mmol) and DMSO (2 mL) were added. The resulting solution was stirred at 110 ^oC for 12 h. After cooling down, the mixture was diluted with water, extracted with ethyl acetate, washed with brine and dried over anhydrous Na_2SO_4. The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 200:1) followed by recycling preparative HPLC to afford **5** in 72% yield (54.3 mg) as a yellow oil. ^1H NMR (400 MHz, C_6D_6) δ 8.57 (s, 1H), 7.62-7.59 (m, 2H), 7.29-7.17 (m, 6H), 7.09-6.96 (m, 6H), 6.83-6.72 (m, 4H); ^{13}C NMR (100 MHz, C_6D_6) δ 139.0, 138.5, 137.7, 135.2, 133.5, 129.5, 129.2, 129.0, 128.9, 128.4, 127.6, 127.1, 126.4, 125.83, 125.78, 125.3, 120.3, 119.9, 109.8, 101.3; IR (neat): 3054, 3029, 2168, 1977, 1580, 1491, 1477, 1431, 1322, 1156, 1025, 842, 774, 755, 737, 695 cm^{-1}; HRMS (ESI) calcd for $C_{26}H_{20}NS$ $[M+H]^+$: 378.1311, found 378.1309.

Synthesis of 6,8-diphenyl-3-((triisopropylsilyl)ethynyl)indolizine (6). To a dry Schlenk tube was added **3a** (53.9 mg, 0.2 mmol). The Schlenk tube was then introduced into a nitrogen-filled glovebox, and AuCl (2.3 mg, 0.01 mmol) was added. The tube with the gold catalyst was then taken out of the glovebox. To this tube were added

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1-((triisopropylsilyl)ethynyl)-1λ^3-benzo[*d*][1,2]iodaoxol-3(1*H*)-one (103 mg, 0.24 mmol) and diethyl ether (4 mL) under argon. The resulting mixture was stirred at room temperature for 2 h. Then, the solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on basic Al_2O_3 (eluent: petroleum ether: ethyl acetate = 100:1) to afford **6** (69.8 mg, 78% yield) as a light yellow oil. ^{1}H NMR (400 MHz, C_6D_6) δ 8.58 (s, 1H), 7.56 (d, *J* = 6.8 Hz, 2H), 7.46 (d, *J* = 8.0 Hz, 2H), 7.27-7.18 (m, 5H), 7.15-7.11 (m, 1H), 7.07 (d, *J* = 4.4 Hz, 1H), 6.94 (d, *J* = 1.2 Hz, 1H), 6.48 (d, *J* = 4.4 Hz, 1H), 1.25-1.14 (m, 21H); ^{13}C NMR (100 MHz, C_6D_6) δ 139.1, 138.7, 133.4, 132.8, 129.2, 129.0, 128.8, 128.4, 127.7, 127.0, 126.3, 121.7, 120.3, 119.5, 109.1, 100.5, 99.3, 98.9, 19.1, 11.8; IR (neat): 2941, 2887, 2863, 2135, 1602, 1464, 1438, 1385, 1160, 1065, 882, 774, 755, 746, 696, 675, 665 cm^{-1}; HRMS (ESI) calcd for $C_{31}H_{36}NSi$ $[M+H]^+$: 450.2612, found 450.2610.

Synthesis of indolizines 7.

Typical procedure for the synthesis of 3-((4-methoxyphenyl)ethynyl)-6,8-diphenylindolizine (7a). To a dry Schlenk tube was added **3a** (53.9 mg, 0.2 mmol). The Schlenk tube was evacuated and back-filled with argon for three times. Then, $Pd(PPh_3)_2Cl_2$ (7.0 mg, 0.01 mmol), KOAc (39.3 mg, 0.4 mmol), 1-(bromoethynyl)-4-methoxybenzene (63.3 mg, 0.3 mmol) and toluene (2 mL) were added. The resulting solution was stirred at 80 ^{o}C for 15 h. Then, the solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on basic Al_2O_3 (eluent: petroleum ether: ethyl acetate = 100:1) to afford **7a** (44.6 mg, 56%

