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Synthesis of Tetracyclic Indoles via Intramolecular α-Arylation of Ketones

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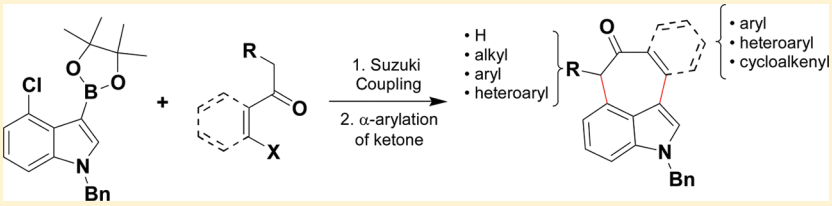
Supporting Information



ABSTRACT: An intramolecular palladium(0)-mediated α-arylation of ketones applied to the synthesis of various substituted tetracyclic indoles is reported. Most significantly, the efficiency of the transformation was enhanced by the use of monoligated Pd(0) complexes. This methodology was extended to double α-arylation of ketones using one-pot reactions with either simultaneous addition or sequential addition of two aryl halides for producing aryl substituted tetracyclic indoles.

Indole is an important heterocycle found in a large number of natural products and bioactive molecules.[1] In particular, carbo- or heterocycles joined at the indole 3,4-positions represent a common structural motif present in a variety of alkaloids. Among these molecules are dragmacidin E,[2] an inhibitor of serine-threonine protein phosphatases, cycloclavine,[3] *N*-methylwelwitindolinone C isothiocyanate,[4] and 9-deacetylfumigaclavine C,[5] which possess anticancer activities. These molecules also present synthetic challenges that inspire the exploration of various methodologies in order to achieve efficient syntheses of the natural product and non-natural derivatives (Figure 1). Various strategies have been used to affect the 3,4-indole connectivity, including use of Pauson–Khand reactions,[6] 6π-electrocyclizations,[7] Diels–Alder reactions,[8] and aminocyclizations.[9]

The palladium-catalyzed α-arylation of carbonyl functional groups has emerged as an attractive method for the rapid construction of C–C bonds.[10] Significant effort has been devoted to developing this methodology. Numerous studies have shown that this transformation is effective for the coupling of various aryl halides with ketones in both intermolecular[11] and intramolecular[12] processes. Nevertheless, the Pd-catalyzed intramolecular α-arylation of ketones has not often been used in indole chemistry,[13] although it may allow the construction of tetracyclic structures in only a few steps. We report herein a concise approach that exploits a Suzuki–Miyaura coupling to introduce *ortho*-ketoaryls, -ketoheteroaryls, or -ketocycloalkenes at the 3-position of indoles, followed by intramolecular α-arylation of the ketones to form tetracyclic derivatives.

The feasibility of this strategy is detailed in Scheme 1. *N*-Benzyl-3,4-dihaloindoles **3a–c** were prepared via a two-step process involving nitrogen alkylation of commercially available

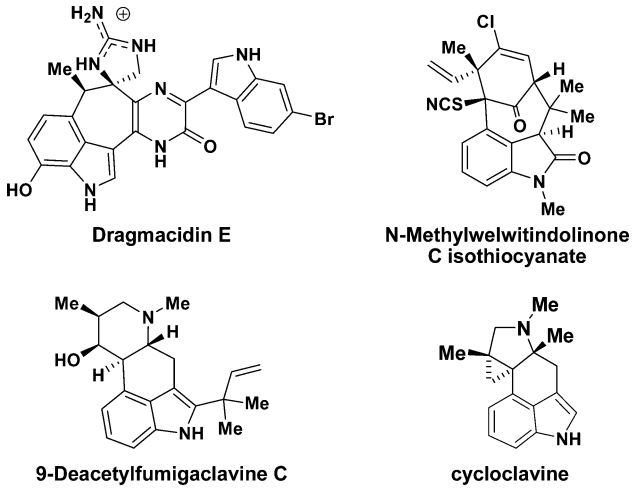


Figure 1. Indole alkaloids joined at the 3,4-positions.

4-bromoindole (**1**) or 4-chloroindole (**2**). The products were used without purification and subjected to regioselective halogenations at the 3-position using *N*-iodo- or *N*-bromosuccinimide generating **3a–c** in 91%, 96%, and 97% overall yield, respectively.[14] Next, two different strategies were explored to introduce the *ortho*-ketoaryl substituents. A Suzuki–Miyaura coupling of **3a** or **3b** with commercially available 2-acetylphenylboronic acid (**4**) gave indoles **7a** and **7b** in 52% and 71% yield, respectively. However, this process was limited by the

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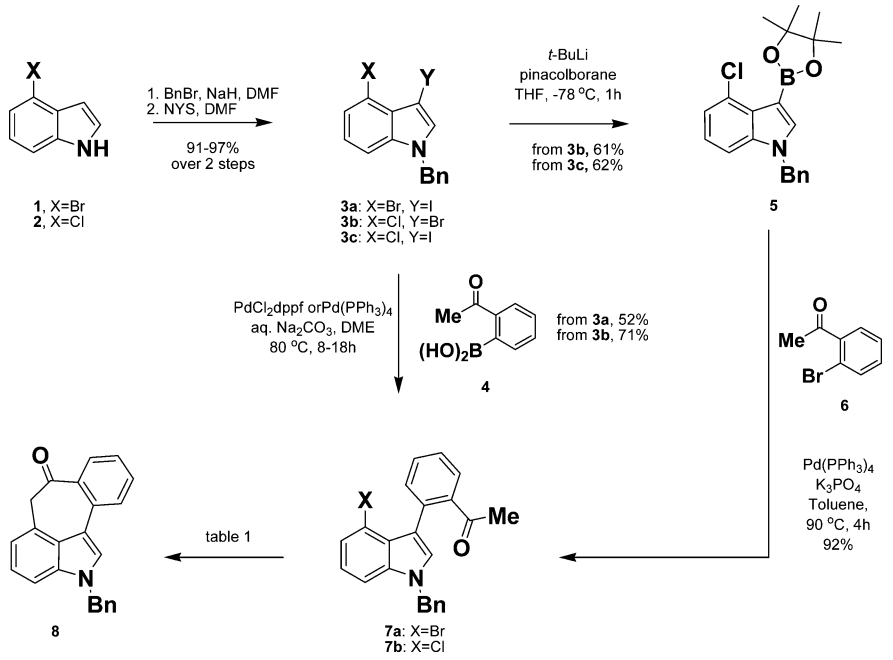
Scheme 1. Preparation of the Key Intermediate 7a–b



access to various commercially available substituted boronic acids necessitating several additional steps to prepare. In the second strategy, the indole boronic ester **5** was prepared from 4-chloroindoles **3b** or **3c** in 61% and 62% yield, respectively. Suzuki–Miyaura coupling of **5** with 2′-bromoacetophenone (**6**) generated indole **7b** in 92% yield.[15]

