Palladium Catalyzed, Multicomponent Synthesis of Fused-Ring Pyrroles from Aryl Iodides, Carbon Monoxide, and Alkyne-Tethered Imines

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Ⓢ _Supporting Information_

ABSTRACT: A palladium-catalyzed multicomponent route to polycyclic pyrroles is described. $Pd(P^tBu_3)_2$ was found to catalyze the coupling of (hetero)aryl iodides, two equivalents of carbon monoxide and alkyne-tethered imines into 1,3-dipoles (Münchnones), which undergo spontaneous, intramolecular 1,3-dipolar cycloaddition to form polycyclic pyrroles. The systematic variation of the alkyne, tethered-imine, or aryl iodide can allow the buildup of a range of pyrrole derivatives, where any of the substituents can be independently varied. In addition, the same palladium catalyst can be employed in an initial Sonogashira-type coupling with aryl iodides, which upon the addition of CO can allow the novel tandem catalytic, five component synthesis of diversely substituted products.
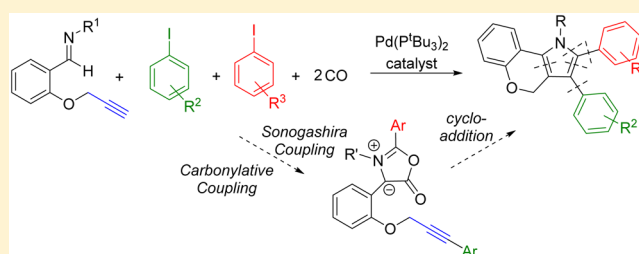
INTRODUCTION

Polycyclic pyrroles and their derivatives are a common motif in natural products and pharmaceutical design.[1] While a range of methods have been developed to synthesize pyrroles, including cyclization strategies (e.g., Paal-Knorr synthesis),[2] or substitution chemistry on preformed pyrroles (e.g., cross coupling or C−H bond functionalization),[3] the design of routes to polycyclic variants of these products that do not require the initial assembly of highly substituted precursors has been less developed. One useful approach to these products and their derivatives is via the intramolecular cycloaddition of alkynes or alkenes to Münchnones (Scheme 1a).[4] This transformation has been exploited by a number of research laboratories, including in targeted synthesis.[5] However, as with many routes to these heterocycles, this chemistry typically entails the buildup of the carboxylic acid precursor to Münchnones prior to dehydration and cycloaddition.

In considering the design of more streamlined routes to these products, we have recently reported that the palladium-catalyzed carbonylation of aryl iodides in the presence of imines can provide a method to construct Münchnones (Scheme 1b).[6] This transformation can be coupled with subsequent addition of alkynes for cycloaddition to provide an overall multicomponent synthesis of substituted pyrroles. A useful feature of this reaction is the availability of imine, alkyne, aryl iodide building blocks, each of which is either commercially available, inexpensive, or easily formed. In light of these features, we questioned if this reaction could be extended to assemble even more complex scaffolds, such as polycyclic products with minimal synthetic effort. For example, alkyne-

Scheme 1. 1,3-Dipolar Cycloaddition Routes to Polycyclic Pyrrole Derivatives

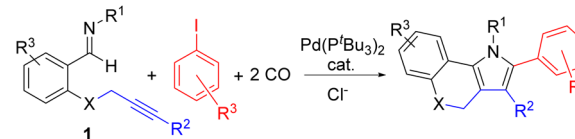_a) Intramolecular Münchnone Cycloaddition_
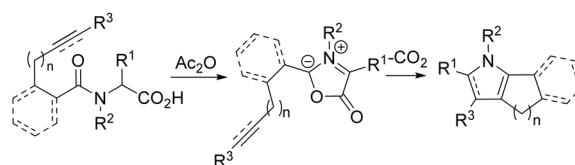
b) Palladium Catalyzed Carbonylative Münchnone Synthesis
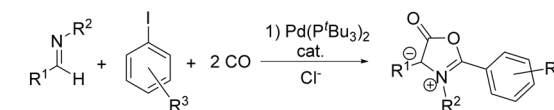
c) This Work

tethered imines are easily synthesized from 2-substituted aromatic aldehydes with amines,[7] and upon use in the palladium catalyzed multicomponent formation of Münchnones would allow the straightforward assembly polycyclic pyrroles in a single operation from combinations of available

substrates (Scheme 1c). A facet of this chemistry would be the presence of the alkyne in the imine substrate, which may allow the use of less activated alkynes to be employed in the Münchnone cycloaddition reaction, and therefore broaden the scope of this transformation.

We describe here our studies toward the design of this palladium-catalyzed route to synthesize fused-ring pyrroles. This can provide an efficient and modular route to these products from building blocks that are both accessible and can be generalized. In addition, this same palladium catalyst can also be employed to derivatize the alkyne in a novel tandem catalytic approach to generate highly substituted polycyclic pyrroles.

■ RESULTS AND DISCUSSION

Our previous research has shown that $Pd(P^tBu_3)_2$ in concert with a chloride source can allow the carbonylation of aryl iodides with imine nucleophiles into Münchnones via two sequential catalytic reactions. This involves an initial *in situ* generation of acid chlorides, which can react with imine to form *N*-acyl iminium salt intermediates for a subsequent palladium-catalyzed cyclocarbonylation to **2** (Scheme 2).[6,8] In principle,

Scheme 2. Mechanism of the Pd-Catalyzed Carbonylative Synthesis of Münchnones
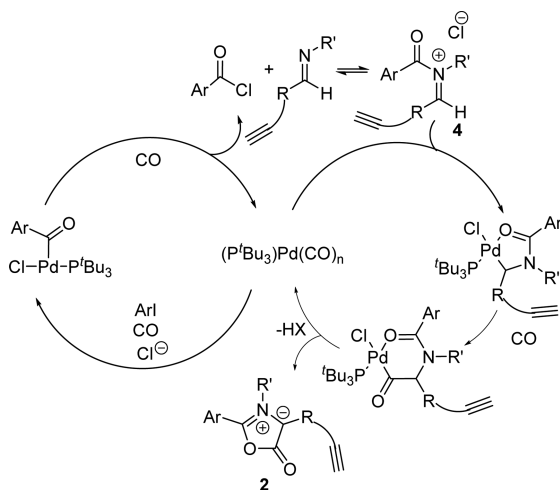
the incorporation of an alkyne-tethered substrate into either on the aryl iodide or imine should allow for spontaneous cycloaddition to generate **3**. A requirement for the success of this reaction will be the compatibility of the alkyne with both the palladium catalyzed carbonylations, and with the imine substrate. For example, Münchnone cycloaddition typically required electron poor dipolarophiles, which are not typically stable in the presence of nucleophilic imines, and have to be added after catalysis to generate pyrroles. Similarly, alkynes are viable insertion substrates, which could also lead to undesired products.

