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Palladium-Catalyzed Oxidative Cyclization for the Synthesis of 2-Alkyl-Imidazo[5,1,2-*cd*]indolizines

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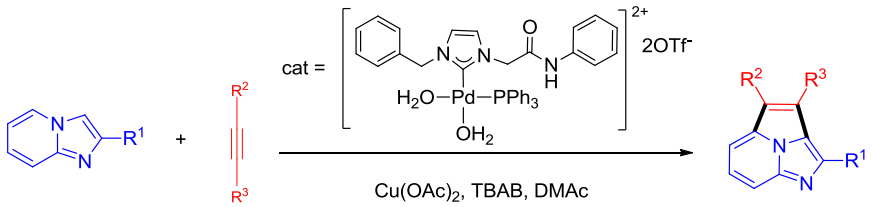

An effective palladium-catalyzed direct arylation of 2-alkyl-imidazo[1,2-*a*]pyridine with alkyne via double C–H functionalization to yield 2-alkyl-imidazo[5,1,2-*cd*]indolizines was successfully developed. The catalyst precursor used was an ionic palladium(II) complex bearing amido-functionalized *N*-heterocyclic carbene and triphenylphosphine ligands.

Key Topic: Organometallic Chemistry

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Abstract

An effective palladium-catalyzed direct arylation of 2-alkyl-imidazo[1,2-*a*]pyridine with alkyne via double C–H functionalization to yield imidazo[5,1,2-*cd*]indolizines was successfully developed. The catalyst system comprised of an ionic palladium(II) complex bearing amido-functionalized *N*-heterocyclic carbene and triphenylphosphine ligands. A mere 2.5 mol% of palladium loading was sufficient for catalyzing the reactions. Copper acetate and *n*-tetrabutylammonium bromide were employed as oxidant and phase transfer catalyst, respectively. Beside imidazo[1,2-*a*]pyridine, desirably, less electron-rich imidazo[1,2-*a*]pyrimidine substrates could also be employed as coupling partners. Also a wide range of diaryl alkynes could also be used. One of the 2-alkyl-imidazo[5,1,2-*cd*]indolizines has been successfully established by single-crystal X-ray diffraction analysis. UV and PL spectra of these compounds confirmed that some of these new compounds were highly fluorescent. The methodology developed provides an easy synthetic route for the preparation of these new fluorescent materials.

Keywords: C–H Functionalization; Imidazo[5,1,2-cd]indolizines; *N*-heterocyclic Carbene; Homogeneous Catalysis

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Introduction

Transition-metal-catalyzed C–H bond functionalization for the construction of fused polycyclic heteroaromatic compounds have been receiving considerable attention.[1],[2],[3] This process provides a green route to π-conjugated heteroaromatic molecules, which exhibit diversified biological and pharmacological activities.[4] This class of compounds can have a wide range of applicability to organic electronics and luminescent materials as well.[5] Previously, we have reported the use of an ionic palladium complex of *N*-heterocyclic carbene (NHC), $[PdL(PPh_3)(H_2O)_2](SO_3CF_3)_2$ (**1a**) to catalyze the double C–H functionalization of various nitrogen- and sulfur-containing heteroarenes to form fused polycyclic heteroaromatic compounds with alkynes (Chart 1).[6] Interestingly, for the coupling reaction employing C2-aryl imidazo[1,2-*a*]pyridine as substrate, beside the major linearly fused tetracyclic compounds, imidazo[5,1,2-*cd*]indolizine featuring a fused tricyclic core was also obtained as minor product. The formation of these two kinds of products can be explained by the possible formation of two different palladacycle intermediates via two possible sites of C–H activation. Imidazo[5,1,2-*cd*]indolizines belonging to a rare class of heterocycle were previously prepared by the tandem [8+2] cycloaddition-[2+6+2]dehydrogenation reactions.[7] Only a few examples of palladium-catalyzed oxidative coupling reactions yielding high yields of imidazo[5,1,2-*cd*]indolizines were known.[8] To avoid the formation of the aforementioned teteracyclic compounds, C2-phenyl group on the imidazo[1,2-*a*]pyridine can be replaced by alkyl substituents, such that 2-alkyl-imidazo[5,1,2-*cd*]indolizines can be formed exclusively. A direct route for the formation of this rare type of π-conjugated heterocyclic scaffold should be of significant interest since earlier work by Gryko *et al*. had demonstrated that related benzo[*a*]imidazo[5,1,2-*cd*]indolizines exhibited interesting photophysical properties.[7b] Herein, we report our results on the palladium-catalyzed double C–H functionalization for the formation of 2-alkyl-imidazo[5,1,2-*cd*]indolizines and their photophysical properties.

Chart 1. Palladium-Catalyzed Oxidative Cyclization

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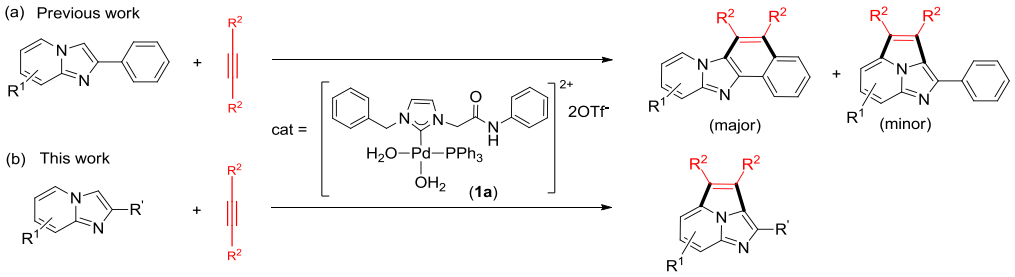
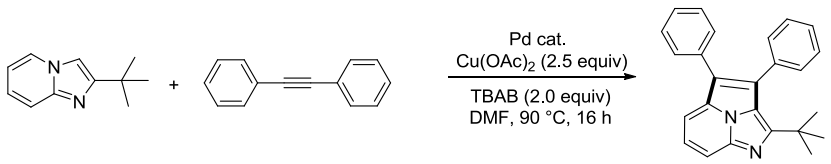


Results and Discussion

Catalytic Investigation.

An initial investigation was carried out to confirm the effectiveness of the ionic complex **1a** in the oxidative coupling reactions (Table 1). The coupling reaction between 2-*tert*-butylimidazo[1,2-*a*]pyridine and diphenylacetylene was carried out as the benchmark reaction and our previous conditions of using 2.5 mol% of palladium complex as precatalyst, a reaction temperature of 90 °C, $Cu(OAc)_2$ as base, a reaction time of 16 h, DMF as solvent, and *n*-tetrabutylammonium bromide (TBAB) as phase transfer catalyst were employed for the reaction.[6] Entry 1 clearly showed that the ionic NHC complex **1a** was the most effective complex, affording a good 74 % yield of coupled product. The neutral dichloropalladium(II) complex **1b** bearing the same NHC ligand and tricyclohexylphosphine,[9] reported by us earlier, was much less effective (entry 2). Palladium(II) NHC complex with IMes ligand (IMes = 1,3-bis(2,4,6-trimethylphenyl)imidazol-2-ylidene) has been proven to be highly effective in various cross-coupling reactions.[10] However, the *in situ* catalyst system of $PdCl_2$/2IMes·HCl with 10 mol% of Pd loading delivered only an inferior product yield of 45 % (entry 3). The catalytic reaction did not work well neither when the imidazolium ligand precursor was replaced by PPh_3 (entry 4). Ligand-free palladium acetate was also less effective than complex **1a** in catalyzing the coupling reaction as the former complex afforded only a 40 % yield of coupled product with 10 mol% of catalyst loading (entries 5 vs. 1).