Optimization of the intramolecular α-arylation of indoles **7a–b** was investigated using a variety of conditions as depicted in Table 1. To our surprise, several of the previously reported methods for α-arylation of ketones using either $Pd(OAc)_2$ or Pd_2dba_3 with BINAP, XantPhos, PPh_3, or DPPF failed to yield the desired product only rendering unreacted starting material.[16] However, $dtBPfPdCl_2$, (SIPr)Pd(allyl)Cl, or precatalysts (Figure 2) proved more efficient. For example, using $dtBPfPdCl_2$, a catalyst developed by Hartwig and co-workers,[17] indole **7a** was converted to **8** in 50% yield in 0.5 h (entry 1). This reaction also proved better in 1,4-dioxane compared to THF or toluene. However, extending the reaction time to 16 h was detrimental, presumably due to decomposition of the tetracyclic indole product (entry 2). Indole **8** was obtained in only 31% yield with a palladium-*N*-heterocyclic carbene catalyst, (SIPr)Pd(allyl)Cl, developed by Nolan and co-workers (entry 3).[18]

More recently, Buchwald and co-workers reported the development of a new class of air- and moisture-stable Pd precatalysts that are activated under standard reaction conditions and ensure the formation of a monoligated active Pd(0)-complex. The $L_1Pd(0)$ species offers the advantage of being highly reactive due to less steric hindrance,[19] which we hypothesized may be beneficial for mediating the intramolecular α-arylation of indoles **7**. The use of these catalysts has also been recently shown to be effective at mediating other processes, including *ortho*- and *para*-arylations of phenols.[20] In the presence of the XPhos precatalyst (5 mol %), NaOt-Bu (1.1 equiv) in 1,4-dioxane at 60 °C for 0.5 h **8** was produced in 94% yield (entry 4). For comparison, α-arylation was not observed using $Pd(OAc)_2$ and XPhos demonstrating the advantage of the precatalyst (entry 5). When the reaction was performed at room temperature, the conversion was very low after 24 h, whereas higher temperatures (i.e., 80 °C) resulted in product

Table 1. Optimization of the Intramolecular Ketone α-Arylation of 7[a]

entry	substrate	catalyst	reaction time (h)	yield (%)[b]
1	**7a**	dtBPf $PdCl_2$	0.5	50
2	**7a**	dtBPf $PdCl_2$	16	25
3	**7a**	(SIPr)Pd(ally)Cl	3	31
4	**7a**	XPhos precat.	0.5	94
5	**7a**	$Pd(OAc)_2$, XPhos	24	0[c]
6	**7a**	BrettPhos precat.	1	95
7	**7a**	SPhos precat.	4	50
8	**7a**	XPhos precat.	3	91[d]
9	**7a**	XPhos precat.	24	59[e]
10	**7b**	XPhos precat.	1	96

[a]Reaction conditions: **7a** or **7b** (1 equiv), [Pd] (5 mol %), NaOtBu (1.1 equiv), 1,4-dioxane, 60 °C. [b]Isolated yield. [c]$Pd(OAc)_2$ (5 mol %), XPhos (10 mol %). [d]XPhos precat. (3 mol %). [e]XPhos precat. (1 mol %).

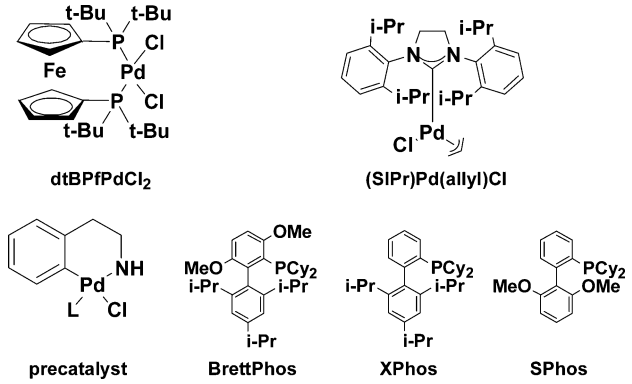


Figure 2. Various palladium catalysts and precatalysts.

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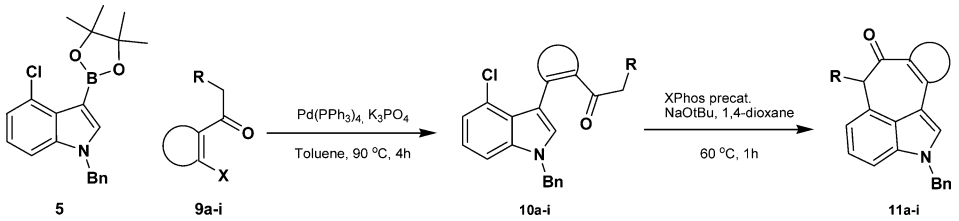
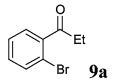
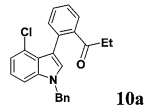
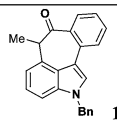
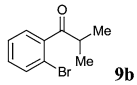
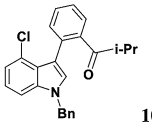
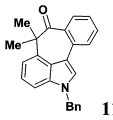
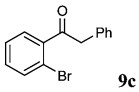
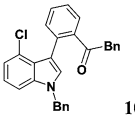
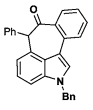
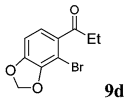
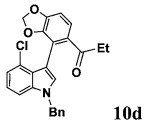
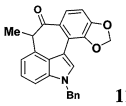
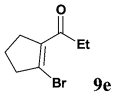
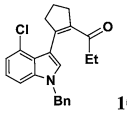
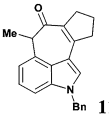
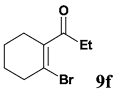
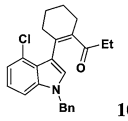
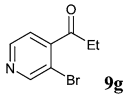
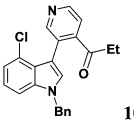
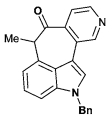
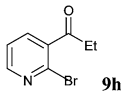
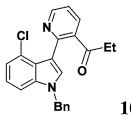
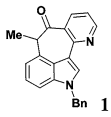
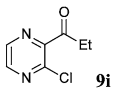
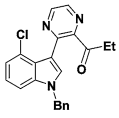
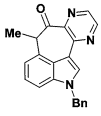
Table 2. Substrate Scope of the Ketone α-Arylation[a]