Our first studies involved the use of *ortho*-alkyne-tethered aryl iodides.[9] This resulted in the formation of a complex mixture of products with a number of catalyst systems potentially arising from the insertion of the alkyne during the initial carbonylation of the aryl iodide (see Table S1 for details). In order to limit this possibility, we moved to the analogous reaction of an alkyne-tethered imine **1a** (Table 1), which can be readily generated in two steps from salicylaldehyde. We were

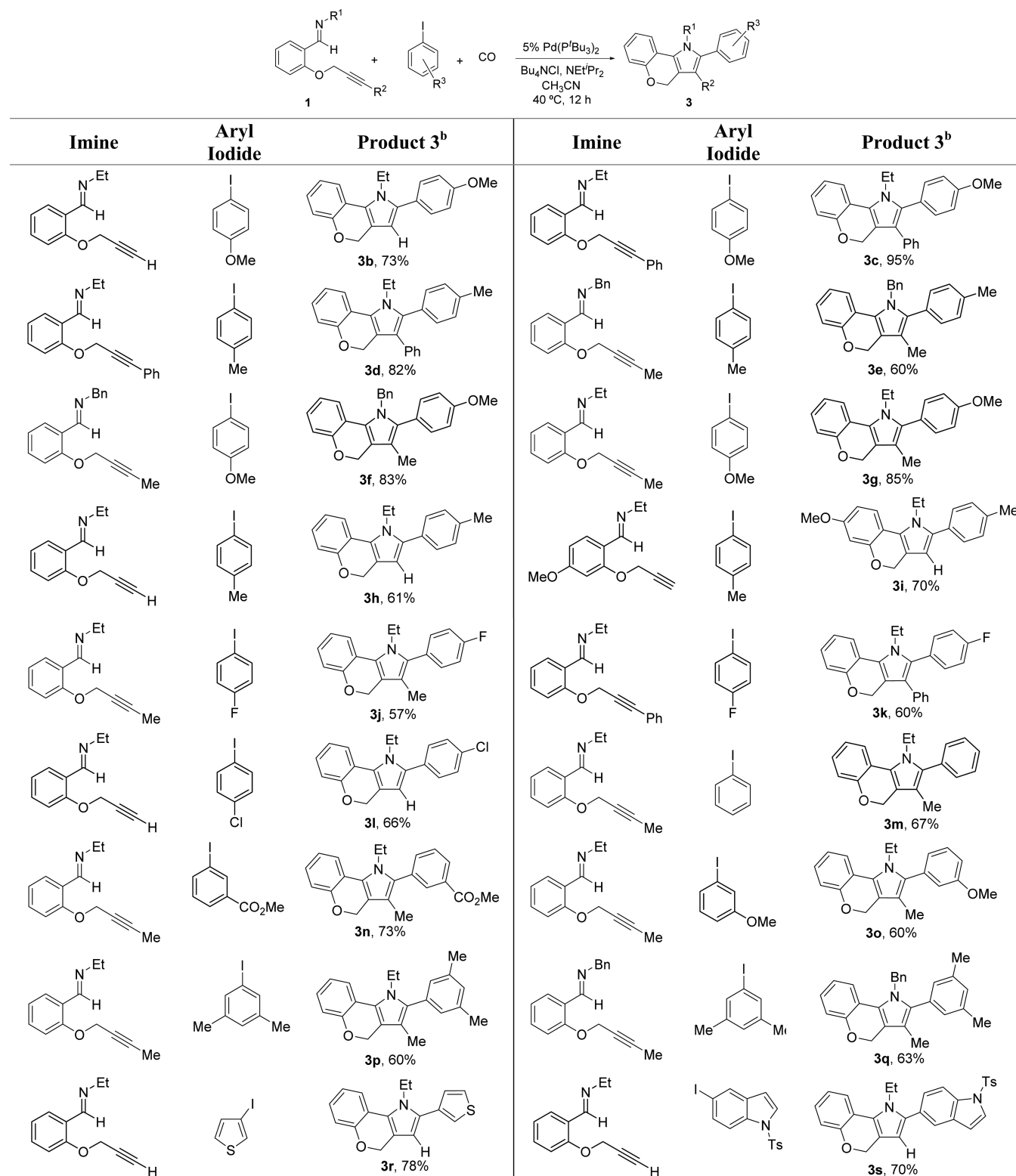**Table 1. Catalyst Design for the Carbonylative Synthesis of 3a**[a]
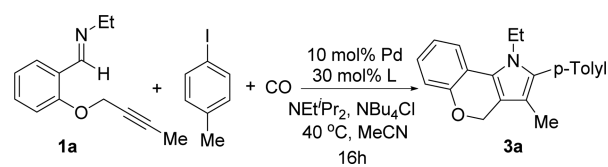
Entry	Pd cat.	Ligand	Yield (%)[b]
1	[Pd(allyl)Cl]₂	P^tBu_3	70
2	[Pd(allyl)Cl]₂	-	0
3	Pd₂dba₃·CH₃Cl	-	0
4	[Pd(allyl)Cl]₂	PCy₃	0
5	[Pd(allyl)Cl]₂	PPh₃	0
6	[Pd(allyl)Cl]₂	P(o-tolyl)₃	23
7	[Pd(allyl)Cl]₂		19
8	[Pd(allyl)Cl]₂		12
9	[Pd(allyl)Cl]₂		40
10	5% $Pd(P^tBu_3)_2$	-	76[c,d]

[a]**1a** (6 mg, 0.03 mmol), 4-iodotoluene (33 mg, 0.15 mmol), Pd (0.003 mmol), L (0.009 mmol) Bu₄NCl (8 mg, 0.03 mmol), NEt^{i}Pr₂ (6 mg, 0.045 mmol), CO (4 atm), CD₃CN. [b]NMR yield. [c]0.5 mmol scale with 5 mol% $Pd(P^tBu_3)_2$ (13 mg, 0.025 mmol), Bu₄NCl (139 mg, 0.5 mmol), 10 atm CO. [d]Isolated yield.

pleased to find that this latter imine in concert with *p*-iodotoluene, CO, and Pd(allyl)Cl/P^tBu_3 catalyst leads to the clean formation of pyrrole **3a** (entry 1). Of note, the unactivated alkyne in **1a** undergoes spontaneous cycloaddition under the palladium catalyzed conditions, and does not appear to participate in insertion of other off-cycle processes. The phosphine ligand plays an important role in the efficiency of this reaction. For example, PPh₃ and PCy₃ completely inhibit catalysis (entries 4, 5), while more sterically encumbered ligands allow the reaction to proceed, albeit in lower yields than with P^tBu_3 (entries 6−9). This is consistent with our previous studies,[10] which showed that the steric bulk of this phosphine is critical to both mediate strain induced acid chloride reductive elimination, and remain sufficiently labile (due to its size) to allow carbonylation of **4** (Scheme 2). The optimized catalyst system with 5 mol% $Pd(P^tBu_3)_2$ and Bu₄NCl allows the synthesis of **3** in good overall yield (76%, entry 10).

A feature of this platform is its ease of diversification. As examples, a number of different alkyne units can be readily incorporated into **1** and participate in cycloaddition to form pyrroles (**3a−c**). This includes internal alkynes, phenylacetylene derivatives, and even terminal alkynes. The use of terminal alkynes is notable, as Sonogashira coupling with the aryl iodide is also a viable reaction pathway (*vide infra*). Both *N*-alkyl and benzyl imines are compatible with this reaction, as

Table 2. Palladium-Catalyzed Polycyclic Pyrrole Synthesis[a]

Imine	Aryl Iodide	Product 3[b]	Imine	Aryl Iodide	Product 3[b]
		3b, 73%			3c, 95%
		3d, 82%			3e, 60%
		3f, 83%			3g, 85%
		3h, 61%			3i, 70%
		3j, 57%			3k, 60%
		3l, 66%			3m, 67%
		3n, 73%			3o, 60%
		3p, 60%			3q, 63%
		3r, 78%			3s, 70%

[a]General: **1** (0.5 mmol), **2** (2.5 mmol), Pd(P^{t}Bu$_3$)$_2$ (13 mg, 0.025 mmol), Bu$_4$NCl (139 mg, 0.5 mmol), NEt^{i}Pr$_2$ (97 mg, 0.75 mmol), CO (10 atm) in CH$_3$CN, 12 h, 40 °C. [b]Isolated yield.

are functionalities on the aromatic backbone (**3i**). However, potentially coordinating substrates, such as those with nitrogen-containing tethers, are not viable substrates.[11] An even broader array of aryl iodides can be incorporated into this transformation as a method to tune the 2-position of the

heterocycle. Electron rich (**3b, c, f, g**), electron poor (**3j–l, n**), and simple aryl iodides (**3m**) are compatible with the reaction conditions, and lead to the formation of pyrroles in good overall yields. This includes *para-* (**3a–l**), *meta-* (**3n,o**), and disubstituted (**3p,q**) aromatic residues. However, ortho-

substituted aryl iodides do not lead to products under these conditions. This chemistry can also be extended to use of heteroaryl iodides, such as thiophenyl iodide (**3r**) and 5-iodoindoles (**3s**). These latter provide facile access to heteroaryl-substituted pyrroles.