yield) as a yellow solid. M.p. 153-154 °C. ^{1}H NMR (400 MHz, C_6D_6) δ 8.57 (s, 1H), 7.60 (d, *J* = 7.2 Hz, 2H), 7.50-7.46 (m, 2H), 7.37 (d, *J* = 7.2 Hz, 2H), 7.28-7.10 (m, 7H), 6.96 (d, *J* = 1.2 Hz, 1H), 6.64-6.62 (m, 3H), 3.20 (s, 3H); ^{13}C NMR (100 MHz, C_6D_6) δ 160.1, 139.2, 138.8, 133.4, 133.2, 132.8, 129.2, 128.9, 128.8, 128.4, 127.5, 127.3, 126.4, 121.5, 120.1, 119.5, 116.0, 114.5, 109.1, 101.0, 97.8, 80.0, 54.8; IR (neat): 3065, 2929, 2834, 2193, 1977, 1606, 1469, 1437, 1388, 1253, 1158, 1029, 827, 773, 764, 757, 719, 699 cm^{-1}; HRMS (ESI) calcd for $C_{29}H_{22}NO$ $[M+H]^+$: 400.1696, found 400.1693.

6,8-Diphenyl-3-((3,4,5-trimethoxyphenyl)ethynyl)indolizine (7b). A mixture of **3a** (134.7 mg, 0.5 mmol), $Pd(PPh_3)_2Cl_2$ (17.5 mg, 0.025 mmol), KOAc (98.1 mg, 1.0 mmol), 5-(bromoethynyl)-1,2,3-trimethoxybenzene (203.3 mg, 0.75 mmol) and toluene (5 mL) were stirred at 80 °C for 18 h. Column chromatography on basic Al_2O_3 (eluent: petroleum ether: ethyl acetate = 20:1 to 8:1) afforded the title product in 48% yield (111 mg) as a light yellow solid. M.p. 162-163 °C. ^{1}H NMR (400 MHz, C_6D_6) δ 8.63 (s, 1H), 7.60 (d, *J* = 6.8 Hz, 2H), 7.38 (d, *J* = 6.8 Hz, 2H), 7.28-7.10 (m, 7H), 6.98 (d, *J* = 1.2 Hz, 1H), 6.87 (s, 2H), 6.66 (d, *J* = 4.4 Hz, 1H), 3.82 (s, 3H), 3.31 (s, 6H); ^{13}C NMR (100 MHz, C_6D_6) δ 154.2, 140.4, 139.1, 138.7, 133.6, 133.0, 129.2, 129.0, 128.8, 128.4, 127.6, 127.3, 126.7, 121.5, 120.4, 119.7, 118.6, 109.5, 108.8, 101.2, 98.4, 80.3, 60.6, 55.7; IR (neat): 2934, 2826, 2190, 1572, 1497, 1400, 1384, 1345, 1327, 1232, 1180, 1127, 1003, 959, 812, 820, 778, 769, 754, 697, 678, 663 cm^{-1}; HRMS (ESI) calcd for $C_{31}H_{26}NO_3$ $[M+H]^+$: 460.1907, found 460.1903.

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Gold-catalyzed reaction of 1-phenyl-2-(1*H*-pyrrol-1-yl)ethanone (1a) with 1-ethynyl-4-methoxybenzene. Under argon, to a Schlenk tube were added PPh_3AuNTf_2 (0.015 mmol, 11.1 mg), **1a** (0.3 mmol, 55.6 mg), toluene (3 mL), and 1-ethynyl-4-methoxybenzene (0.36 mmol, 47.6 mg). The reaction mixture was stirred at 80 ℃ for 3 h. The solvent was evaporated under the reduced pressure and the residue was purified by column chromatography on silica gel (eluent: petroleum ether: ethyl acetate = 200:1 to 50:1) to afford **3b** in 10% yield (9.1 mg) and 8-(4-methoxyphenyl)-3-(1-(4-methoxyphenyl)vinyl)-6-phenylindolizine in 13% yield (16.9 mg) as a light yellow oil. ^{1}H NMR of the latter product: (400 MHz, C_6D_6) δ 7.99 (s, 1H), 7.67 (d, *J* = 8.0 Hz, 2H), 7.27 (t, *J* = 8.4 Hz, 4H), 7.11 (t, *J* = 7.2 Hz, 2H), 7.06-7.02 (m, 2H), 6.99 (s, 1H), 6.90-6.88 (m, 3H), 6.68 (d, *J* = 8.0 Hz, 2H), 5.56 (s, 1H), 5.48 (s, 1H), 3.37 (s, 3H), 3.23 (s, 3H); ^{13}C NMR (100 MHz, C_6D_6) δ 160.3, 160.2, 140.6, 139.2, 133.5, 133.4, 132.5, 132.1, 130.0, 129.1, 128.9, 127.3, 127.0, 126.7, 125.1, 121.1, 117.2, 117.0, 114.50, 114.47, 114.2, 100.7, 54.9, 54.8; IR (neat): 2954, 2929, 2831, 1730, 1606, 1507, 1244, 1174, 1030, 832, 773, 760, 697 cm^{-1}; HRMS (ESI) calcd for $C_{30}H_{26}NO_2$ $[M+H]^+$: 432.1958, found 432.1956.