entry	ketones	Suzuki product	yield (%)[b]	α-arylation product	yield (%)[b]
1	 **9a**	 **10a**	86	 **11a**	89
2	 **9b**	 **10b**	82	 **11b**	99
3	 **9c**	 **10c**	79	 **11c**	98
4	 **9d**	 **10d**	88	 **11d**	0
5	 **9e**	 **10e**	94	 **11e**	96
6	 **9f**	 **10f**	97	 **11f**	94
7	 **9g**	 **10g**	64	 **11g**	50
8	 **9h**	 **10h**	65	 **11h**	0
9	 **9i**	 **10i**	93	 **11i**	0

[a]Reaction conditions. Suzuki coupling: **5** (1 equiv), **9a–i** (1.5 equiv), $Pd(PPh_3)_4$ (5 mol%), K_3PO_4 (3 equiv), Toluene, 90 °C, 4 h; α-arylation: **10a–i** (1 equiv), XPhos precat. (5 mol%), NaOtBu (1.1 equiv), 1,4-dioxane, 60 °C, 1 h. [b]Isolated yield.

decomposition. Further investigation revealed that the reaction was also dependent on the choice of ligand. For example, **8** was obtained in only 50% yield using a precatalyst where the ligand was SPhos (entry 6) but in 95% yield when the ligand was BrettPhos (entry 7). Decreasing the catalyst loading to 3 mol % resulted in 91% yield of **8** after 3 h (entry 8). However, the reaction was less efficient with 1 mol % catalyst (entry 9). The XPhos precatalyst was also effective at mediating the α-arylation of the 4-chloroindole substrate **7b** giving **8** in 96% yield after 1 h (entry 10). Unfortunately, to date indole **8** has not been obtained via a one-step process utilizing boronic ester **5** and ketone **6**.

With the optimized conditions identified, the scope of the Suzuki coupling/ketone α-arylation sequence was examined. As shown in Table 2, a variety of *ortho*-ketoaryls, -ketoheteroaryls, and -ketocycloalkenes were tolerated in the Suzuki coupling step. This allowed a phenyl, cyclopentenyl, cyclohexenyl, pyridyl, and pyrazinyl containing indole substrate (**10a–i**) to be obtained in 64–97% yields. These substrates were then subjected to the ketone α-arylation conditions with XPhos precatalyst (5 mol %)

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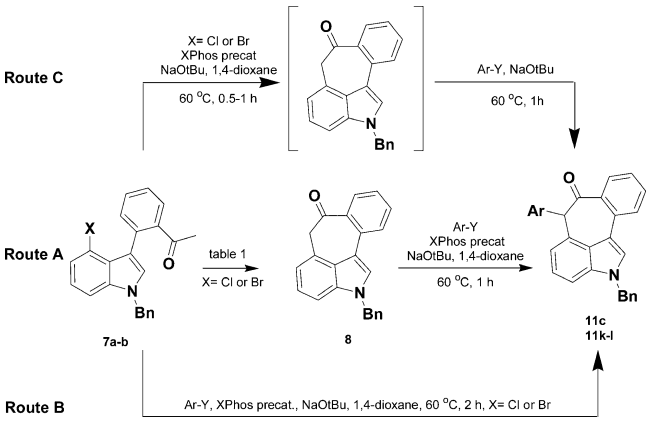
and NaOt-Bu (1.1 equiv), in 1,4-dioxane at 60 °C for 1 h. Gratifyingly, various substituted (i.e., methyl, gem-dimethyl, or phenyl) phenylketones could be efficiently coupled generating tetracyclic indoles **11a−c** in 89%, 99%, and 98% yields, respectively (entries 1−3). However, **10d** did not undergo ketone α-arylation, possibly due to steric hindrance between the methylenedioxy group and the 2-position of the indole (entry 4). Cyclization of both the cyclopentenyl and cyclohexenyl substrates **10e−f** gave **11e−f** in excellent yields (entries 5 and 6). Cyclization of the 3-pyridyl substrate **10g** generated **11g** in a moderate 50% yield (entry 7). However, the 2-pyridyl and pyrazinyl substrates **10h−i** did not give the desired products (entries 7−9), presumably due to chelation of nitrogen to the palladium after metal insertion into the C−Cl bond.[21] A number of parameters were modified, including catalyst, solvent, temperature, and addition of additives (i.e., Cu or Ag), in an attempt to induce α-arylation of **10h−i**, but so far all have failed.

Next, more convergent syntheses using one-pot reactions (with either simultaneous addition or sequential addition of the two aryl halides) for producing aryl substituted tetracyclic indoles (e.g., **11c**) were investigated (Table 3). The efficiencies

Table 3. Double α-Arylation of Ketones



entry	route	X	Ar−Y	product	yield (%)[a]
1	A	Cl or Br	3-bromoanisole	**11j**	94
2	B	Br	3-bromoanisole	**11j**	64
3	B	Cl	3-bromoanisole	**11j**	0
4	C	Br	3-bromoanisole	**11j**	96
5	C	Cl	3-bromoanisole	**11j**	98
6	C	Cl	chlorobenzene	**11c**	88
7	C	Cl	bromobenzene	**11c**	93
8	C	Cl	3-bromopyridine	**11k**	75
9	C	Cl	2-bromopyridine	**11l**	0

[a]Isolated yield.

of these methods were compared to the stepwise process of intramolecular ketone α-arylation of **7a−b** to give **8** (isolated and purified), followed by an intermolecular ketone α-arylation with 3-bromoanisole to generate **11j** in 94% overall yield (entry 1), which used 10 mol % precatalyst over the two steps. In the one-pot process (route B) using the bromine substrate **7a**, the product **11j** was obtained in 64% yield (entry 2). However, no reaction was observed starting with the chloroindole **7b** (entry 3). Finally, sequential ketone α-arylations (route C) of **7a** and **7b** were performed generating **11j** in 96% and 95% yields, respectively (entries 4 and 5). Route C was extended to other aryl halides, such as chlorobenzene, bromobenzene, and 3-bromopyridine, giving **11c** and **11k** in good yields (entries 6−8). However, with 2-bromopyridine the sequential one-pot reaction failed, again probably due to nitrogen chelation by palladium following metal insertion into the C−Cl bond (entry 9).