The reaction in Table 2 provides an alternative to the more classical assembly of aryl-substituted pyrroles from aryl halides via cross coupling or C−H activation chemistry, where in this case the polycyclic pyrrole core is generated at the same time as the (hetero)aryl-pyrrole bond. In considering this more traditional use of palladium catalysis in C−C bond formation, we questioned if these functions might be coupled to create a more modular synthesis of **3**. It is well-established that terminal alkynes, such as those in **1c**, can undergo a Sonogashira coupling with the aryl iodides. We see no evidence for this transformation above (Table 2), presumably due to the presence of carbon monoxide that diverts the aryl iodide coupling toward reaction with the imine and Münchnone generation. As such, CO might be employed to control selectivity between these two pathways, such that the absence of CO could allow an initial Sonogashira coupling reaction on **1c**. The subsequent addition of CO would in principle lead to a second carbonylative cyclization, and provide a one pot, five component synthesis of diaryl-substituted polycyclic pyrroles. From a mechanistic perspective, this would involve coupling three separate palladium catalyzed reactions with both nucleophilic attack and spontaneous cycloaddition (Scheme 3).

Scheme 3. Mechanistic Postulate for a Tandem Catalytic, Palladium Catalyzed Coupling
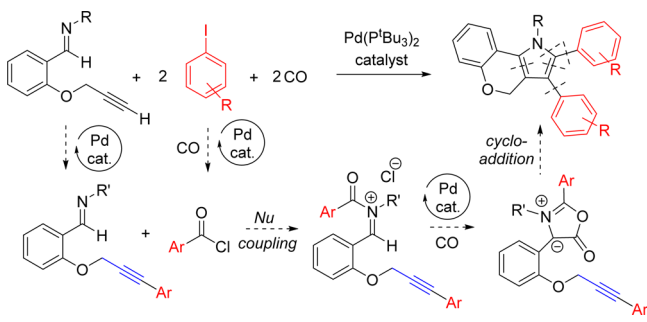
After probing various reaction conditions, it was found that the same palladium catalyst could mediate all of these steps. Thus, the Pd(P^{t}Bu$_3$)$_2$/CuI catalyzed Sonogashira coupling of a terminal-alkyne tethered imine, *p*-iodotoluene followed by the addition of CO to the same reaction vessel leads to the formation of polysubstituted **5a** in good yield (Table 3). While a number of phosphine ligands can be employed in the initial Sonogashira coupling, this tandem catalytic reaction once again requires the use of P^{t}Bu$_3$ in order to facilitate the subsequent carbonylation chemistry, as well as the addition of a chloride source (Bu$_4$NCl).

As with the pyrrole synthesis in Table 2, this tandem catalytic, multicomponent reaction can tolerate substituents on the imine unit, and the use of *N*-benzyl protected imines (**5b−h**). The 2- and 3-aryl positions in **5** can also be modulated. This includes, for example, the use of donor-substituted aryls, those with electron withdrawing units, and even other heterocycles. Finally, we have found that this reaction can also allow different aryl iodides to be incorporated into the core of **5**. For this, the CO controlled cyclization is useful, where an initial, high

Table 3. Tandem Catalytic, Five Component Polycyclic Pyrrole Synthesis[a]

Imine	Ar-I	Product 5
		5a, 72%
		5b, 62%
		5c, 63%
		5d, 60%
		5e, 70%
		5f, 65%
	1) / 2)	**5g**, 70%
	1) / 2)	**5h**, 53%

[a](a) **1** (0.5 mmol), ArI (5 mmol), Pd(P^{t}Bu$_3$)$_2$ (26 mg, 0.05 mmol), CuI (4.8 mg, 0.025 mmol), P^{t}Bu$_3$ (20 mg, 0.1 mmol), NEt^{i}Pr$_2$ (258 mg, 2 mmol), CH$_3$CN, 5 h, r.t. (b) Bu$_4$NCl (278 mg, 1 mmol), CO (10 atm), 40 °C, 16 h.

yielding non-CO based Sonogashira reaction can be followed by the addition of a second aryl iodide in concert with CO for cyclization. This approach allows the selective preparation of pyrroles **5g** and **5h** (Table 3). As far as we are aware, this represents one of the few CO controlled tandem catalytic reactions, and allows the generation of **5** in an efficient fashion from five different reagents (two aryl iodides, two equivalents of carbon monoxide, and the alkyne-tethered imine).

■ CONCLUSION

In conclusion, we have described a new palladium catalyzed approach to assemble polycyclic pyrroles from aryl iodides, CO, and alkyne-tethered imines. This reaction exploits the dicarbonylative formation of Münchnone, which undergo spontaneous cycloaddition with tethered alkynes, and provides access to these products from available reagents and minimal byproducts (HI and CO_2). The transformation can be diversified, and expanded to a one pot synthesis of polysubstituted variants of **3** via a tandem Sonogashira/ carbonylation reaction employing a single palladium catalyst. In principle, this platform should be adaptable to access a range of alternative classes of heterocyclic products. Experiments directed toward the latter are in progress.

■ EXPERIMENTAL SECTION

General Procedures. All experiments were conducted in an inert atmospheres glovebox or using standard Schlenk techniques, unless otherwise noted. Research grade carbon monoxide (99.99%) was used as received. All reagents were purchased from commercial sources and used as received. $CDCl_3$ and CD_3CN were distilled from CaH_2 under nitrogen, vacuum transferred, and stored over 4 Å molecular sieves. Acetonitrile, dichloromethane, and diethyl ether were dried with a solvent purification system. Tetrabutylammonium chloride was dried in the glovebox by dissolving in dichloromethane, allowing it to stand overnight over activated 4 Å molecular sieves, then filtering and removing the solvent *in vacuo*. $Pd(P^tBu_3)_2$ was prepared as previously described.[10b] Nuclear magnetic resonance (NMR) characterization was performed on 500 MHz spectrometers for proton, and 126 MHz for carbon. ^{1}H and ^{13}C NMR chemical shifts were referenced to residual solvent. Mass spectra were recorded on a high-resolution electrospray ionization quadrupole mass spectrometer.

Typical Synthesis of Alkyne-Tethered Imines 1. In analogy to previous reports,[12] a solution of salicylaldehyde (366 mg, 3.0 mmol) and K_2CO_3 (1.0 g, 7.5 mmol) in DMF (15 mL) was prepared in a 100 mL round-bottom flask equipped with a magnetic stir bar. The solution was allowed to stir for 20 min at room temperature. To the solution was added 1-bromo-2-butyne (519 mg, 3.9 mmol). The reaction mixture was allowed to stir overnight at room temperature. Water (20 mL) was then added and the resulting mixture was extracted three times with diethyl ether (15 mL portions). The ether fractions were combined and filtered through $MgSO_4$. The solvent was removed *in vacuo* and the product was recrystallized in ethanol to afford 2-(but-2-yn-1-yloxy)benzaldehyde (435 mg, 2.5 mmol) as a yellow powder in 83% yield. To a solution of this 2-(but-2-yn-1-yloxy)benzaldehyde (435 mg, 2.5 mmol) in dichloromethane (10 mL) was added Na_2SO_4 (1.0 g, 7.0 mmol) and ethylamine (2.0 M in THF) (1.6 mL, 3.25 mmol). The heterogeneous mixture was stirred at room temperature for 18 h. The reaction mixture was filtered, and the solvent and excess amine were removed *in vacuo* to afford 1-(2-(but-2-yn-1-yloxy)phenyl)-*N*-ethylmethanimine **1a** (453 mg, 2.2 mmol) as a clear oil (88%). In the case of *N*-benzyl-1-(2-(but-2-yn-1-yloxy)-phenyl)methanimine **1b** exactly 1.0 equiv of benzylamine was added.