ASSOCIATED CONTENT

Supporting Information

X-ray crystallography of compound **7b** (CCDC 1570337) and spectroscopic characterization of all new compounds are given in the Supporting Information.

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Notes

The authors declare no competing financial interest.

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REFERENCES

(1) (a) V. Sharma and V. Kumar, *Med. Chem. Res.*, 2014, **23**, 3593-3606. (b) L.-L. Gundersen, C. Charnock, A. H. Negussie, F. Rise and S. Teklu, *Eur. J. Pharm. Sci.*, 2007, **30**, 26-35. (c) Y.-M. Shen, P.-C. Lv, W. Chen, P.-G. Liu, M.-Z. Zhang and H.-L. Zhu, *Eur. J. Med. Chem.* 2010, **45**, 3184-3190. (d) S. Teklu, L.-L. Gundersen, T. Larsen, K. E. Malterud and F. Rise, *Bioorg. Med. Chem.*, 2005, **13**, 3127-3139. (e) W. Chai, J. G. Breitenbucher, A. Kwok, X. Li, V. Wong, N. I. Carruthers, T. W. Lovenberg, C. Mazur, S. J. Wilson, F. U. Axe and T. K. Jones, Bioorg. *Med. Chem. Lett.*, 2003, **13**, 1767-1770.

(2) (a) Y. R. Song, C. W. Lim and T. W. Kim, *Luminescence*, 2016, **31**, 364-371. (b) E. Kim,

View Article Online
DOI: 10.1039/C7OB02102J

Y. Lee, S. Lee and S. B. Park, *Acc. Chem. Res.*, 2015, **48**, 538-547. (c) H. Sonnenschein, G. Hennrich, U. Resch-Genger and B. Schulz, *Dyes Pigm.*, 2000, **46**, 23-27.

(3) For reviews on the synthesis of indolizines, see: (a) B. Sadowski, J. Klajn and D. T. Gryko, *Org. Biomol. Chem.*, 2016, **14**, 7804-7828. (b) G. S. Singh and E. E. Mmatli, *Eur. J. Med. Chem.* 2011, 46, 5237-5257.

(4) M. Scholtz, *Ber. Dtsch. Chem. Ges.*, 1912, **45**, 734-746.

(5) A. E. Tschitschibabin, *Ber. Dtsch. Chem. Ges. B*, 1927, **60**, 1607-1617.

(6) (a) J. Brioche, C. Meyer and J. Cossy, *Org. Lett.*, 2015, **17**, 2800-2803. (b) K. Wu and Q.-Y. Chen, *Synthesis*, 2003, 35-40.