In summary, monoligated Pd(0) catalysts efficiently mediated intramolecular α-arylation of ketones to generate a variety of tetracyclic indoles in good to excellent yields. Low catalyst loading (5 mol %) and short reaction times (≤1 h) were generally sufficient to perform this process. The methodology was also extended to double α-arylation of ketones by one-pot procedures with either simultaneous or sequential additions of the two aryl halides to yield aryl substituted tetracyclic indoles.

EXPERIMENTAL SECTION

General Information. All reagents and solvents were purchased from commercial sources and used without further purification. All reactions were conducted under an argon atmosphere in flame-dried or oven-dried glassware with magnetic stirring. Purification of products was performed on an automated system using disposable silica gel columns. Analytical thin layer chromatography was performed on 0.25 mm silica gel 60-F plates. Visualization was accomplished with UV light and ninhydrin solution, $KMnO_4$ or anisaldehyde staining followed by heating. ^{1}H NMR spectra were recorded on a 400 or 500 MHz spectrometer and are reported in ppm using solvent as the internal standard ($CDCl_3$ at 7.26 ppm). Data are reported as follows: b = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet; coupling constant(s) in Hz, integration. ^{13}C NMR spectra were recorded on a 100 or 125 MHz spectrometer. Chemical shifts are reported in ppm from tetramethylsilane, with the solvent resonance employed as the internal standard ($CDCl_3$ at 77.0 ppm). High-resolution mass spectra were obtained on MALDI-FT-ICR MS, using 150 mg/mL 2,5-dihydroxybenzoic acid dissolved in MeOH/H_2O (50:50) as the matrix.

Procedure for the Synthesis of Indoles 3a−c. *1-Benzyl-4-bromo-3-iodoindole (**3a**).* To a solution of 4-bromoindole (1.01 g, 5.0 mmol) in dry DMF (8 mL) at 0 °C was added NaH (60% dispersal in mineral oil, 300 mg, 7.5 mmol). The mixture was stirred at 0 °C for 10 min, and then it was allowed to warm to ambient temperature and stirred for 30 min. The solution was cooled to 0 °C, and then benzyl bromide (0.89 mL, 2.30 mmol) was added. The ice bath was removed, and the reaction mixture was warmed to 45 °C and stirred for 1 h. The mixture was cooled to room temperature, concentrated, and then diluted with EtOAc and saturated NH_4Cl. The organic layer was washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated. The residue of 1-benzyl-4-bromoindole was used without further purification.

To a solution at 0 °C of 1-benzyl-4-bromoindole (1.43 g, 5.0 mmol) in dry DMF (10 mL) was added *N*-iodosuccinimide (1.30 g, 5.5 mmol). The reaction was stirred for 30 min and then quenched with saturated $NaHCO_3$, stirred for 10 min, concentrated, diluted with H_2O, and extracted with EtOAc. The organic layers were combined, washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated. Purification by chromatography (SiO_2, 0−5% EtOAc in cyclohexane) gave **3a** (1.9 g, 4.6 mmol, 91% over two steps) as an unstable white solid (stored at 0 °C). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.34−7.26 (m, 6H), 7.11−7.09 (m, 2H), 7.01 (t, J = 8.0 Hz, 1H), 5.28 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 136.3, 135.5, 129.2, 128.3, 127.1, 125.6, 123.5, 110.0, 50.8.

*1-Benzyl-3-bromo-4-chloroindole (**3b**).* Unstable white solid (1.82 g, 5.7 mmol, stored at 0 °C), yield 96%. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.34−7.27 (m, 3H), 7.19 (dd, J = 9.0 and 1.0 Hz, 1H), 7.16 (s, 1H), 7.13−7.05 (m, 4H), 5.26 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 137.4, 136.4, 129.2, 128.3, 127.1, 123.4, 121.9, 109.3, 50.7.

*1-Benzyl-4-chloro-3-iodoindole (**3c**).* Unstable white solid (1.76 mmol, 4.8 mmol, stored at 0 °C), yield 97%.^{1}H NMR (500 MHz, $CDCl_3$): δ 7.34−7.27 (m, 3H), 7.25 (s, 1H), 7.21 (dd, J = 8.0 and 1.0

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Hz, 1H), 7.12−7.05 (m, 4H), 5.27 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 136.4, 135.0, 129.2, 128.3, 127.1, 123.2, 121.9, 109.3, 50.8.

*1-Benzyl-4-chloro-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-indole (**5**).* To a solution of **3b** (1.28 g, 4.0 mmol) in THF (40 mL) at −78 °C was added *t*-BuLi (1.59 M in pentane, 5.53 mL, 8.8 mmol) dropwise over 5 min. The reaction mixture was stirred for 15 min at −78 °C, and then dioxaborolane (1.68 mL, 8.0 mmol) was added. The mixture was stirred at −78 °C for 1 h, quenched with saturated NH_4Cl, and allowed to warm to room temperature. The aqueous layer was extracted with Et_2O. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated. Purification by chromatography (SiO_2, 0−10% EtOAc in cyclohexane) gave **5** (896 mg, 2.44 mmol, 61% yield) as a moderately stable pale yellow solid (stored at 0 °C). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.60 (s, 1H), 7.30−7.24 (m, 3H), 7.16−7.12 (m, 2H), 7.09−7.04 (m, 3H), 5.31 (s, 2H), 1.38 (s, 12H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.0, 136.8, 129.9, 129.0, 128.0, 126.9, 122.8, 127.5, 108.7, 83.6, 50.8, 25.0. HRMS (MALDI-TOF, M + Na) calcd for $C_{21}H_{23}BClNNaO_2$ 389.1439, found 389.1437.