1-(2-(But-2-yn-1-yloxy)phenyl)-N-ethylmethanimine (1a).[13] Isolated yield 88% (453 mg, 2.20 mmol). Yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.73 (s, 1H), 7.96 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.40–7.30 (m, 1H), 7.00 (m, 2H), 4.71 (q, *J* = 2.3 Hz, 2H), 3.65 (qd, *J* = 7.3, 1.3 Hz, 2H), 1.85 (t, *J* = 2.3 Hz, 3H), 1.29 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (125

MHz, $CDCl_3$) δ 156.9, 156.3, 131.4, 127.2, 125.4, 121.4, 112.7, 84.0, 73.9, 56.9, 56.0, 16.4, 3.6. HRMS: Calculated for $C_{13}H_{15}NNaO$ (MNa⁺): 224.1046, found: 224.1052.

N-Benzyl-1-(2-(but-2-yn-1-yloxy)phenyl)methanimine (1b). Isolated yield 90% (593 mg, 2.25 mmol). Yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.87 (d, *J* = 1.5 Hz, 1H), 8.04 (dd, *J* = 7.7, 1.8 Hz, 1H), 7.42–7.36 (m, 1H), 7.37–7.31 (m, 4H), 7.28–7.23 (m, 1H), 7.06–6.98 (m, 2H), 4.83 (d, *J* = 1.1 Hz, 2H), 4.73 (q, *J* = 2.3 Hz, 2H), 1.87 (t, *J* = 2.3 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.9, 157.1, 139.7, 131.7, 128.4, 127.9, 127.5, 126.8, 125.2, 121.4, 112.8, 84.1, 73.8, 65.4, 57.0, 3.7. HRMS: Calculated for $C_{18}H_{18}NO$ (MH⁺): 264.1383, found: 264.1385.

N-Ethyl-1-(2-(prop-2-yn-1-yloxy)phenyl)methanimine (1c). Isolated yield 95% (445 mg, 2.40 mmol). Yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.73 (s, 1H), 7.97 (dd, *J* = 8.1, 1.6 Hz, 1H), 7.42–7.33 (m, 1H), 7.03 (m, 2H), 4.76 (d, *J* = 2.4 Hz, 2H), 3.65 (qd, *J* = 7.3, 1.4 Hz, 2H), 2.53 (t, *J* = 2.4 Hz, 1H), 1.30 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.6, 156.1, 131.4, 127.4, 125.6, 121.8, 112.6, 78.3, 75.8, 56.3, 56.1, 16.3. HRMS: Calculated for $C_{12}H_{14}NO$ (MH⁺) 188.1070, found: 188.1070.

N-Benzyl-1-(2-(prop-2-yn-1-yloxy)phenyl)methanimine (1d). Isolated yield 90% (561 mg, 2.25 mmol). Yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.87 (d, *J* = 1.5 Hz, 1H), 8.06 (dd, *J* = 8.0, 1.8 Hz, 1H), 7.44–7.37 (m, 1H), 7.37–7.32 (m, 4H), 7.29–7.23 (m, 1H), 7.07–7.01 (m, 2H), 4.84 (d, *J* = 1.3 Hz, 2H), 4.78 (d, *J* = 2.4 Hz, 2H), 2.54 (t, *J* = 2.4 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.8, 157.0, 139.8, 131.9, 128.6, 128.1, 127.8, 127.0, 125.6, 122.0, 112.9, 78.4, 76.0, 65.6, 56.5. HRMS. Calculated for $C_{17}H_{16}NO$ (MH⁺) 250.1226, found: 250.1225.

(E)-N-Ethyl-1-(4-methoxy-2-(prop-2-yn-1-yloxy)phenyl)-methanimine (1e). Isolated yield 85% (463 mg, 2.10 mmol). Yellow powder. mp 57–58 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.61 (s, 1H), 7.93–7.87 (m, 1H), 6.59–6.52 (m, 2H), 4.72 (d, *J* = 2.4 Hz, 2H), 3.82 (s, 3H), 3.60 (qd, *J* = 7.3, 1.4 Hz, 2H), 2.54 (t, *J* = 2.4 Hz, 1H), 1.27 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.6, 157.9, 155.7, 128.6, 118.8, 106.6, 99.7, 78.3, 76.1, 56.4, 56.1, 55.5, 16.6. HRMS: Calculated for $C_{13}H_{16}NO_2$ (MH⁺) 218.1176, found: 218.1178.

Typical Synthesis of Polycyclic Pyrroles 3. In a glovebox, 1-(2-(but-2-yn-1-yloxy)phenyl)-*N*-ethylmethanimine **1a** (101 mg, 0.5 mmol), 4-iodotoluene (545 mg, 2.5 mmol), NEt^iPr_2 (97 mg, 0.75 mmol) in 3.3 mL acetonitrile were added to $Pd(P^tBu_3)_2$ (13 mg, 0.025 mmol) and Bu_4NCl (139 mg, 0.5 mmol) in a 4 mL glass vial equipped with a magnetic stir bar. The vial was capped with a pierced plastic cap and placed inside a 50 mL Parr steel autoclave, which was sealed and taken out of the glovebox. The reactor was charged with 10 atm CO using a Parr Multiwell Reactor 5000. The reactor was heated to 40 °C for 12 h in an oil bath. After allowing sufficient time to cool to room temperature, the CO atmosphere was evacuated and the crude residue was purified by column chromatography on silica gel (eluent: *n*-hexane/ethyl acetate 10:1) to afford 1-ethyl-3-methyl-2-(p-tolyl)-1,4-dihydrochromeno[4,3-*b*]pyrrole **3a** as a light yellow solid in 76% yield (115 mg, 0.38 mmol).

1-Ethyl-3-methyl-2-(p-tolyl)-1,4-dihydrochromeno[4,3-b]pyrrole (3a). Isolated yield 76% (115 mg, 0.38 mmol). Light yellow solid, mp 113–115 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.32–7.27 (m, 2H), 7.25 (d, *J* = 8.1 Hz, 2H), 7.08 (ddd, *J* = 8.7, 7.3, 1.6 Hz, 1H), 7.03–6.95 (m, 2H), 5.24 (s, 2H), 4.11 (q, *J* = 7.1 Hz, 2H), 2.45 (s, 3H), 1.94 (s, 3H), 1.26 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.2, 137.3, 134.0, 130.7, 129.3, 129.1, 126.1, 122.1, 121.6, 120.2, 119.9, 117.2, 116.2, 112.1, 64.9, 30.3, 21.3, 16.6, 9.3. HRMS: Calculated for $C_{21}H_{21}NNaO$ (MNa⁺): 326.1515, found: 326.1516.