Table 1. Catalysts Screening[a]



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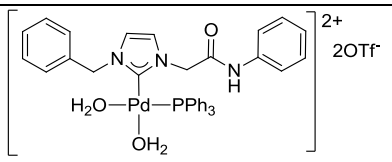
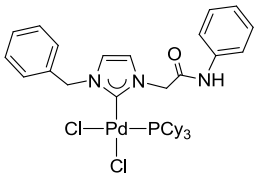
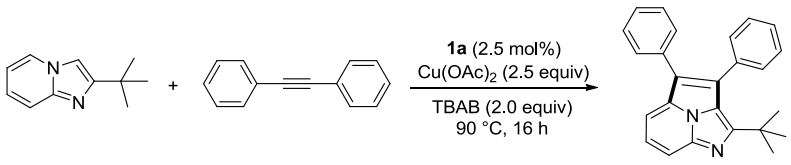
Entry	Cat.	Yield (%)
1	 **1a**	74
2	 **1b**	28
3	$PdCl_2$/2IMesHCl	45[b]
4	$PdCl_2$/2PPh_3	32[b]
5	$Pd(OAc)_2$	40[c]

[a]Conditions (unless otherwise specified): 2-*tert*-butylimidazo[1,2-*a*]pyridine (0.5 mmol), diphenylacetylene (0.6 mmol), Pd(II) complex (2.5 mol%), $Cu(OAc)_2$ (1.25 mmol), TBAB (1.0 mmol), DMF (1.5 mL), 16 h, 90 °C, isolated yield. [b]10 mol% $PdCl_2$, 20 mol% ligand additive. [c]10 mol% $Pd(OAc)_2$.

Next, the solvent system for catalyzing the coupling reaction was screened (Table 2). As shown in entries 1 and 2, both high polar DMA and DMF were good solvents for the reaction, affording good product yields of 70 and 74 %, respectively. DMSO which is also a high polar solvent, however, delivered an inferior product yield of 53 % (entry 3). Protic and nonpolar solvents were proven to be unsuitable for the catalytic reactions (entries 4 and 5).

Table 2. Solvent Screening[a]



Entry	Cat.	Yield (%)
1	DMA	70
2	DMF	74
3	DMSO	53
4	toluene	5
5	AcOH	0

[a]Conditions: 2-*tert*-butylimidazo[1,2-*a*]pyridine (0.5 mmol), diphenylacetylene (0.6 mmol), complex **1a** (2.5 mol%), $Cu(OAc)_2$ (1.25 mmol), TBAB (1.0 mmol), solvent (1.5 mL), 16 h, 90 °C, isolated yield.

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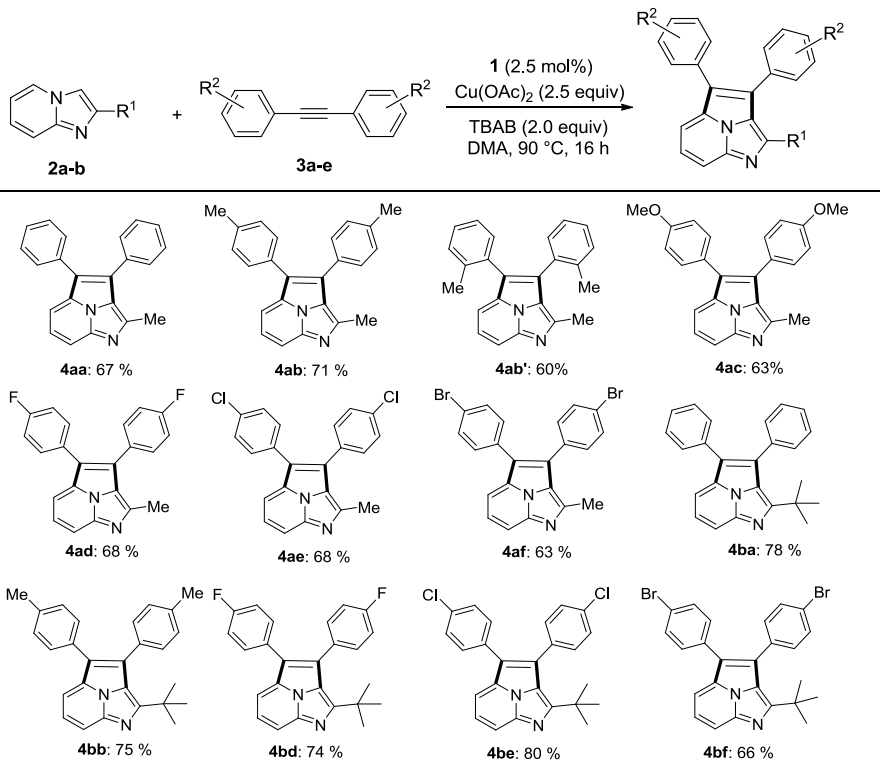
With the best conditions in hand, the substrate scope of the catalyst system was then explored. Initially, we evaluated the coupling reaction of 2-methylimidazo[1,2-*a*]pyridine (**2a**) with different acetylenes (Table 3). Using diphenylacetylene (**3a**) as substrate, a decent 67 % yield of coupled product **4aa** was obtained. The reaction between di-*p*-tolylacetylene (**3b**) with **2a** also went smoothly to afford the product **4ab** in 71 % yield. Sterically demanding di-*o*-tolylacetylene substrate could be successfully applied as substrate as well albeit with a slightly lower 60 % yield of product **4ab'**. Bis(4-methoxyphenyl)acetylene (**3c**) coupled with **2a** leading to a 63 % yield of product **4ac**. Compounds **4ad**–**f** were obtained in 63–68% yield in reactions with **2a** and bis(4-halophenyl)acetylenes. Noteworthy, the halide groups on the products allowed these compounds amenable to further functionalization via C—C coupling reactions. We then replaced the methyl group on **2a** with the sterically hindered *tert*-butyl group and investigated the coupling activities of this 2-*tert*-butylimidazo[1,2-*a*]pyridine (**2b**) with different acetylenes. In general, slightly better yields of imidazo[5,1,2-*cd*]indolizine products were obtained. For example, using **2b** as substrate, the coupling reaction led to the coupled product **4ba** in 78 % yield which is better than that of 67 % yield of **4aa** using **2a** as substrate. The coupling reaction between **2b** and bis(4-chlorophenyl)acetylene went well affording the coupled product **4be** in a good 80 % yield.