General Procedure for the Preparation of Ketones 9d−h. To a solution of aldehyde (1 equiv) in dry THF (2 mL/1 mmol of starting material) under an argon atmosphere at −78 °C was added dropwise a Grignard reagent (1.1 equiv). After stirring at room temperature for 18 h, the reaction mixture was quenched with saturated NH_4Cl and extracted twice with EtOAc. The organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated. Purification by chromatography (SiO_2, 10−50% EtOAc in cyclohexane) afforded the alcohol as a colorless oil.

To a solution of alcohol (1 equiv) in dry CH_2Cl_2 (3 mL/1 mmol of starting material) at 0 °C under an argon atmosphere was added Dess-Martin periodinane (1.6 equiv). The reaction mixture was stirred at 0 °C for 1 h and then overnight at room temperature. The reaction mixture was concentrated, and the residue was purified by chromatography (SiO_2, 10−25% EtOAc in cyclohexane) to give the corresponding ketone.

*1-(4-Bromo-benzo[1,3]dioxol-5-yl)-propan-1-one (**9d**).* Colorless oil (214 mg, 0.83 mmol), yield 56%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.05 (d, *J* = 8.0 Hz, 1H), 6.71 (d, *J* = 8.0 Hz, 1H), 6.03 (s, 2H), 2.89 (q, *J* = 7.2 Hz, 2H), 1.20 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 201.6, 147.6, 146.0, 126.4, 124.2, 110.6, 109.7, 102.4, 37.4, 7.8. HRMS (EI, M^+) calcd for $C_{10}H_9BrO_3$ 255.9735, found 255.9738.

*1-(2-Bromo-cyclopent-1-enyl)-propan-1-one (**9e**).* Colorless oil (180 mg, 0.87 mmol), yield 52%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.88−2.81 (m, 4H), 2.68−2.63 (m, 2H), 1.97−1.89 (m, 2H), 1.11 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 199.6, 140.2, 129.1, 44.1, 35.5, 33.7, 21.6, 7.9. HRMS (EI, M^+) calcd for $C_8H_{11}BrO$ 201.9993, found 201.9990.

*1-(2-Bromo-cyclohex-1-enyl)-propan-1-one (**9f**).* Colorless oil (147 mg, 0.68 mmol), yield 77%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.70 (q, *J* = 7.2 Hz, 2H), 2.54−2.50 (m, 2H), 2.26−2.24 (m, 2H), 1.75−1.68 (m, 4H), 1.11 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 207.8, 139.8, 119.7, 36.2, 34.9, 29.0, 24.3, 21.5, 7.8. HRMS (EI, M^+) calcd for $C_9H_{13}BrO$ 216.0150, found 216.0145.

*1-(3-Bromopyridin-4-yl)propan-1-one (**9g**).* Colorless oil (65 mg, 0.30 mmol), yield 45%. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.79 (s, 1H), 8.60 (d, *J* = 5.0 Hz, 1H), 7.23 (d, *J* = 5.0 Hz, 1H), 2.91 (q, *J* = 7.0 Hz, 2H), 1.23 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 203.3, 153.1, 148.8, 148.7, 121.8, 116.3, 36.1, 7.9. HRMS (EI, M^+) calcd for C_8H_8BrNO 212.9789, found 212.9788.

*1-(2-Bromopyridin-3-yl)propan-1-one (**9h**).* Colorless oil (237 mg, 1.11 mmol), yield 56%. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.44 (dd, *J* = 4.5 and 2.0 Hz, 1H), 7.66 (dd, *J* = 7.5 and 2.0 Hz, 1H), 7.35 (dd, *J* = 7.5 and 4.5 Hz, 1H), 2.98 (q, *J* = 7.0 Hz, 2H), 1.24 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 203.6, 151.3, 139.2, 137.9, 136.9, 122.9, 36.3, 8.3.

*1-(3-Chloropyrazin-2-yl)propan-1-one (**9i**).* A Schlenk flask was charged with 2,3-dichloropyrazine (596 mg, 4.0 mmol), Pd_2dba_3 (83 mg, 0.08 mmol), PPh_3 (84 mg, 0.32 mmol), and dry toluene (8 mL). The reaction vessel was flushed with argon for 5 min, and then (1-ethoxypropenyl)tributyltin (1.5 g, 4.0 mmol) was added. The reaction was heated at 110 °C for 2 h. After cooling, the reaction mixture was quenched with saturated NH_4Cl and extracted with EtOAc. The organic layers were combined, washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated. Purification by chromatography (SiO_2, 0−5% EtOAc in cyclohexane) gave 2-chloro-3-(1-ethoxyprop-1-enyl)pyrazine (339 mg, 1.71 mmol, 43%) as a yellow oil.

To a solution of 2-chloro-3-(1-ethoxyprop-1-enyl)pyrazine (330 mg, 1.66 mmol) in DME (2 mL) was added 2 N HCl (2 mL). The reaction mixture was heated at 60 °C for 2 h and then allowed to cool to room temperature, neutralized with saturated $NaHCO_3$, and extracted with EtOAc. The organic layers were combined, washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated. Purification by chromatography (SiO_2, 0−5% EtOAc in cyclohexane) gave **9i** (240 mg, 1.41 mmol, 85%) as a pale yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.54 (d, *J* = 2.4 Hz, 1H), 8.50 (d, *J* = 2.4 Hz, 1H), 3.12 (q, *J* = 7.2 Hz, 2H), 1.22 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 200.8, 148.5, 146.6, 145.7, 141.6, 33.9, 7.8.

*1-(2-(1-Benzyl-4-bromoindol-3-yl)phenyl)ethanone (**7a**).* A Schlenk flask was charged with **3a** (1.0 g, 2.43 mmol), **4** (609 mg, 3.64 mmol), and $PdCl_2$dppf (178 mg, 0.24 mmol). The flask was evacuated and backfilled with argon (3 times), and then DME (20 mL) followed by a solution of Na_2CO_3 (514 mg, 4.86 mmol) in water (4 mL) was added. The reaction mixture was sparged with argon and then heated to 80 °C for 6 h. After cooling, the reaction mixture was dissolved with water and extracted with EtOAc. The organic layers were combined, washed with brine (20 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated. Purification by chromatography (SiO_2, 5−20% EtOAc in cyclohexane) gave **7a** (510 mg, 1.26 mmol, 52%) as a yellowish solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.63 (d, *J* = 7.0 Hz, 1H), 7.47−7.40 (m, 3H), 7.34−7.27 (m, 5H), 7.14−7.11 (m, 2H), 7.06 (t, *J* = 8.0 Hz, 1H), 7.05 (s, 1H), 5.34 (s, 2H), 2.07 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 204.1, 142.3, 137.5, 136.8, 134.2, 133.3, 129.9, 129.6, 129.2, 1127.4, 127.0, 125.7, 124.8, 123.4, 116.8, 114.8, 109.7, 50.7, 30.3. HRMS (MALDI-TOF, M + H) calcd for $C_{23}H_{19}BrNO$ 404.0644, found 404.0642.