1-Ethyl-2-(4-ethylphenyl)-3-methyl-1,4-dihydrochromeno[4,3-b]-pyrrole (3b). Isolated yield 73% (111 mg, 0.36 mmol). White solid, 111–114 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.38–7.31 (m, 2H), 7.07 (ddd, *J* = 8.6, 7.3, 1.5 Hz, 1H), 7.02–6.93 (m, 4H), 5.97 (s, 1H), 5.22 (s, 2H), 4.20 (q, *J* = 7.1 Hz, 2H), 3.87 (s, 3H), 1.30 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.2, 153.2, 137.0, 130.9, 126.3, 125.6, 123.5, 121.6, 120.1, 120.0,

117.3, 116.8, 113.9, 104.6, 65.9, 55.3, 40.4, 16.6. HRMS Calculated for $C_{20}H_{19}NNaO_2$ (MNa$^+$): 328.1308, found: 328.1309.

1-Ethyl-2-(4-methoxyphenyl)-3-phenyl-1,4-dihydrochromeno-[4,3-b]pyrrole (3c). Isolated yield 95% (181 mg, 0.47 mmol). Light yellow solid, mp 138–140 °C. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.45 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.24–7.16 (m, 4H), 7.15–7.07 (m, 2H), 7.04–6.96 (m, 4H), 6.94–6.87 (m, 2H), 5.28 (s, 2H), 4.16 (q, *J* = 7.1 Hz, 2H), 3.84 (s, 3H), 1.30 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 159.2, 153.6, 134.8, 133.1, 132.6, 129.1, 128.0, 126.5, 125.3, 124.4, 122.7, 121.7, 120.5, 119.8, 119.2, 117.3, 115.1, 113.9, 65.0, 55.2, 40.0, 16.5. HRMS: Calculated for $C_{26}H_{24}NO_2$ (MH$^+$): 382.1802, found: 382.1795.

1-Ethyl-3-phenyl-2-(p-tolyl)-1,4-dihydrochromeno[4,3-b]pyrrole (3d).[14] Isolated yield 82% (150 mg, 0.41 mmol). Light yellow solid, 150–151 °C. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.46 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.19 (d, *J* = 8.4 Hz, 6H), 7.14–7.08 (m, 2H), 7.05–6.96 (m, 4H), 5.28 (s, 2H), 4.16 (q, *J* = 7.1 Hz, 2H), 2.39 (s, 3H), 1.30 (t, *J* = 7.1 Hz, 3H).^{13}C NMR (125 MHz, CDCl$_3$) δ 153.6, 137.6, 134.8, 133.4, 131.3, 129.2, 129.18, 129.16, 128.0, 126.5, 125.4, 122.8, 121.7, 120.5, 119.8, 119.2, 117.3, 115.2, 65.0, 40.0, 21.3, 16.5. HRMS: Calculated for $C_{26}H_{23}NNaO$ (MNa$^+$): 388.1672, found: 388.1667.

1-Benzyl-3-methyl-2-(p-tolyl)-1,4-dihydrochromeno[4,3-b]pyrrole (3e). Isolated yield 60% (110 mg, 0.30 mmol). Light yellow solid, mp 150–153 °C. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.34 (t, *J* = 7.4 Hz, 2H), 7.30–7.23 (m, 1H), 7.15 (d, *J* = 7.7 Hz, 2H), 7.13–7.03 (m, 5H), 7.03–6.93 (m, 2H), 6.75 (td, *J* = 7.4, 1.9 Hz, 1H), 5.31 (s, 2H), 5.26 (s, 2H), 2.38 (s, 3H), 2.05 (s, 3H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 153.2, 139.1, 137.3, 134.7, 130.4, 129.0, 128.88, 128.83, 127.0, 126.2, 125.6, 123.2, 121.5, 120.5, 119.4, 117.0, 116.2, 112.3, 64.9, 49.2, 21.2, 9.6. HRMS: Calculated for $C_{26}H_{23}NO$ (M$^+$): 365.1774, found: 365.1764.

1-Benzyl-2-(4-methoxyphenyl)-3-methyl-1,4-dihydrochromeno-[4,3-b]pyrrole (3f). Isolated yield 83% (158 mg, 0.41 mmol). Light yellow solid, 133–138 °C. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.32 (td, *J* = 7.2, 6.3, 1.3 Hz, 2H), 7.28–7.21 (m, 1H), 7.14–7.07 (m, 2H), 7.07–7.00 (m, 3H), 7.00–6.93 (m, 2H), 6.88–6.81 (m, 2H), 6.72 (ddd, *J* = 7.7, 6.9, 1.8 Hz, 1H), 5.28 (s, 2H), 5.22 (s, 2H), 3.80 (s, 3H), 2.00 (s, 3H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 159.0, 153.2, 139.1, 134.4, 131.7, 128.8, 127.0, 126.2, 125.6, 124.1, 123.0, 121.5, 120.4, 119.5, 117.0, 116.0, 113.7, 112.2, 64.9, 55.2, 49.1, 9.6. HRMS: Calculated for $C_{26}H_{23}NNaO_2$ (MNa$^+$): 404.1621, found: 404.1614.

1-Ethyl-2-(4-methoxyphenyl)-3-methyl-1,4-dihydrochromeno-[4,3-b]pyrrole (3g). Isolated yield 85% (136 mg, 0.42 mmol). Light yellow solid, mp 114–116 °C. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.39 (dd, *J* = 7.7, 1.5 Hz, 1H), 7.29–7.23 (m, 2H), 7.08–7.02 (m, 1H), 7.02–6.93 (m, 4H), 5.21 (s, 2H), 4.07 (q, *J* = 7.1 Hz, 2H), 3.87 (s, 3H), 1.91 (s, 3H), 1.24 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 159.1, 153.1, 133.7, 132.1, 126.1, 124.6, 121.9, 121.6, 120.1, 119.9, 117.2, 116.1, 113.8, 112.0, 64.9, 55.2, 40.2, 16.6, 9.3. HRMS: Calculated for $C_{21}H_{22}NO_2$ (MH$^+$): 320.1645, found: 320.1638.

1-Ethyl-2-(p-tolyl)-1,4-dihydrochromeno[4,3-b]pyrrole (3h). Isolated yield 61% (88 mg, 0.31 mmol). White solid, 122–125 °C. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.46 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.36–7.30 (m, 2H), 7.30–7.23 (m, 2H), 7.09 (ddd, *J* = 8.5, 7.2, 1.6 Hz, 1H), 7.04–6.96 (m, 2H), 6.02 (s, 1H), 5.24 (s, 2H), 4.24 (q, *J* = 7.1 Hz, 2H), 2.43 (s, 3H), 1.32 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 153.3, 137.4, 137.3, 130.3, 129.5, 129.2, 126.4, 123.7, 121.7, 120.1, 120.0, 117.3, 117.0, 104.8, 65.9, 40.5, 21.3, 16.6. HRMS: Calculated for $C_{20}H_{19}NNaO$ (MNa$^+$): 312.1359, found: 312.1364.

1-Ethyl-7-methoxy-2-(p-tolyl)-1,4-dihydrochromeno[4,3-b]-pyrrole (3i). Isolated yield 70% (112 mg, 0.35 mmol). Light yellow solid. mp 103–105 °C. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.36 (d, *J* = 8.6 Hz, 1H), 7.33–7.29 (m, 2H), 7.24 (d, *J* = 7.9 Hz, 2H), 6.62 (d, *J* = 2.6 Hz, 1H), 6.56 (dd, *J* = 8.6, 2.7 Hz, 1H), 5.99 (s, 1H), 5.22 (s, 2H), 4.19 (q, *J* = 7.1 Hz, 2H), 3.81 (s, 3H), 2.42 (s, 3H), 1.30 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 158.6, 154.8, 137.3, 136.4, 130.5, 129.5, 129.3, 124.1, 121.0, 114.9, 113.3, 107.4, 104.7, 103.5, 66.3, 55.4, 40.5, 21.4, 16.7. HRMS: Calculated for $C_{21}H_{22}NO_2$ (MH$^+$): 320.1645, found: 320.1644.