Table 3. Pd-Catalyzed Oxidative Coupling of Imidazo[1,2-*a*]pyridine Substrates with Alkynes[a]



[a]Conditions: heteroarene (0.16 mmol), alkyne (0.20 mmol), **1** (2.5

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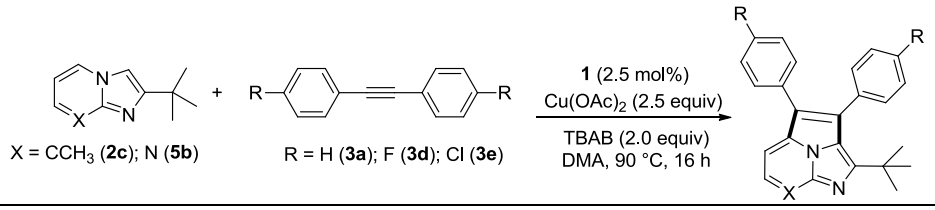
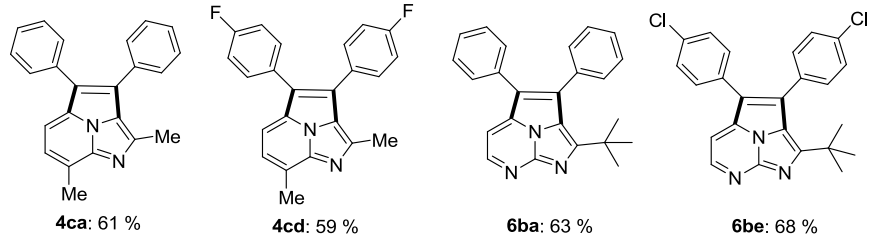
mol%), $Cu(OAc)_2$ (0.4 mmol), TBAB (0.32 mmol), DMA (1 mL), 16 h, 90 °C, isolated yield.

Instead of imidazo[1,2-*a*]pyridine, we then investigated the possible utilization of the less electron-rich imidazo[1,2-*a*]pyrimidine as substrate. Fused pyrimidines were found to possess remarkable pharmacological properties and they are essential components of important naturally occurring substances such as nucleic acids.[11] As shown in Table 4, a decent 61 % yield for **6ba** was obtained using 2-*tert*-butylimidazo[1,2-*a*]pyrimidine (**5b**) and diphenylacetylene as coupling partners. This yield was lower than that of 78 % for **4ba** using 2-*tert*-butylimidazo[1,2-*a*]pyridine and diphenylacetylene as substrates. Similarly, the 68 % yield of **6be** from **5b** was also lower than the 80 % yield of **4be** obtained from **2b**. Substitution on the pyridine ring in **2a** also affect the yields of coupling reactions. In the reaction of **2c** bearing a methyl group on the C7 position, the coupled product **4ca** was obtained in 63 % yield, which was slightly inferior to that of 67 % yield of **4aa** produced from the unsubstituted **2a** as substrate. The coupling reaction between **2c** and bis(4-fluorophenyl)acetylene afforded a 59 % yield of coupled product **4cd** which was also slightly inferior to the 68 % yield of **4ad** obtained from the unsubstituted **2a**. Noteworthy, the coupling reaction did not work when dialkylacetylene was used as substrate. Thus no coupling product was obtained when di-*n*-hexylacetylene was reacted with 2-*tert*-butylimidazo[1,2-*a*]pyridine. The desired tricyclic product was not formed neither in the reaction between 2-*tert*-butylimidazo[1,2-*a*]pyridine and an unsymmetrically aryl/alkyl substituted alkyne, 1-phenyl-1-propyne. Our results on the failure of using such internal alkynes was in line with similar observations published in the work by Hajra *et. al.*[8a]

Table 4. Pd-Catalyzed Oxidative Coupling of Imidazo[1,2-*a*]pyridine Substrates with Alkynes[a]





[a]Conditions: heteroarene (0.16 mmol), alkyne (0.20 mmol), **1** (2.5

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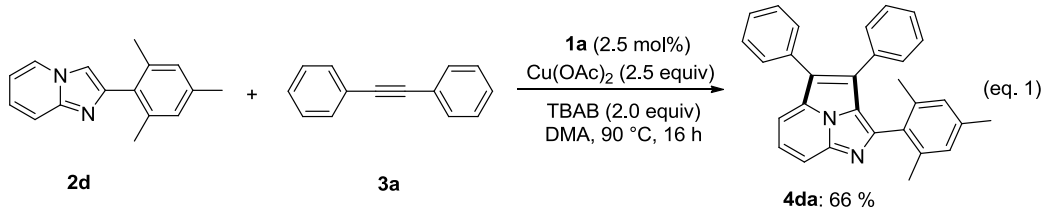
mol%), $Cu(OAc)_2$ (0.4 mmol), TBAB (0.32 mmol), DMA (1 mL), 16 h, 90 °C, isolated yield.

Previously, we have shown that for C2-aryl imidazo[1,2-*a*]pyridine bearing *ortho*-phenyl protons, deprotonation at these sites were possible leading to the fused tetracyclic compounds. Therefore, blocking of these *ortho*-phenyl protons with methyl groups should avoid the tetracyclic product but favor the formation of imidazo[5,1,2-*cd*]indolizine. Pleasingly, the reaction between 2-mesityl-*H*-imidazo[1,2-*a*]pyridine (**2d**) and diphenylacetylene successfully allowed the construction of imidazo[5,1,2-*cd*]indolizine product **4da** in 66 % yield (eq. 1). Similar strategy has been employed by Fan *et al.* in obtaining similar imidazo[5,1,2-*cd*]indolizine product.[8c] Ethyl imidazo[1,2-*a*]pyridine-2-carboxylate was attempted as coupling partner in reactions with diphenylacetylene. However, no desired imidazo[5,1,2-*cd*]indolizine product was obtained. Noteworthy, free imidazo[1,2-*a*]pyridine without C2-substituition did not yield the desired coupling product with diphenylacetylene neither using our new protocol. This result was in contrast to that published by Mira *et. al.* who observed a 49 % of the desired tricyclic product using free $Pd(OAc)_2$ as catalyst precursor.[8b] A higher reaction temperature of 120 °C (instead of 90 °C in our case) in a mixed pivalic acid/DMA solvent system was used in their conditions.



To further understand the coupling efficiency of substrates with different electronic properties, competition experiments were performed (Scheme 1). Consistent with our aforementioned findings, 2-*tert*-butylimidazo[1,2-*a*]pyridine (**2b**) reacted more favorably compared with the electron-poor 2-*tert*-butylimidazo[1,2-*a*]pyrimidine (**5b**) giving the coupled products **4ba** and **6ba** in a ratio of 66:34. The competition experiment involving a mixture of **2b**, di-*p*-tolyacetylene, and bis(4-fluorophenyl)acetylene led to coupled products **4bb** and **4bd** in a ratio of 35:65, indicating that the electronic-poor alkynes reacted preferentially.

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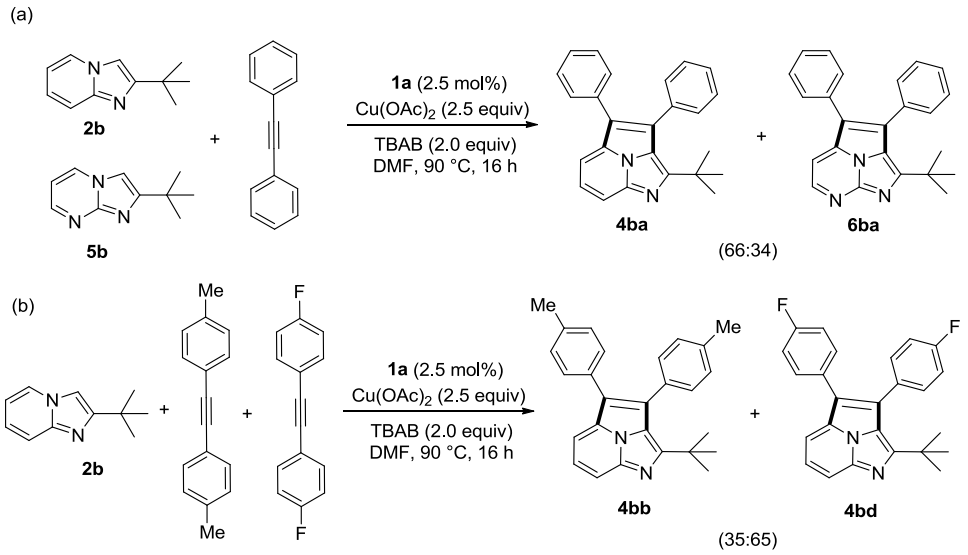
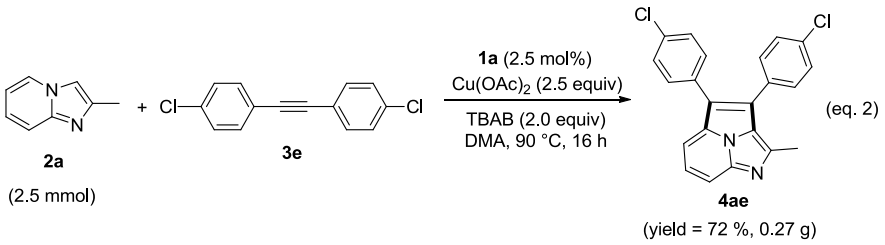