*1-(2-(1-Benzyl-4-chloroindol-3-yl)phenyl)ethanone (**7b**).* A Schlenk flask was charged with **3b** (1.84 g, 5.74 mmol), **4** (1.44 g, 8.61 mmol), and $Pd(PPh_3)_4$ (332 mg, 0.29 mmol). The flask was evacuated and backfilled with argon (3 times), and then DME (40 mL) followed by a solution of Na_2CO_3 (445 mg, 4.20 mmol) in water (4 mL) was added. The reaction mixture was sparged with argon and then heated to 80 °C for 18 h. After cooling, the reaction was dissolved with water and extracted with EtOAc. The organic layers were combined, washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated. Purification by chromatography (SiO_2, 5−20% EtOAc in cyclohexane) gave **7b** (1.46 g, 4.05 mmol, 71%) as a yellowish solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.63 (d, *J* = 7.5 Hz, 1H), 7.49−7.39 (m, 3H), 7.34−7.32 (m, 4H), 7.15−7.10 (m, 4H), 7.03 (s, 1H), 5.34 (s, 2H), 2.08 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 204.1, 142.0, 137.9, 136.8, 133.7, 133.6, 130.0, 129.4, 129.2, 128.2, 127.4, 127.3, 127.0, 126.8, 124.3, 123.1, 121.3, 116.1, 109.1, 50.7, 30.2. HRMS (MALDI-TOF, M + H) calcd for $C_{23}H_{19}ClNO$ 360.1150, found 360.1153.

General Procedure for the Synthesis of Indoles 10a−i. A Schlenk flask was charged with **5** (1 equiv), the corresponding aryl, vinyl or heteroaryl halide **6** or **9a−i** (1.5 equiv), anhydrous K_3PO_4 (3 equiv), and $Pd(PPh_3)_4$ (5 mol %). The flask was evacuated and backfilled with argon (3 times), and then dry toluene (1 mL/0.1 mmol of starting material) was added. The reaction mixture was sparged with argon and then heated at 90 °C for 4−24 h. After cooling, the reaction mixture was diluted with EtOAc and then filtered through a pad of Celite. The solvent was removed in vacuo. Purification by chromatography (SiO_2, 5−20% EtOAc in cyclohexane) gave **10a−i**.

*1-(2-(1-Benzyl-4-chloroindol-3-yl)phenyl)propan-1-one (**10a**).* Pale yellow solid (64 mg, 0.17 mmol), yield 86%. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.57−7.48 (m, 2H), 7.45 (ddd, *J* = 8.0, 7.5, and 1.5 Hz, 1H), 7.39 (ddd, *J* = 8.0, 7.5, and 1.5 Hz, 1H), 7.33−7.27 (m, 3H), 7.25 (dd, *J* = 7.0 and 2.0 Hz, 1H), 7.15−7.10 (m, 4H), 7.01 (s, 1H), 5.32 (s, 2H), 2.39 (q, *J* = 7.5 Hz, 1H), 0.84 (2, *J* = 7.5 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 208.2, 142.3, 137.9, 136.8, 133.8, 132.8,

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129.6, 129.4, 129.2, 128.2, 127.2, 127.0, 126.9, 124.2, 123.1, 121.4, 115.8, 109.1, 50.7, 35.8, 8.7. HRMS (MALDI-TOF, M + H) calcd for $C_{24}H_{21}ClNO$ 374.1306, found 374.1307.

*1-(2-(1-Benzyl-4-chloroindol-3-yl)phenyl)-2-methylpropan-1-one (**10b**).* Pale yellow solid (40 mg, 0.10 mmol), yield 82%. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.51 (d, J = 7.5 Hz, 1H), 7.46−7.35 (m, 3H), 7.32−7.24 (m, 4H), 7.16 (m, 4H), 6.98 (s, 1H), 5.30 (s, 2H), 2.69−2.60 (m, 1H), 0.94−0.67 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 212.7, 142.2, 137.9, 136.7, 133.8, 132.2, 129.9, 129.1, 128.9, 128.2, 127.1, 126.9, 124.2, 123.2, 121.4, 115.4, 109.1, 50.7, 39.9, 19.7. HRMS (MALDI-TOF, M + H) calcd for $C_{25}H_{23}ClNO$ 388.1463, found 388.1464.

*1-(2-(1-Benzyl-4-chloroindol-3-yl)phenyl)-2-phenylethanone (**10c**).* Pale yellow solid (43 mg, 0.10 mmol), yield 79%. ^{1}H NMR (500 MHz, $CDCl_3$): δ 0.56−7.33 (m, 4H), 7.31−7.24 (m, 4H), 7.19−7.07 (m, 7H), 6.91 (s, 1H), 6.83−6.77 (m, 2H), 5.29−5.16 (m, 2H), 3.75−3.55 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 204.9, 142.1, 138.0, 136.6, 134.8, 133.9, 132.9, 130.1, 129.6, 129.2, 128.4, 128.2, 127.3, 127.2, 127.1, 126.9, 126.7, 124.1, 123.3, 121.6, 115.4, 109.2, 50.6, 49.3. HRMS (MALDI-TOF, M + H) calcd for $C_{29}H_{23}ClNO$ 436.1463, found 436.1457.