1-Ethyl-2-(4-fluorophenyl)-3-methyl-1,4-dihydrochromeno[4,3-b]pyrrole (3j). Isolated yield 57% (88 mg, 0.28 mmol). Light yellow solid, mp 116–118 °C. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.40 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.34–7.28 (m, 2H), 7.19–7.13 (m, 2H), 7.07 (ddd, *J* = 8.7, 7.3, 1.5 Hz, 1H), 7.02–6.94 (m, 2H), 5.21 (s, 2H), 4.07 (q, *J* = 7.1 Hz, 2H), 1.91 (s, 3H), 1.23 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 162.5 (d, *J* = 247.4 Hz), 153.4, 132.9, 132.7 (d, *J* = 8.1 Hz), 128.5 (d, *J* = 3.4 Hz), 126.5, 122.6, 121.8, 120.4, 119.9, 117.5, 116.4, 115.6 (d, *J* = 21.4 Hz), 112.6, 65.0, 40.4, 16.7, 9.5. HRMS: Calculated for $C_{20}H_{19}FNO$ (MH$^+$): 308.1445, found: 308.1437.

1-Ethyl-2-(4-fluorophenyl)-3-phenyl-1,4-dihydrochromeno[4,3-b]pyrrole (3k). Isolated yield 60% (111 mg, 0.30 mmol). Light yellow solid, mp 180–183 °C. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.46 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.31–7.24 (m, 2H), 7.24–7.17 (m, 2H), 7.16–6.99 (m, 6H), 6.99–6.92 (m, 2H), 5.27 (s, 2H), 4.15 (q, *J* = 7.2 Hz, 2H), 1.30 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 162.6 (d, *J* = 247.9 Hz), 153.9, 134.6, 133.4 (d, *J* = 8.1 Hz), 132.2, 129.3, 128.4 (d, *J* = 3.5 Hz), 128.3, 126.9, 125.8, 123.3, 121.9, 120.8, 119.8, 119.8, 117.6, 115.7 (d, *J* = 21.5 Hz), 115.5, 65.1, 40.2, 16.7. HRMS: Calculated for $C_{25}H_{21}FNO$ (MH$^+$): 370.1602, found: 370.1599.

2-(4-Chlorophenyl)-1-ethyl-1,4-dihydrochromeno[4,3-b]pyrrole (3l). Isolated yield 66% (102 mg, 0.33 mmol). White solid, mp 134–136 °C. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.47–7.37 (m, 3H), 7.37–7.32 (m, 2H), 7.09 (ddd, *J* = 8.4, 7.2, 1.5 Hz, 1H), 7.02–6.94 (m, 2H), 6.02 (s, 1H), 5.20 (s, 2H), 4.21 (q, *J* = 7.2 Hz, 2H), 1.29 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 153.3, 135.9, 133.5, 131.6, 130.6, 128.7, 126.7, 124.5, 121.7, 120.3, 119.7, 117.4, 117.1, 105.3, 65.7, 40.6, 16.5. HRMS: Calculated for $C_{19}H_{17}ClNO$ (MH$^+$) 310.0993, found: 310.0993.

1-Ethyl-3-methyl-2-phenyl-1,4-dihydrochromeno[4,3-b]pyrrole (3m).[13] Isolated yield 67% (97 mg, 0.33 mmol). Light yellow solid, mp 98–101 °C. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.47 (tt, *J* = 7.9, 1.4 Hz, 2H), 7.44–7.37 (m, 2H), 7.37–7.31 (m, 2H), 7.07 (ddd, *J* = 8.6, 7.3, 1.6 Hz, 1H), 7.03–6.93 (m, 2H), 5.23 (s, 2H), 4.11 (q, *J* = 7.1 Hz, 2H), 1.94 (s, 3H), 1.24 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 153.2, 134, 132.4, 130.8, 128.3, 127.5, 126.2, 122.4, 121.6, 120.3, 119.9, 117.2, 116.3, 112.3, 64.9, 40.3, 16.6, 9.4. HRMS: Calculated for $C_{20}H_{19}NO$ (M$^+$): 289.1461, found: 289.1452.

Methyl 3-(1-Ethyl-3-methyl-1,4-dihydrochromeno[4,3-b]pyrrol-2-yl)benzoate (3n). Isolated yield 73% (127 mg, 0.36 mmol). Light yellow oil. ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.09–8.01 (m, 2H), 7.56–7.51 (m, 2H), 7.41 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.08 (ddd, *J* = 8.7, 7.2, 1.5 Hz, 1H), 6.98 (ddd, *J* = 14.7, 7.6, 1.4 Hz, 2H), 5.20 (s, 2H), 4.09 (q, *J* = 7.1 Hz, 2H), 3.95 (s, 3H), 1.93 (s, 3H), 1.22 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 167.0, 153.5, 135.3, 132.9, 132.0, 130.6, 128.8, 128.7, 126.6, 123.1, 121.8, 120.5, 119.9, 117.5, 116.6, 113.0, 64.9, 52.4, 40.6, 16.7, 9.5. HRMS: Calculated for $C_{22}H_{22}NO_3$ (MH$^+$): 348.1594, found: 348.1587.

1-Ethyl-2-(3-methoxyphenyl)-3-methyl-1,4-dihydrochromeno-[4,3-b]pyrrole (3o). Isolated yield 60% (96 mg, 0.30 mmol). Light yellow solid, mp 105–106 °C. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.45–7.34 (m, 2H), 7.07 (ddd, *J* = 8.6, 7.3, 1.6 Hz, 1H), 7.02–6.91 (m, 4H), 6.89 (dd, *J* = 2.6, 1.5 Hz, 1H), 5.22 (s, 2H), 4.12 (q, *J* = 7.1 Hz, 2H), 3.86 (s, 3H), 1.95 (s, 3H), 1.25 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 159.6, 153.4, 134.0, 133.8, 129.5, 126.4, 123.4, 122.6, 121.8, 120.4, 120.0, 117.4, 116.5$_1$, 116.4$_8$, 113.3, 112.4, 65.0, 55.4, 40.6, 16.8, 9.5. HRMS: Calculated for $C_{21}H_{21}NNaO_2$ (MNa$^+$): 342.1464, found: 342.1467.

2-(3,5-Dimethylphenyl)-1-ethyl-3-methyl-1,4-dihydrochromeno-[4,3-b]pyrrole (3p). Isolated yield 60% (95 mg, 0.30 mmol). Light yellow solid, mp 107–110 °C. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.40 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.09–7.00 (m, 2H), 7.00–6.90 (m, 4H), 5.21 (s, 2H), 4.09 (q, *J* = 7.1 Hz, 2H), 2.38 (s, 6H), 1.92 (s, 3H), 1.23 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 153.1, 137.7, 134.3, 132.2, 129.2, 128.6, 126.0, 122.1, 121.6, 120.2, 120.0, 117.2, 116.3, 112.0, 64.9, 40.3, 21.3, 16.6, 9.4. HRMS: Calculated for $C_{22}H_{24}NO$ (MH$^+$): 318.1852, found: 318.1854.

1-Benzyl-2-(3,5-dimethylphenyl)-3-methyl-1,4-dihydrochromeno[4,3-b]pyrrole (3q). Isolated yield 63% (119 mg, 0.31 mmol). Light yellow solid, mp 119–121 °C. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.31 (dd, *J* = 8.1, 6.9 Hz, 2H), 7.24 (t, *J* = 7.5 Hz, 1H),

7.10−7.03 (m, 3H), 7.01−6.90 (m, 3H), 6.78−6.71 (m, 3H), 5.28 (d, J = 1.1 Hz, 2H), 5.21 (s, 2H), 2.21 (s, 6H), 2.02 (d, J = 1.1 Hz, 3H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 153.2, 139.3, 137.6, 135.0, 131.6, 129.1, 128.7, 128.3, 127.0, 126.2, 125.7, 124.2, 123.3, 121.5, 120.4, 119.5, 117.0, 116.1, 112.2, 64.9, 21.2, 9.6. HRMS: Calculated for C$_{27}$H$_{25}$NNaO (MNa$^+$): 402.1828, found: 402.1831.