Scheme 1. Competitive Experiments.

Finally, to prove the practicability of the catalyst system based on complex **1a** in organic synthesis, an upscaling reaction between **2a** and di-*p*-4-chlorophenylacetylene was performed (eq. 2). Desirably, the coupled product **4ae** was obtained in 0.27 g (72 % yield) using a 2.5 mmol of starting material.



Structural Description

The structure of **4bd** was successfully established by single-crystal X-ray diffraction analysis (Figure 1). The summation of bond angles around the central nitrogen atom N1 is 360°, reflecting the planarity nature of the fused tricyclic ring. The three peripheral bond angles of ∠C14─C13─C21, ∠C7─C8─C9, and ∠C11─C12─N2 defining the shape of the fused ring system are 153.52(17), 142.69(18) and 137.48(16)°, respectively. Noteworthy, the bond angle of 153.52(17) ° around C13 atom is exceptionally large for a sp^2 carbon on a cyclic ring. One of the aryl rings forms a large 72.96(4)° interplanar angle with the central tricyclic core, whereas the corresponding interplanar angle of 39.25(4)° with the other aryl ring was much smaller.

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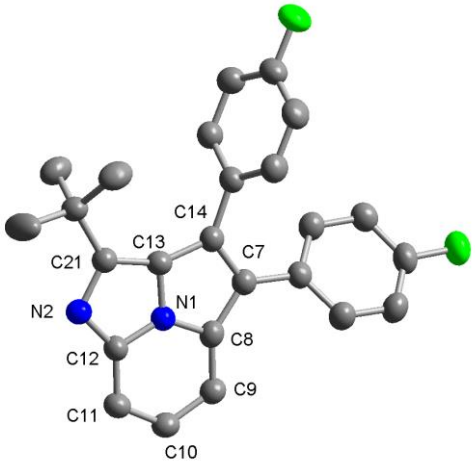

Figure 1. Molecular structure of **4bd** with 50 % probability ellipsoids for non-H atoms. H-atoms were omitted for clarity. Selected bond distances (Å) and angles (deg) around N1 in **4bd**: C13—N1, 1.358(2); C12—N1, 1.360(2); C8—N1, 1.636(2); C13—N1—C8, 115.87(15); C13—N1—C12, 112.34(15); C12—N1—C8, 131.78(15).

Proposed Mechanism

A catalytic cycle for the annulation reaction between 2-alkyl-imidazo[1,2-*a*]pyridine and alkyne is proposed in Scheme 2. The catalytic reaction should be initiated by the palladium(II) complex **A** and an initial C–H activation of the heteroaromatic substrate and its coordination via the C3 atom led to the formation of the palladium(II) complex **B**. The insertion of the alkyne substrate into the Pd–C bond produced the intermediate **C**. Further C–H activation generated the palladacycle intermediate **D** with the release of HX. An subsequent reductive elimination afforded the imidazo[5,1,2-*cd*]indolizine product and the palladium(0) complex **E** which was oxidized and transformed back to palladium complex **A** by copper(II) acetate.

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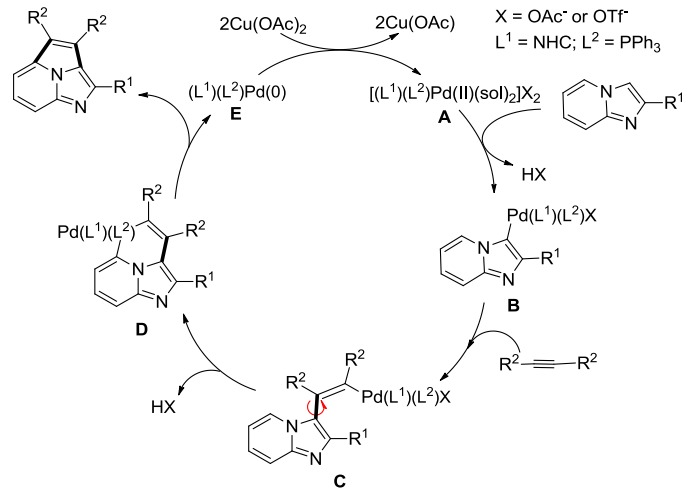

Scheme 2. Mechanistic Proposal for the Oxidative Annulation Reaction of 2-Alkyl-imidazo[1,2-*a*]pyridine with Alkyne.

Optical Properties.

The UV and PL spectra of selected compounds in THF (10^{-5} M) are summarized in Table 5. The new imidazo[5,1,2-*cd*]indolizine **4** exhibited absorption maxima in the range of 388–396 nm. Their PL spectra except that of **4ac** exhibit single broad emission in the range of 518–532 nm. Interestingly, compound **4ac** with 4-methoxy groups on the phenyl rings exhibits the strongest fluorescence among the new compounds (Φ_F = 0.445) with dual emission maxima at 427 nm and 536 nm (Figure 2). This anomalous emission should be related to the methoxy groups. Noteworthy, Gryko *et al*. also observed dual emission but in the solid-state for a benzo[*a*]imidazo[5,1,2-*cd*]indolizine bearing an OMe group.[7b] In their case, the methoxy group acts as an additional hydrogen-bond acceptor, altering crystal packing and thus the formation of polymorphs. The emission of compound **4af** bearing 4-bromophenyl rings at 520 nm was slightly blue-shifted compared with those of other imidazo[5,1,2-*cd*]indolizine **4a** bearing C2-methyl groups at ca. 530 nm or above (see Figure 2). The emission maxima of compound **4b** with C2-*t*-butyl groups were blue shifted at ca. 520 nm compared with those of **4a**. (Figure 3). The absorption maxima of compound **6ba** and **6be** with nitrogen atoms replacing carbon atoms on the tricyclic ring cores are bathochromatically shifted by 23 nm in comparison to those of parent imidazo[5,1,2-*cd*]indolizines **4ba** and **4be** (Figure 4). Their emission maxima were also red shifted by 46 and 36 nm, respectively. These red shift of emission maximum wavelength for **6ba** and **6be** suggests the intramolecular charge transfer involving the extra pyrimidine nitrogen lone pairs at the excited state.