*1-[4-(1-Benzyl-4-chloroindol-3-yl)-benzo[1,3]dioxol-5-yl]-propan-1-one (**10d**).* Pale yellow solid (55 mg, 0.13 mmol), yield 88%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33−7.25 (m, 3H), 7.22−7.17 (m, 1H), 7.12−7.06 (m, 4H), 7.01 (s, 1H), 6.89 (dd, J = 12.4 and 8.0 Hz, 2H), 6.06 (s, 2H), 5.30 (s, 2H), 2.59−2.43 (m, 2H), 0.88 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 203.8, 147.2, 145.0, 137.6, 136.9, 129.5, 129.1, 128.1, 126.9, 126.7, 126.3, 124.7, 12.6, 122.8, 121.1, 115.0, 109.0, 101.8, 50.6, 37.1, 8.1. HRMS (MALDI-TOF, M + H) calcd for $C_{25}H_{21}ClNO_3$ 418.1204, found 418.1197.

*1-[2-(1-Benzyl-4-chloroindol-3-yl)-cyclopent-1-enyl]-propan-1-one (**10e**).* White solid (51 mg, 0.14 mmol), yield 94%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33−7.27 (m, 3H), 7.24−7.20 (m, 1H), 7.13−7.08 (m, 4H), 6.96 (s, 1H), 5.31 (s, 2H), 2.94−2.86 (m, 2H), 2.82−2.76 (m, 2H). 2.20 (q, J = 7.2 Hz, 2H), 2.00−1.93 (m, 2H), 0.82 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 202.7, 147.0, 142.1, 138.0, 1136.8, 129.1, 128.2, 127.0, 126.9, 126.6, 124.4, 123.1, 121.1, 113.1, 109.0, 50.5, 44.5, 34.5 (2C), 22.3, 8.4. HRMS (MALDI-TOF, M + H) calcd for $C_{23}H_{23}ClNO$ 364.1463, found 364.1464.

*1-[2-(1-Benzyl-4-chloroindol-3-yl)-cyclohex-1-enyl]-propan-1-one (**10f**).* White solid (56 mg, 0.15 mmol), yield 97%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31−7.25 (m, 3H), 7.17−7.03 (m, 5H), 6.85 (s, 1H), 5.22 (s, 2H), 2.89−2.51 (m, 2H), 2.20−2.02 (m, 4H), 1.90−1.56 (m, 2H), 0.70 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 210.8, 139.6, 136.8, 135.1, 129.1, 128.3, 128.1, 126.9, 126.5, 124.5, 123.1, 120.9, 117.3, 108.9, 50.5, 35.5, 34.7, 26.7, 22.8, 22.4, 8.5. HRMS (MALDI-TOF, M + H) calcd for $C_{24}H_{25}ClNO$ 378.1619, found 378.1613.

*1-(3-(1-Benzyl-4-chloroindol-3-yl)pyridin-4-yl)propan-1-one (**10g**).* Pale yellow solid (30 mg, 0.08 mmol), yield 64%. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.78 (s, 1H), 8.65 (d, J = 5.5 Hz, 1H), 7.34−7.26 (m, 5H), 7.18−7.10 (m 4H), 7.08 (s, 1H), 5.35 (s, 2H), 2.43 (q, J = 7.5 Hz, 2H), 0.87 (t, J = 7.5 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 206.4, 154.1, 148.6, 147.9, 137.9, 136.5, 130.2, 129.2, 128.3, 127.3, 127.0, 126.7, 124.3, 123.5, 121.6, 120.0, 111.6, 109.3, 50.8, 35.7, 8.1. HRMS (MALDI-TOF, M + H) calcd for $C_{23}H_{20}ClN_2O$ 375.1259, found 375.1268.

*1-(2-(1-Benzyl-4-chloroindol-3-yl)pyridin-3-yl)propan-1-one (**10h**).* Pale yellow solid (196 mg, 0.52 mmol), yield 65%. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.77 (dd, J = 5.0 and 2.0 Hz, 1H), 7.87 (dd, J = 7.5 and 2.0 Hz, 1H), 7.35−7.23 (m, 5H), 7.18 (s, 1H), 7.16−7.11 (m, 4H), 5.34 (s, 2H), 2.45 (q, J = 7.5 Hz, 2H), 0.87 (t, J = 7.5 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 206.2, 151.8, 150.5, 138.0, 137.6, 136.5, 135.3, 130.3, 129.2, 128.2, 127.0, 126.7, 124.5, 123.5, 121.8, 121.8, 116.1, 109.1, 50.8, 35.5, 8.6. HRMS (MALDI-TOF, M + H) calcd for $C_{23}H_{20}ClN_2O$ 375.1259, found 375.1259.

*1-(3-(1-Benzyl-4-chloroindol-3-yl)pyrazin-2-yl)propan-1-one (**10i**).* Pale yellow solid (53 mg, 0.14 mmol), yield 93%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.68 (d, J = 2.4 Hz, 1H), 8.54 (d, J = 2.4 Hz, 1H), 7.46 (s, 1H), 7.35−7.22 (m, 4H), 7.21 (m, 2H), 7.13−7.06 (m, 2H), 5.38 (s, 2H), 3.17 (q, J = 7.2 Hz, 2H), 1.09 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 202.8, 149.8, 148.0, 144.6, 140.9, 138.0, 136.4, 131.1, 129.2, 128.2, 127.2, 126.2, 124.0, 123.2, 121.7, 114.2, 109.5, 51.0, 33.3, 8.1. HRMS (MALDI-TOF, M + H) calcd for $C_{22}H_{19}ClN_3O$ 376.1211, found 376.1215.

General Procedure for the Intramolecular α-Arylations. A reaction tube was charged with the corresponding indole (1 equiv), Xphos precat. (5 mol %), and NaOtBu (1.1 equiv). The tube was evacuated and backfilled with argon (3 times), and then dry 1,4-dioxane (1 mL/0.1 mmol of starting material) was added. The reaction mixture was sparged with argon and then heated to 60 °C for 0.5−1 h. After cooling, the reaction was quenched with saturated NH_4Cl and extracted with EtOAc. The organic layers were combined, washed with brine, dried over anhudrous Na_2SO_4, filtered, and concentrated. Purification by chromatography (SiO_2, 5−25% EtOAc in cyclohexane) gave the products.