1-Ethyl-2-(thiophen-3-yl)-1,4-dihydrochromeno[4,3-b]pyrrole (3r). Isolated yield 78% (110 mg, 0.39 mmol). White solid, 85−90 °C. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.44 (dd, J = 7.7, 1.6 Hz, 1H), 7.40 (dd, J = 5.0, 3.0 Hz, 1H), 7.28 (dd, J = 3.0, 1.3 Hz, 1H), 7.18 (dd, J = 4.9, 1.3 Hz, 1H), 7.08 (ddd, J = 8.4, 7.2, 1.5 Hz, 1H), 7.02−6.95 (m, 2H), 6.06 (s, 1H), 5.21 (s, 2H), 4.26 (q, J = 7.2 Hz, 2H), 1.39 (t, J = 7.2 Hz, 3H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 153.3, 133.4, 131.6, 128.7, 126.5, 125.6, 123.9, 122.6, 121.6, 120.1, 119.7, 117.3, 116.7, 104.9, 65.7, 40.5, 16.6. HRMS: Calculated for C$_{17}$H$_{15}$NNaOS (MNa$^+$): 304.0767, found: 304.0771.

1-Ethyl-2-(1-tosyl-1H-indol-5-yl)-1,4-dihydrochromeno[4,3-b]-pyrrole (3s). Isolated yield 70% (164 mg, 0.35 mmol). White solid, mp 160−163 °C. ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.06−8.00 (m, 1H), 7.86−7.79 (m, 2H), 7.62 (d, J = 3.7 Hz, 1H), 7.55 (dd, J = 1.7, 0.7 Hz, 1H), 7.43 (dd, J = 7.7, 1.6 Hz, 1H), 7.35 (dd, J = 8.5, 1.7 Hz, 1H), 7.27 (d, J = 8.6 Hz, 2H), 7.07 (ddd, J = 8.5, 7.2, 1.5 Hz, 1H), 7.01−6.94 (m, 2H), 6.69 (dd, J = 3.7, 0.8 Hz, 1H), 5.98 (s, 1H), 5.21 (s, 2H), 4.20 (q, J = 7.1 Hz, 2H), 2.37 (s, 3H), 1.26 (t, J = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 153.2, 145.1, 137.1, 135.3, 134.1, 130.8, 129.9, 128.3, 130.0, 129.9, 126.4, 126.3, 123.8, 122.3, 121.6, 120.1, 119.8, 117.3, 116.9, 113.3, 108.8, 105.0, 65.8, 40.5, 21.6, 16.5. HRMS: Calculated for C$_{28}$H$_{24}$N$_2$NaO$_3$S (MNa$^+$): 491.1400, found: 491.1417.

Typical Synthesis of Polycyclic Pyrroles with Two Aryl Iodides (Table 3).

In a glovebox, *N*-ethyl-1-(2-(prop-2-yn-1-yloxy)-phenyl)methanimine **1c** (93 mg, 0.5 mmol), 4-iodotoluene (1090 mg, 5 mmol), and NEt^{i}Pr$_2$ (250 mg, 2 mmol) in 3.3 mL acetonitrile were added to Pd(P^{t}Bu$_3$)$_2$ (26 mg, 0.05 mmol), CuI (4.8 mg, 0.025 mmol), and P^{t}Bu$_3$ (20 mg, 0.1 mmol) in a 4 mL glass vial equipped with a magnetic stir bar. The mixture was allowed to stir at room temperature for 5 h. Bu$_4$NCl (278 mg, 1.0 mmol) was then added, and the vial was capped with a pierced plastic cap and placed inside a 50 mL Parr steel autoclave, which was sealed and taken out of the glovebox. The reactor was charged with 10 atm CO using a Parr Multiwell Reactor 5000. The reactor was heated to 40 °C for 12 h. After allowing sufficient time to cool to room temperature, the CO atmosphere was evacuated and the crude residue was purified by column chromatography on silica gel (eluent: *n*-hexane/ethyl acetate 10:1) to afford 1-ethyl-2,3-di-p-tolyl-1,4-dihydrochromeno[4,3-*b*]pyrrole **5a** as a light yellow solid in 72% yield (137 mg, 0.36 mmol).

Pyrrole **5g** was synthesized in a similar fashion with the use of 4-iodotoluene (120 mg, 0.55 mmol) in the first step (6 h), followed by the addition of Bu$_4$NCl (278 mg, 1.0 mmol) and 4-iodoanisole (585 mg, 2.5 mmol) for cyclization. For **5h**, the procedure was modified as follows: imine **1e** (109 mg, 0.5 mmol), 1-chloro-4-iodobenzene (119 mg, 0.5 mmol), DABCO (168 mg, 1.5 mmol), and P^{t}Bu$_3$ (20 mg, 0.1 mmol) were dissolved in 9 mL of MeCN and added to a 20 mL vial containing CuI (2.4 mg, 0.0125 mmol) and Pd(P^{t}Bu$_3$)$_2$ (26 mg, 0.05 mmol). The vial was equipped with a stir bar and the mixture was allowed to stir at room temperature for 48 h. Bu$_4$NCl (278 mg, 1.0 mmol) and 3-iodothiophene (525 mg, 2.5 mmol) were added to the solution together with 3 mL MeCN. The system was sealed, taken out of the glovebox, and charged with 10 atm CO. Similar isolation to that above afforded 3-(4-chlorophenyl)-1-ethyl-7-methoxy-2-(thiophen-3-yl)-1,4-dihydrochromeno[4,3-*b*]pyrrole **5h** as a light yellow solid (112 mg, 0.26 mmol) in 53% yield.

1-Ethyl-2,3-di-p-tolyl-1,4-dihydrochromeno[4,3-b]pyrrole (5a). Isolated yield 72% (137 mg, 0.36 mmol). Light yellow solid, mp 125−130 °C. ^{1}H NMR (500 MHz, CD$_3$CN) δ 7.54 (dd, J = 7.8, 1.5 Hz, 1H), 7.25−7.21 (m, 2H), 7.21−7.16 (m, 2H), 7.11 (td, J = 7.7, 1.6 Hz, 1H), 7.05−6.99 (m, 3H), 6.97 (dd, J = 8.0, 1.4 Hz, 1H), 6.91−6.85 (m, 2H), 5.18 (s, 2H), 4.11 (q, J = 7.2 Hz, 2H), 2.37 (s, 3H), 2.26 (s, 3H), 1.20 (t, J = 7.2 Hz, 3H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 154.4, 139.0, 136.3, 134.2, 132.7, 132.4, 130.2, 130.0$_2$, 130.0$_0$, 129.7, 127.6, 123.2, 122.9, 121.9, 120.5, 119.9, 118.0, 116.1, 65.6, 40.9, 21.3,

21.0, 16.7. HRMS: Calculated for C$_{27}$H$_{25}$NNaO (MNa$^+$): 402.1828, found: 402.1824.