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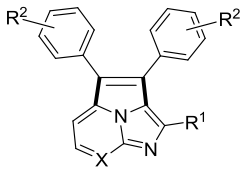
Table 5. Photophysical Properties of New Compounds[a]



Compound	R^1	R^2	X	Absorption λ_{max} (nm)	log ε	Emission λ_{max} (nm)	Φ_F[b]
4aa	Me	H	CH	393	3.82	531	0.164
4ac	Me	OMe	CH	396	3.54	427, 536	0.445
4ad	Me	F	CH	392	3.89	532	0.141
4ae	Me	Cl	CH	394	3.84	531	0.160
4af	Me	Br	CH	395	3.90	520	0.146
4ba	*t*-Bu	H	CH	389	3.90	519	0.136
4bd	*t*-Bu	F	CH	389	3.86	518	0.159
4be	*t*-Bu	Cl	CH	389	3.97	525	0.117
4bf	*t*-Bu	Br	CH	393	3.90	520	0.142
4ca	Me	H	CMe	388	3.89	526	0.149
6ba	*t*-Bu	H	N	412	3.94	565	0.119
6be	*t*-Bu	Cl	N	412	3.87	561	0.139

[a]Measured in THF. [b]Determined with reference to anthracene in ethanol (Φ_F = 0.27)

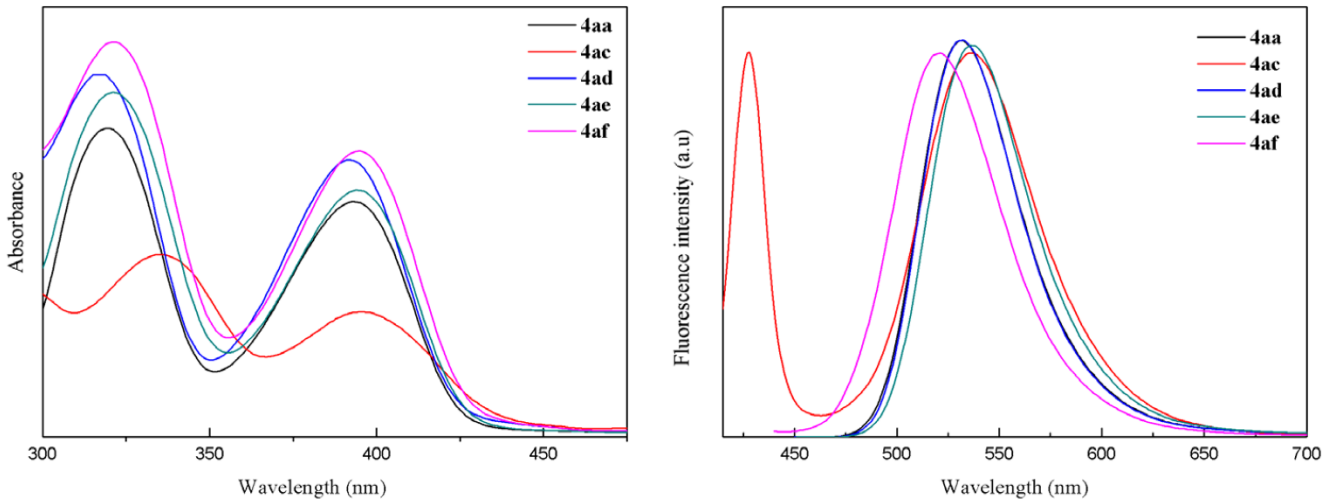


Figure 2. UV and PL spectra of **4aa**, **4ac**, **4ad**, **4ae**, and **4af** in THF

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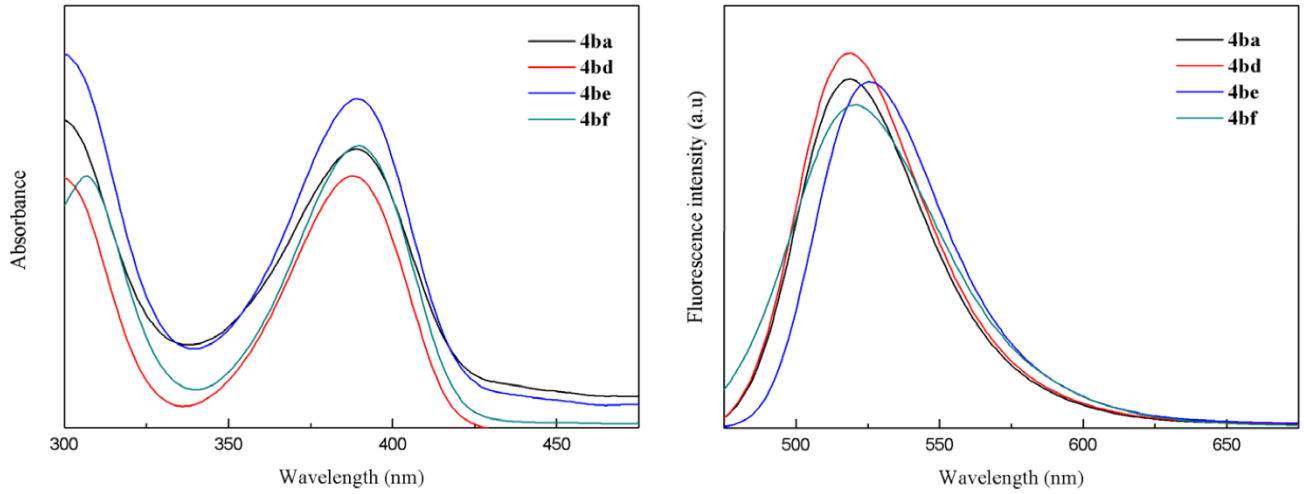

Figure 3. UV and PL spectra of **4ba**, **4bd**, **4be**, and **4bf** in THF

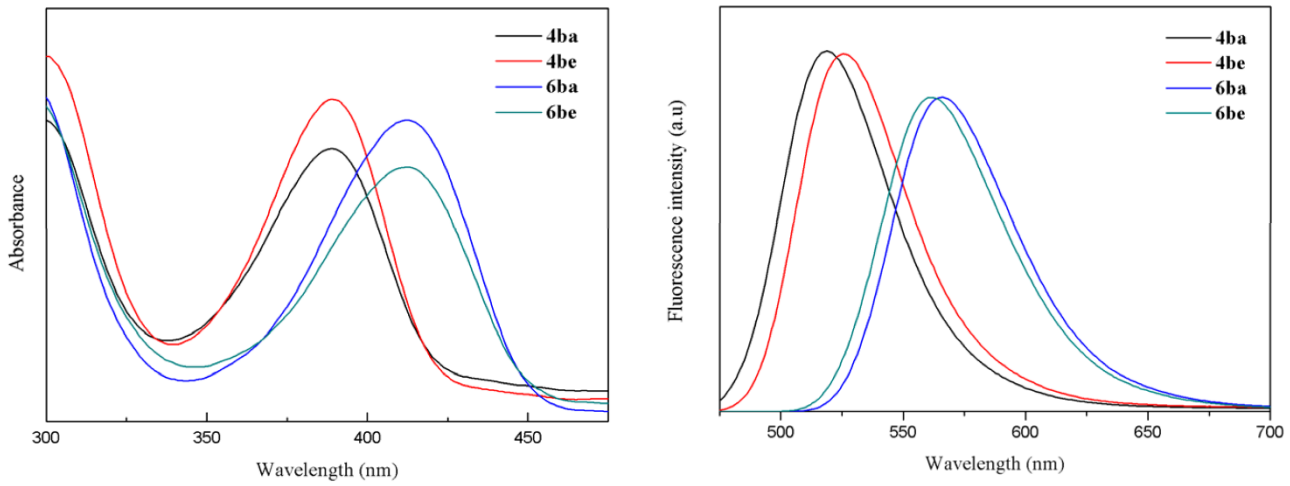

Figure 4. UV and PL spectra of **6ba** and **6be** vs. those of **4ba** and **4be** in THF