(7) For a review, see: (a) L.-X. Wang and Y.-L. Tang, *Eur. J. Org. Chem.*, 2017, 2207-2213. For selected papers, see: (b) I. V. Seregin and V. Gevorgyan, *J. Am. Chem. Soc.*, 2006, **128**, 12050-12051. (c) C. R. Smith, E. M. Bunnelle, A. J. Rhodes and R. Sarpong, *Org. Lett.*, 2007, **9**, 1169-1171. (d) Y. Liu, Z. Song and B. Yan, *Org. Lett.*, 2007, **9**, 409-412. (e) B. Yan and Y. Liu, *Org. Lett.*, 2007, **9**, 4323-4326. (f) B. Yan, Y. Zhou, H. Zhang, J. Chen and Y. Liu, *J. Org. Chem.* 2007, **72**, 7783-7786. (g) A. R. Hardin and R. Sarpong, *Org. Lett.*, 2007, **9**, 4547-4550. (h) D. Chernyak, S. B. Gadamsetty and V. Gevorgyan, *Org. Lett.*, 2008, **10**, 2307-2310. (i) Z. Li, D. Chernyak and V. Gevorgyan, *Org. Lett.*, 2012, **14**, 6056-6059. (j) X. Meng, P. Liao, J. Liu and X. Bi, *Chem. Commun.*, 2014, **50**, 11837-11839. (k) T. Xu and H. Alper, *Org. Lett.*, 2015, **17**, 4526-4529. (l) L. Zhang, X. Li, Y. Liu and D. Zhang, *Chem. Commun.*, 2015, **51**, 6633-6636. (m) R.-R. Liu, C.-J. Lu, M.-D. Zhang, J.-R. Gao and Y.-X. Jia, *Chem. Eur. J.*, 2015, **21**, 7057-7060.

(8) For indolizine synthesis by construction of the pyridine ring, see: (a) H. Zhu, J. Stöckigt,

View Article Online
DOI: 10.1039/C7OB02102J

Y. Yu and H. Zou, *Org. Lett.*, 2011, **13**, 2792-2794. (b) M. Kucukdisli and T. Opatz, *J. Org. Chem.*, 2013, **78**, 6670-6676. (c) J. H. Lee and I. Kim, *J. Org. Chem.*, 2013, **78**, 1283-1288. (d) W. Hao, H. Wang, Q. Ye, W.-X. Zhang and Z. Xi, *Org. Lett.*, 2015, **17**, 5674-5677. (e) A. K. Verma, S. P. Shukla, J. Singh and V. Rustagi, *J. Org. Chem.*, 2011, **76**, 5670-5684. (f) D. I. Chai and M. Lautens, *J. Org. Chem.*, 2009, **74**, 3054-3061. (g) A. K. Verma, T. Kesharwani, J. Singh, V. Tandon and R. C. Larock, *Angew. Chem., Int. Ed.*, 2009, **48**, 1138-1143. (h) S. E. Kiruthika, A. Nandakumar and P. T. Perumal, *Org. Lett.*, 2014, **16**, 4424-4427.

(9) X. Li, X. Xie and Y. Liu, *J. Org. Chem.*, 2016, **81**, 3688-3699.

(10) For the application of gold catalysis in the synthesis of heterocycles, see: (a) M. Rudolph and A. S. K. Hashmi, *Chem. Commun.*, 2011, **47**, 6536–6544. (b) A. Arcadi, *Chem. Rev.*, 2008, **108**, 3266–3325. For the use of gold catalysis in synthesis, see: (c) D. Pflästerer and A. S. K. Hashmi, *Chem. Soc. Rev.*, 2016, **45**, 1331-1367. (d) M. Rudolph and A. S. K. Hashmi, *Chem. Soc. Rev.*, 2012, **41**, 2448–2462. (e) N. Bongers and N. Krause, *Angew. Chem. Int. Ed.*, 2008, **47**, 2178-2181.

(11) For example, gold-catalyzed reaction of 1-phenyl-2-(1*H*-pyrrol-1-yl)ethanone with 1-ethynyl-4-methoxybenzene afforded the desired indolizine in only 10% yield, along with 2-vinylated indolizine in 13% yield by this method. See experimental section. For the regioselectivity problems in gold-catalyzed conversion of pyrroles, see: A. S. K. Hashmi, R. Salathé and W. Frey, *Eur. J. Org. Chem.*, 2007, 1648-1652.

(12) For gold-catalyzed intramolecular hydroarylation of alkynes with pyrroles, see: (a) Y. Lu, X. Du, X. Jia and Y. Liu, *Adv. Synth. Catal.*, 2009, **351**, 1517-1522. (b) M. Gruit, D.