1-Ethyl-2,3-diphenyl-1,4-dihydrochromeno[4,3-b]pyrrole (5b). Isolated yield 62% (109 mg, 0.31 mmol). Light yellow solid, mp 96−100 °C. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.46 (dd, J = 7.7, 1.6 Hz, 1H), 7.39−7.34 (m, 3H), 7.32−7.27 (m, 2H), 7.22−7.16 (m, 2H), 7.11 (ddt, J = 8.5, 7.3, 1.5 Hz, 2H), 7.05−6.99 (m, 2H), 6.99−6.94 (m, 2H), 5.28 (s, 2H), 4.18 (q, J = 7.1 Hz, 2H), 1.31 (t, J = 7.2 Hz, 3H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 153.6, 134.6, 132.2, 131.5, 129.1, 128.4, 128.0, 127.8, 126.6, 126.2, 125.4, 122.9, 121.7, 120.5, 119.7, 119.3, 117.4, 115.3, 65.0, 40.1, 16.5. HRMS: Calculated for C$_{25}$H$_{21}$NNaO (MNa$^+$): 374.1515, found: 374.1521.

1-Ethyl-2,3-bis(4-fluorophenyl)-1,4-dihydrochromeno[4,3-b]pyrrole (5c). Isolated yield 63% (122 mg, 0.31 mmol). Light yellow solid, mp 170−173 °C. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.45 (dd, J = 7.8, 1.5 Hz, 1H), 7.28−7.22 (m, 2H), 7.14−7.05 (m, 3H), 7.05−6.98 (m, 2H), 6.93−6.88 (m, 4H), 5.23 (s, 2H), 4.15 (q, J = 7.1 Hz, 2H), 1.30 (t, J = 7.2 Hz, 3H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 162.7 (d, J = 248.4 Hz), 161.3 (d, J = 245.1 Hz), 153.8, 133.3 (d, J = 8.2 Hz), 132.2, 130.7 (d, J = 7.8 Hz), 130.6 (d, J = 3.2 Hz), 128.2 (d, J = 3.4 Hz), 127.0, 123.3, 122.0, 120.8, 119.7, 118.9, 117.6, 115.8 (d, J = 21.5 Hz), 115.3, 115.3 (d, J = 21.2 Hz), 65.0, 40.3, 16.7. HRMS Calculated for C$_{25}$H$_{20}$F$_2$NO (MH$^+$): 388.1507, found: 388.1508.

1-Benzyl-2,3-bis(4-fluorophenyl)-1,4-dihydrochromeno[4,3-b]-pyrrole (5d). Isolated yield 65% (146 mg, 0.32 mmol). Light yellow solid, 150−155 °C. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.35 (t, J = 7.4 Hz, 2H), 7.13−7.01 (m, 9H), 6.99−6.91 (m, 5H), 6.80 (td, J = 7.7, 1.3 Hz, 1H), 5.33 (s, 2H), 5.32 (s, 2H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 162.6 (d, J = 248.4 Hz), 161.4 (d, J = 245.2 Hz), 153.8, 138.4, 133.1 (d, J = 8.0 Hz), 130.9 (d, J = 7.8 Hz), 130.6 (d, J = 3.2 Hz), 129.1, 127.7 (d, J = 3.3 Hz), 127.5, 127.1, 125.7, 124.5, 121.9, 121.0, 119.2, 119.1, 117.4, 115.7 (d, J = 21.5 Hz), 115.4 (d, J = 21.4 Hz), 115.3, 113.2, 65.0, 49.2. HRMS: Calculated for C$_{30}$H$_{21}$F$_2$NNaO (MNa$^+$): 472.1483, found: 472.1494.

1-Benzyl-2,3-di-p-tolyl-1,4-dihydrochromeno[4,3-b]pyrrole (5e). Isolated yield 70% (154 mg, 0.35 mmol). Light yellow solid, 156−160 °C. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.34 (t, J = 7.5 Hz, 2H), 7.27 (m, 2H), 7.13−7.03 (m, 9H), 7.00 (m, 3H), 6.77 (m, 1H), 5.36 (s, 2H), 5.35 (s, 2H), 2.33 (s, 6H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 135.5, 138.6, 137.5, 135.1, 134.2, 131.8, 131.1, 129.1, 129.0, 128.9, 128.8, 128.7, 127.1, 126.5, 125.6, 123.9, 121.5, 120.7, 119.4, 119.3, 117.1, 115.2, 65.1, 48.9, 21.2, 21.1. HRMS: Calculated for C$_{32}$H$_{27}$NNaO (MNa$^+$): 464.1985, found: 464.1993.

1-Benzyl-2,3-diphenyl-1,4-dihydrochromeno[4,3-b]pyrrole (5f). Isolated yield 65% (134 mg, 0.32 mmol). Light yellow solid, mp 150−153 °C. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.34 (t, J = 7.5 Hz, 2H), 7.25 (m, 6H), 7.20−7.14 (m, 4H), 7.13−7.04 (m, 5H), 7.04−6.99 (m, 1H), 6.79 (td, J = 7.7, 1.5 Hz, 1H), 5.37 (s, 4H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 153.6, 138.4, 134.7, 134.3, 131.7, 131.2, 129.3, 128.8, 128.3, 128.1, 127.8, 127.1, 126.7, 125.7, 125.6, 124.2, 121.6, 120.8, 119.6, 119.2, 117.1, 115.3, 65.0, 49.0. HRMS: Calculated for C$_{30}$H$_{23}$NNaO (MNa$^+$): 436.1672, found: 436.1682.

1-Ethyl-2-(4-methoxyphenyl)-3-(p-tolyl)-1,4-dihydrochromeno-[4,3-b]pyrrole (5g). Isolated yield 70% (138 mg, 0.35 mmol). Light yellow solid, mp 133−136 °C. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.45 (dd, J = 7.7, 1.3 Hz, 1H), 7.25−7.19 (m, 2H), 7.12−7.07 (m, 1H), 7.04−6.97 (m, 4H), 6.94−6.90 (m, 2H), 6.88 (d, J = 8.1 Hz, 2H), 5.28 (s, 2H), 4.15 (q, J = 7.1 Hz, 2H), 3.84 (s, 3H), 2.29 (s, 3H), 1.30 (t, J = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 159.4, 153.8, 135.0, 133.1, 132.8, 131.9, 129.1, 129.0, 126.6, 124.7, 122.7, 121.8, 120.6, 120.0, 119.3, 117.5, 115.3, 114.0, 65.2, 55.4, 40.1, 21.2, 16.7. HRMS: Calculated for C$_{27}$H$_{26}$NO$_2$ (MH$^+$): 396.1958, found: 396.1961.

3-(4-Chlorophenyl)-1-ethyl-7-methoxy-2-(thiophen-3-yl)-1,4-dihydrochromeno[4,3-b]pyrrole (5h). Isolated yield 53% (112 mg, 0.26 mmol). Light orange solid. mp 132−134 °C. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.40−7.33 (m, 2H), 7.22−7.14 (m, 3H), 7.01−6.97 (m, 1H), 6.91 (d, J = 8.4 Hz, 2H), 6.64 (d, J = 2.6 Hz, 1H), 6.59 (dd, J = 8.6, 2.6 Hz, 1H), 5.23 (s, 2H), 4.16 (q, J = 7.1 Hz, 2H), 3.82 (s, 3H), 1.34 (t, J = 7.2 Hz, 3H). ^{13}C NMR (125 MHz, CDCl$_3$) δ 159.0, 155.3, 133.5, 132.0, 131.5, 130.3, 130.0, 128.5, 126.9, 126.1, 125.9, 123.8,

121.5, 118.9, 113.1, 112.8, 107.8, 103.5, 65.2, 55.5, 40.3, 16.7. HRMS: Calculated for $C_{24}H_{20}NClSO_2$ (M^+): 421.0898, found: 421.0890.

■ ASSOCIATED CONTENT

ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b02102.

^1H and ^{13}C NMR spectra for compounds 1−5 (PDF)

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Notes

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