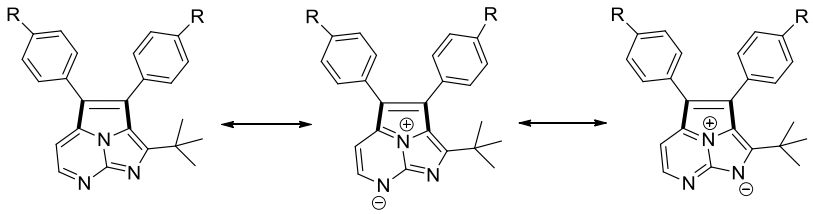

Figure 5. Charge transfer in compounds **6ba** (R = H) and **6be** (R = Cl)

Conclusion

In summary, the catalyst system based on **1a** was highly effective in catalyzing the oxidative coupling reactions between diarylacetylenes and imidazo[1,2-*a*] pyridines leading to imidazo[5,1,2-*cd*]indolizines

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product. Less electron-rich imidazo[1,2-*a*]pyrimidines could also be applied as substrate leading to similar coupled products albeit with slightly inferior yields. Importantly, the methodology was based on C2 substituted imidazo[1,2-*a*] pyridines and imidazo[1,2-*a*]pyrimidine without C2 phenyl protons, which were crucial in avoiding the formation of previously reported fused tetracyclic product. This simple palladium-catalyzed direct arylation protocol allows an easy access of fluorescent imidazo[5,1,2-*cd*]indolizines and related compounds. Further studies on introducing different functionality on the tricyclic skeleton and fine tuning of their photophysical properties are underway.

Experimental Section

All manipulations were performed under a dry nitrogen atmosphere using standard Schlenk techniques. Unless otherwise noted, all the catalytic reactions were carried out in thick walled sealable tubes. All the solvents were directly used as received without any further purification unless otherwise specified. Common starting chemicals were purchased from commercial source and used as received. ^{1}H, and $^{13}C\{^{1}H\}$ NMR spectra were recorded at 300.13 and 75.48 MHz, respectively. $CDCl_3$ as solvent and tetramethylsilane (TMS) as the internal standard were employed. Chemical shifts were reported in units (ppm) by assigning TMS resonance in the ^{1}H NMR spectrum as 0.00 ppm. The data of ^{1}H NMR was reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet and br = broad), coupling constant (*J* values) in Hz and integration. Chemical shifts for ^{13}C NMR spectra were recorded in ppm from TMS using the central peak of $CDCl_3$ (77.0 ppm) as the internal standard. Flash chromatography was performed using 230-400 mesh silica gel. EI-MS was carried out on a sector field mass spectrometer. UV-vis spectra were recorded on a HP-8453 spectrophotometer with a diode array detector, and the resolution was set at 1 nm. Photoluminescence spectra were recorded on a Cary Eclipse Fluorescence spectrophotometer. Compound **2a**,[12] **2b**,[13] and **2c**[14] were prepared following a literature procedure of similar compounds.[15]

2-Mesity-l*H*-imidazo[1,2-*a*]pyridine (2d). To a stirred solution of 2-bromo-1-mesitylethanone (1.2 g, 5.0 mmol) in ethanol (30 mL) was added 2-aminoypyridine (470 mg, 5.0 mmol) in portions, followed by addition of $NaHCO_3$ (1.2 g, 15 mmol). The mixture was refluxed for 4 h. The reaction mixture was then cooled to room temperature, filtered and concentrated under reduced pressure. The crude material was purified by flash chromatography using ethyl acetate/hexane (4:6) as eluent. A brown oil was obtained (80

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mg, 68% yield). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.12 (dd, *J* = 6.9, 1.8 Hz, 1H), 7.60 (dd, *J* = 6.9, 1.8 Hz, 1H), 7.42 (s, 1H), 7.17-7.12 (m, 1H), 6.92 (s, 2H), 6.77 (td, J = 6.9, 1.8 Hz, 1H), 2.30 (s, 3H), 2.12 (s, 6H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 145.1, 144.8, 137.7, 137.5, 131.0, 128.1, 125.5, 124.0, 117.6, 112.1, 110.9, 21.2, 20.7. HRMS (EI) calcd. for $C_{16}H_{16}N_2$ [M^+]: 236.1313. Found: 236.1310.

2-*tert*-Butylimidazo[1,2-*a*]pyrimidine (5b). To a stirred solution of 2-aminopyrimidine (0.5 g, 5.25 mmol) in ethanol (25.0 mL) was added 1-bromo-3,3-dimethylbutan-2-one (1.41 g, 7.9 mmol). The mixture was stirred at reflux for overnight. After the reaction was completed, the mixture was evaporated, diluted with ethyl acetate (50.0 mL) and washed with 1N NaOH solution (50.0 mL). The organic layer was dried over anhydrous $MgSO_4$ and concentrated in vacuo. The crude product was purified by flash column chromatography. An off-white solid was obtained (0.59 g, 64 % yield). mp = 185.8.–186.6 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.39 (s, 1H), 8.30 (dd, *J* = 6.6, 1.8 Hz, 1H), 7.20 (s, 1H), 6.74-6.70 (m, 1H), 1.34 (s, 9H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 159.2, 149.0, 148.2, 132.8, 108.1, 104.9, 32.7, 29.9. HRMS (EI) calcd. for $C_{10}H_{13}N_3$ [M^+]: 175.1109. Found: 175.1102.

Typical Procedure for Pd(II)-Catalyzed Double C-H Functionalization. To a 15 mL oven-dried sealed tube containing stir bar were added heteroarene (0.16 mmol), Pd catalyst (2.5 mol%), $Cu(OAc)_2$ (72 mg, 0.40 mmol), alkyne (0.20 mmol), TBAB (103 mg, 0.32 mmol) in DMF or DMA (1－1.5 mL). The reaction mixture was stirred at 90 ^{o}C for 16 h. Upon completion, EtOAc was added to dilute the mixture which was then washed with water (2 x 20 mL) and saturated NaCl (aq). The organic layer was dried over $MgSO_4$, evaporated, and purified by flash column chromatography on silica gel with a gradient eluent of hexane and ethyl acetate (25:1 v/v) to afford the corresponding cyclized product.

2-Methyl-3,4-diphenyl*H*-imidazo[5,1,2-*cd*]indolizine (4aa). Off-white solid (33 mg, 67% yield), mp = 135.0–135.8 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.90-7.85 (m, 3H), 7.54 (d, *J* = 6.0 Hz, 2H), 7.47 (d, *J* = 6.0 Hz, 2H), 7.42-7.28 (m, 6H), 2.90 (s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 150.1, 139.6, 134.1, 133.7, 131.4, 130.9, 130.5, 130.2, 128.8, 128.7, 128.0, 127.1, 126.3, 125.5, 112,1, 110.0, 16.8. HRMS (EI) calcd. for $C_{22}H_{16}N_2$ [M^+]: 308.1313. Found: 308.1310.