Michalik, K. Krüger, A. Spannenberg, A. Tillack, A. Pews-Davtyan and M. Beller, *Tetrahedron*, 2010, **66**, 3341-3352. (c) E. Borsini, G. Broggini, A. Fasana, C. Baldassarri, A. M. Manzo and A. D. Perboni, *Beilstein J. Org. Chem.*, 2011, **7**, 1468-1474. (d) S. Sarkar, K. Bera, S. Jalal and U. Jana, *Eur. J. Org. Chem.*, 2013, 6055-6061. (e) B. Pan, X. Lu, C. Wang, Y. Hu, F. Wu and B. Wan, *Org. Lett.*, 2014, **16**, 2244-2247. (f) D. Hack, C. C. J. Loh, J. M. Hartmann, G. Raabe and D. Enders, *Chem. Eur. J.*, 2014, **20**, 3917-3921. (g) L. Boiaryna, M. S. Azizi, A. El Bouakher, B. Picard, C. Taillier, M. Othman, M. Trabelsi-Ayadi and V. Dalla, *Org. Lett.*, 2015, **17**, 2130-2133. (h) Z. Li, A. Kumar, S. K. Sharma, V. S. Parmar and E. V. Van der Eycken, *Tetrahedron*, 2015, **71**, 3333-3342.

(13) (a) L. Florentino, F. Aznar and C. Valdés, *Chem. Eur. J.*, 2013, **19**, 10506-10510. (b) J. A. Schiffner, T. H. Wöste and M. Oestreich, *Eur. J. Org. Chem.*, 2010, 174-182.

(14) The same method has been used for the synthesis of α-(*N*-pyrrolyl)ketone bearing alkyl substituents in our previous report, see Ref 9.

(15) X. Li, M. Chen, X. Xie, N. Sun, S. Li and Y. Liu, *Org. Lett.*, 2015, **17**, 2984-2987.

(16) D. C. Mohan, C. Ravi, V. Pappula and S. Adimurthy, *J. Org. Chem.*, 2015, **80**, 6846-6855.

(17) J. P. Brand, J. Charpentier and J. Waser, *Angew. Chem. Int. Ed.*, 2009, **48**, 9346-9349.

(18) I. V. Seregin, V. Ryabova and V. Gevorgyan, *J. Am. Chem. Soc.*, 2007, **129**, 7742-7743.

(19) See Supporting Information.

(20) For the discussion of the reaction mechanism in gold catalysis, see: A. S. K. Hashmi, *Angew. Chem. Int. Ed.* 2010, **49**, 5232-5241.

(21) For elimination of water to form the aromatic rings in gold catalysis, see: (a) A. S. K. Hashmi and Michael Wölfle, *Tetrahedron*, 2009, **65**, 9021-9029. (b) C. M. Grisé and L. Barriault, *Org. Lett.*, 2006, **8**, 5905-5908. (c) For elimination of silanol, see: A. S. K. Hashmi, W. Yang and F. Rominger, *Angew. Chem. Int. Ed.*, 2011, **50**, 5762-5765.

(22) P. Braunstein, H. Lehner and D. Matt, K. Burgess and Ohlmeyer, M. J. *Inorg. Synth.*, 1990, **27**, 218-221.

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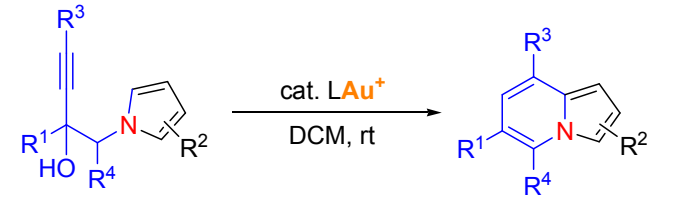
Graphic abstract:



R^2 = H, alkyl, aryl, EWG *20 examples with up to 98% yield*

- *pyridine ring construction*
- *mild reaction conditions*
- *wide functional group compatibility*
- *high efficiency*

Abstract: Gold-catalyzed intramolecular hydroarylation/aromatization of pyrrole-ynes to functionalized indolizines through the construction of the pyridine ring of indolizines has been developed.