2-Methyl-3,4-di*p*-tolyl*H*-imidazo[5,1,2-*cd*]indolizine (4ab). Off-white solid (38 mg, 71% yield), mp = 135.4-136.3 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.88 (s, 3H), 7.44 (d, *J* = 7.8 Hz, 2H), 7.38 (d, *J* = 7.8 Hz, 2H), 7.24-7.19 (m, 4H), 2.90 (s, 3H), 2.40 (s, 3H), 2.39 (s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 149.6, 137.8,

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136.8, 131.7, 131.2, 130.9, 130.8, 130.3, 129.9, 129.5, 129.4, 129.3, 129.1, 126.3, 125.4, 112.0, 109.9, 21.4, 21.3, 16.7. HRMS (EI) calcd. for $C_{24}H_{20}N_2$ [M^+]: 336.1626. Found: 336.1617.

2-Methyl-3,4-di*o*-tolyl*H*-imidazo[5,1,2-*cd*]indolizine (4ab'). Off-white solid (32 mg, 60% yield), mp. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.92-7.84 (m, 2H), 7.69 (d, *J* = 6.9 Hz, 1H), 7.28-7.18 (m, 8H), 2.74 (s, 3H), 2.12 (s, 3H), 2.04 (s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 149.9, 138.8, 131.7, 131.6, 130.5, 130.4, 130.3, 128.1, 127.7, 126.8, 125.9, 125.7, 125.6, 112.1, 109.9, 20.4, 16.1. HRMS (EI) calcd. for $C_{24}H_{20}N_2$ [M^+]: 336.1626. Found: 336.1632.

3,4-Bis(4-methoxyphenyl)-2-methyl*H*-imidazo[5,1,2-*cd*]indolizine (4ac). Off-white solid (37 mg, 63% yield), mp = 172.9-173.6 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.83 (s, 3H), 7.46 (d, *J* = 8.7 Hz, 2H), 7.40 (d, *J* = 8.7 Hz, 2H), 6.95-6.91 (m, 4H), 3.84 (s, 3H), 3.83 (s, 3H), 2.89 (s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 159.4, 158.7, 148.2, 145.7, 131.7, 131.6, 131.2, 130.4, 126.5, 126.1, 126.0, 124.8, 119.8, 114.3, 114.2, 111.8, 109.7, 55.3, 16.8. HRMS (EI) calcd. for $C_{24}H_{20}N_2O_2$ [M^+]: 368.1525. Found: 368.1528.

3,4-Bis(4-flurophenyl)-2-methyl*H*-imidazo[5,1,2-*cd*]indolizine (4ad). Yellow solid (35 mg, 68% yield), mp = 167.0-167.9 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.89-7.82 (m, 3H), 7.53 (dd, *J* = 8.7, 5.4 Hz, 2H), 7.40 (dd, *J* = 8.7, 5.7 Hz, 2H), 7.14-7.06 (m, 4H), 2.87 (s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 162.8 (d, *J* = 247 Hz), 162.1 (d, *J* = 247 Hz), 150.2, 139.7, 132.0 (d, *J* = 8.3 Hz), 131.7 (d, *J* = 7.5 Hz), 131.3, 129.9 (d, *J* = 3.0 Hz), 129.7, 129.6 (d, *J* = 3.0 Hz), 126.4, 125.1, 124.4, 115.9 (d, *J* = 21.8 Hz), 111.9, 110.3, 16.7. HRMS (EI) calcd. for $C_{22}H_{14}N_2F_2$ [M^+]: 344.1125. Found: 344.1120.

3,4-Bis(4-chlorophenyl)-2-methyl*H*-imidazo[5,1,2-*cd*]indolizine (4ae). Off-white solid (54 mg, 68% yield), mp = 160.3-161.2 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.91-7.89 (m, 3H), 7.47-7.38 (m, 8H), 2.88 (s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 150.4, 139.7, 134.3, 133.3, 132.3, 131.9, 131.6, 131.3, 131.1, 129.6, 129.2, 129.1, 126.7, 125.0, 124.3, 112.2 110.5, 16.8. HRMS (EI) calcd. for $C_{22}H_{14}Cl_2N_2$ [M^+]: 376.0534. Found: 376.0531.

3,4-Bis(4-bromophenyl)-2-methyl*H*-imidazo[5,1,2-*cd*]indolizine (4af). Light yellow solid (47 mg, 63% yield), mp = 164.6-165.8 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.89-7.83 (m, 3H), 7.56-7.49 (m, 4H), 7.37 (d, *J* = 8.7 Hz, 2H), 7.30 (d, *J* = 8.4 Hz, 2H), 2.86 (s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 150.5, 139.8, 132.8, 132.4, 132.1, 132.0, 131.9, 131.6, 131.0, 129.5, 126.6, 124.9, 124.1, 122.6, 121.5, 112.1, 110.5, 16.8. HRMS (EI) calcd. for $C_{22}H_{14}Br_2N_2$ [M^+]: 463.9524. Found: 463.9532.

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2-*tert*-Butyl-3,4-diphenyl*H*-imidazo[5,1,2-*cd*]indolizine (4ba). Off-white solid (44 mg, 78% yield), mp = 207.3-208.2 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.00-7.88 (m, 3H), 7.46-7.38 (m, 7H), 7.32-7.22 (m, 3H), 1.38 (s, 9H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 164.7, 138.8, 135.8, 134.2, 131.6, 131.0, 130.6, 130.0, 128.4, 128.2, 128.0, 127.0, 126.7, 125.9, 124.7, 112.2, 110.3, 35.0, 30.9. HRMS (EI) calcd. for $C_{25}H_{22}N_2$ [M^+]: 350.1783. Found: 350.1787.

2-*tert*-Butyl-3,4-di-*p*-tolyl*H*-imidazo[5,1,2-*cd*]indolizine (4bb). Off-white solid (45 mg, 75% yield), mp = 250.7–251.8 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.92-7.81 (m, 3H), 7.27-7.22 (m, 4H), 7.19-7.14 (m, 2H), 7.05 (d, *J* = 7.8 Hz, 2H), 2.36 (s, 3H), 2.27 (s, 3H), 1.33 (s, 9H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 164.4, 138.7, 137.6, 136.3, 132.8, 131.5, 131.3, 130.8, 130.7, 129.8, 129.2, 128.9, 127.0, 125.8, 124.8, 112.1, 110.1, 34.9, 30.9, 21.5. HRMS (EI) calcd. for $C_{27}H_{26}N_2$ [M^+]: 378.2096. Found: 378.2092.

2-*tert*-Butyl-3,4-bis(4-fluorophenyl)*H*-imidazo[5,1,2-*cd*]indolizine (4bd). Off-white solid (46 mg, 74% yield), mp = 201.2-202.0 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.00-7.96 (m, 1H), 7.91 (d, *J* = 4.8 Hz, 2H), 7.41-7.37 (m, 2H), 7.34-7.29 (m, 2H), 7.12 (t, *J* = 8.7 Hz, 2H), 7.00 (t, *J* = 8.7 Hz, 2H), 1.38 (s, 9H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 164.3, 162.9 (d, *J* = 282.8 Hz), 161.8 (d, *J* = 247 Hz), 138.8, 132.6 (d, *J* = 4.7 Hz), 131.5 (d, *J* = 4.7 Hz), 131.4, 130.3, 129.9 (*J* = 3.0 Hz), 126.2, 126.1, 124.5, 115.6 (d, *J* = 21 Hz), 115.4 (d, *J* = 20 Hz), 112.1, 110.5, 35.0, 30.9. HRMS (EI) calcd. for $C_{25}H_{20}F_2N_2$ [M^+]: 386.1595. Found: 386.1587.

2-*tert*-Butyl-3,4-bis(4-chlorophenyl)*H*-imidazo[5,1,2-*cd*]indolizine (4be). Off-white solid (46 mg, 80% yield), mp = 212.9-213.7 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.00-7.96 (m, 1H), 7.91 (d, *J* = 4.8 Hz, 2H), 7.41-7.36 (m, 4H), 7.28 (s, 4H), 1.38 (s, 9H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 165.0, 138.8, 134.3, 134.0, 132.9, 132.3, 132.2, 131.1, 130.2, 130.1, 128.9, 128.7, 126.3, 125.8, 124.4, 112.2, 110.7, 35.0, 31.0. HRMS (EI) calcd. for $C_{24}H_{20}Cl_2N_2$ [M^+]: 418.1004. Found: 418.1003.

3,4-Bis(4-bromophenyl)-2-tert-butyl*H*-imidazo[5,1,2-*cd*]indolizine (4bf). Light yellow solid (53 mg, 66% yield), mp = 210.7-211.5 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.95-7.87 (m, 3H), 7.50 (d, *J* = 8.4 Hz, 2H), 7.39 (d, *J* = 8.4 Hz, 2H), 7.25 (d, *J* = 8.1 Hz, 2H), 7.16 (d, *J* = 8.4 Hz, 2H), 1.33 (s, 9H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 156.0, 138.8, 134.5, 132.8, 132.5, 131.8, 131.6, 131.4, 130.9, 130.1, 126.4, 125.8, 124.4, 122.6, 121.1, 112.2, 110.7, 35.0, 31.0. HRMS (EI) calcd. for $C_{25}H_{20}Br_2N_2$ [M^+]: 505.9993. Found: 505.9991.

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2,7-Dimethyl-3,4-diphenyl*H*-imidazo[5,1,2-*cd*]indolizine (4ca). Off-white solid (32 mg, 61% yield), mp = 125.1–125.9 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.77 (d, *J* = 7.8 Hz, 1H), 7.65 (d, *J* = 7.8 Hz, 1H), 7.53 (dd, *J* = 7.5, 1.5 Hz, 2H), 7.46 (dd, *J* = 8.4, 1.5 Hz, 2H), 7.42-7.29 (m, 6H), 2.94 (s, 3H), 2.88 (s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 148.3, 138.9, 134.3, 133.9, 130.4, 130.1, 130.0, 129.8, 128.7, 128.6, 127.8, 127.7, 127.0, 125.5, 125.4, 121.3, 112.2, 16.7, 15.9. HRMS (EI) calcd. for $C_{23}H_{18}N_2$ [M^+]: 322.1470. Found: 322.1477.

3,4-Bis(4-fluorophenyl)-2,7-dimethyl*H*-imidazo[5,1,2-*cd*]indolizine (4cd). Light yellow solid (34 mg, 59% yield), mp = 106.1-107.3 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.71 (d, *J* = 7.8 Hz, 1H), 7.65 (d, *J* = 8.1 Hz, 1H), 7.46-7.34 (m, 4H), 7.10-7.02 (m, 4H), 2.91 (s, 3H), 2.83 (s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ. 162.5 (d, *J* = 246.8 Hz), 162.1 (d, *J* = 245.3 Hz), 148.2, 138.9, 132.0 (d, *J* = 8.3 Hz), 131.6 (d, *J* = 8.3 Hz), 130.0 (d, *J* =3.8 Hz), 129.7 (d, *J* = 3.0 Hz), 129.6, 128.7, 127.7, 126.1, 124.4, 121.6, 115.9 (d, *J* = 22 Hz), 115.8 (d, *J* = 22 Hz), 112.1, 16.6, 15.9. HRMS (EI) calcd. for $C_{23}H_{16}F_2N_2$ [M^+]: 358.1282. Found: 358.1276.

2-Mesityl-3,4-diphenyl*H*-imidazo[5,1,2-*cd*]indolizine (4da). Light yellow solid (44 mg, 66% yield), mp = 136.7–137.8 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.99-7.89 (m, 3H), 7.51 (dd, *J* = 6.9, 1.8 Hz, 2H), 7.40-7.30 (m, 3H), 7.12-7.08 (m, 3H), 7.00-6.94 (m, 2H), 6.82 (s, 2H), 2.27 (s, 3H), 1.91 (s, 9H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 138.9, 138.0, 137.1, 134.3, 133.0, 132.2, 131.1, 130.9, 130.2, 129.9, 128.9, 128.2, 128.1, 127.8, 127.3, 126.5, 125.7, 112.5, 111.3, 21.3, 20.4. HRMS (EI) calcd. for $C_{30}H_{24}N_2$ [M^+]: 412.1939. Found: 412.1943.

2-(*tert*-Butyl)-3,4-diphenyl-1,2*a*^{1},7-triazacyclopenta[*cd*]indene (6ba). Light yellow solid (35 mg, 63% yield), mp = 235.8–236.7 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.93 (d, *J* = 5.7 Hz, 1H), 7.84 (d, *J* = 5.4 Hz, 1H), 7.39 (s, 5H), 7.31-7.20 (m, 5H), 1.34 (s, 9H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 172.0, 146.6, 145.8, 135.9, 134.7, 133.7, 133.1, 130.5, 129.6, 128.7, 128.5, 128.4, 127.2, 127.1, 123.3, 107.9, 35.7, 30.6. HRMS (EI) calcd. for $C_{24}H_{21}N_3$ [M^+]: 351.1735. Found: 351.1741.

2-(*tert*-Butyl)-3,4-bis(4-chlorophenyl)-1,2*a*^{1},7-triazacyclopenta[*cd*]indene (6be). Light yellow solid (46 mg, 68% yield), mp = 217.2-218.0 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.92 (d, *J* = 5.4 Hz, 1H), 7.78 (d, *J* = 5.4 Hz, 1H), 7.38 (d, *J* = 6.6 Hz, 2H), 7.31-7.16 (m, 6H), 1.33 (s, 9H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 172.4, 146.7, 146.1, 135.0, 134.3, 133.4, 133.3, 132.9, 131.8, 131.3, 130.8, 129.1, 129.0, 126.0, 123.1, 107.8, 35.8, 30.7. HRMS (EI) calcd. for $C_{24}H_{19}Cl_2N_3$ [M^+]: 419.0956. Found: 419.0951.

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X-ray Crystallography. Samples were collected at 150(2) K on a X-ray diffractometer equipped with a CCD area detector and a graphite monochromater utilizing MoKα radiation (λ = 0.71073 Å). The unit cell parameters were obtained by least-squares refinement. Data collection and reduction were performed using the APEX2 and SAINT software.[16] Absorption corrections were performed using the SADABS program.[17] All the structures were solved by direct methods and refined by full-matrix least squares methods against F^2 with the SHELXTL software package.[18] All non-H atoms were refined anisotropically. All H-atoms were fixed at calculated positions and refined with the use of a riding model. Crystallographic data are listed in Table S1 of the Supporting Information. CCDC files 1487706 (**4bd**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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Supporting Information Available. NMR spectra for all products and crystallographic data of **4bd**. This material is available free of cost via the Internet at http://pubs.acs.org. We also thank the National Center for High-performance Computing of Taiwan for computing time and financial support of the Conquest software.

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