*2-Benzyl-2,6-dihydro-2-aza-dibenzo[cd,h]azulen-7-one (**8**).* White solid (345 mg, 1.07 mmol), yield 96%. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.81 (d, J = 7.5 Hz, 1H), 7.63 (dd, J = 7.5 and 1.5 Hz, 1H), 7.55 (s, 1H), 7.43 (ddd, J = 8.0, 7.5, and 1.5 Hz, 1H), 7.35−7.27 (m, 3H), 7.25−7.15 (m, 5H), 7.00−6.96 (m, 1H), 5.37 (s, 2H), 4.32 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 198.9, 139.4, 137.1, 136.9, 132.6, 131.5, 129.5, 129.2, 128.2, 127.3, 127.1, 126.9, 125.4, 124.6, 124.4, 123.7, 120.2, 115.8, 109.0, 51.3, 50.7. HRMS (MALDI-TOF, M + Na) calcd for $C_{23}H_{17}NNaO$ 346.1202, found 346.1209.

*2-Benzyl-6-methyl-2,6-dihydro-2-aza-dibenzo[cd,h]azulen-7-one (**11a**).* White solid (56 mg, 0.17 mmol), yield 89%. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.81 (d, 1H, J = 8.0 Hz), 7.61 (dd, 1H, J = 8.0 and 1.5 Hz), 7.59 (s, 1H), 7.43 (ddd, 1H, J = 8.0, 8.0, and 1.5 Hz), 7.35−7.27 (m, 3H), 7.25−7.21 (m, 3H), 7.19−7.16 (m, 2H), 7.07−7.03 (m, 1H), 5.37 (s, 2H), 4.29 (q, 1H, J = 7.0 Hz), 1.41 (d, 3H, J = 7.0 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 203.5, 137.5, 137.4, 136.8, 133.2, 132.2, 131.2, 130.0, 129.2, 128.2, 127.3, 127.2, 125.6, 124.1, 123.7, 123.2, 119.0, 115.4, 109.0, 54.8, 50.7, 20.3. HRMS (MALDI-TOF, M + Na) calcd for $C_{24}H_{19}NNaO$ 360.1359, found 360.1363.

*2-Benzyl-6,6-dimethyl-2,6-dihydro-2-aza-dibenzo[cd,h]azulen-7-one (**11b**).* White solid (18 mg, 0.05 mmol), yield 99%. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.78 (d, 1H, J = 8.0 Hz), 7.60 (s, 1H), 7.51 (dd, 1H, J = 7.5 and 1.5 Hz), 7.41 (ddd, 1H, J = 8.0, 7.5, and 1.5 Hz), 7.35−7.28 (m, 3H), 7.26−7.20 (m, 4H), 7.18−7.14 (m, 2H), 5.38 (s, 2H), 1.57 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 206.1, 138.4, 137.4, 137.2, 136.8, 131.7, 130.6, 129.3, 129.2, 128.2, 127.1, 127.0, 125.6, 123.4, 123.3, 115.9, 115.7, 109.2, 51.8, 50.7, 27.0. HRMS (MALDI-TOF, M + Na) calcd for $C_{25}H_{21}NNaO$ 374.1515, found 374.1516.

*2-Benzyl-6-phenyl-2,6-dihydro-2-aza-dibenzo[cd,h]azulen-7-one (**11c**).* Pale yellow solid (18 mg, 0.04 mmol), yield 98%. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.76 (d, 1H, J = 8.0 Hz), 7.59 (s, 1H), 7.45 (dd, 1H, J = 8.0 and 1.5 Hz), 7.37−7.27 (m, 6H), 7.22−7.19 (m, 2H), 7.11−7.03 (m, 5H), 6.96−6.92 (m, 2H), 5.58 (s, 1H), 5.42 (AB, 2H, J=16.0 and 8.0 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 200.9, 139.5, 137.5, 137.4, 136.8, 131.4, 131.1, 130.8, 129.4, 129.2, 128.6, 128.3, 128.0, 127.5, 127.2, 127.1, 125.5, 124.7, 124.3, 124.0, 123.8, 121.6, 115.8, 109.5, 67.4, 50.8. HRMS (MALDI-TOF, M + Na) calcd for $C_{29}H_{21}NNaO$ 422.1515, found 422.1515.

*2-Benzyl-6-methyl-2,8,9,10-tetrahydro-6H-2-aza-benzo[cd]-cyclopenta[h]azulen-7-one (**11e**).* White solid (17 mg, 0.05 mmol), yield 96%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35−7.28 (m, 3H), 7.25−7.15 (m, 5H), 7.02−6.99 (m, 1H), 5. 31 (s, 2H), 4.09 (q, J = 7.2 Hz, 1H), 3.06−2.88 (m, 3H), 2.77−2.70 (m, 1H), 2.08−1.88 (m, 2H), 1.40 (d, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 198.5, 144.6, 137.4, 136.7, 134.4, 134.0, 129.2, 128.8, 128.2, 127.2, 124.6, 123.8, 120.8, 114.0, 108.7, 56.2, 50.7, 36.0, 34.8, 23.9, 22.0. HRMS (MALDI-TOF, M + H) calcd for $C_{23}H_{22}NO$ 328.1696, found 328.1699.

*2-Benzyl-6-methyl-2,6,8,9,10,11-hexahydro-2-aza-dibenzo[cd,h]-azulen-7-one (**11f**).* White solid (16 mg, 0.05 mmol), yield 94%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34−7.28 (m, 4H), 7.22−7.13 (m, 4H), 6.99−6.97 (m, 1H), 5.35−5.24 (m, 2H), 4.10 (q, J = 7.2 Hz, 1H), 2.85−2.77 (m, 1H), 2.71−2.66 (m, 2H), 2.32−2.24 (m, 1H), 1.82−1.68 (m, 4H), 1.42 (d, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 203.7, 137.1, 137.0, 134.3, 133.7, 131.2, 129.1, 128.1, 127.3, 127.1,

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123.9, 123.4, 119.0, 117.5, 108.5, 55.7, 50.6, 28.0, 27.7, 22.8, 22.6, 20.8. HRMS (MALDI-TOF, M + H) calcd for $C_{24}H_{24}NO$ 342.1852, found 342.1859.

*2-Benzyl-6-methyl-2,6-dihydro-2,10-diaza-dibenzo[cd,h]azulen-7-one (**11g**).* Yellow solid (18 mg, 0.05 mmol), yield 50%. ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.16 (s, 1H), 8.47 (d, 1H, J = 5.0 Hz), 7.71 (s, 1H), 7.44 (d, 1H, J = 5.0 Hz), 7.37−7.30 (m, 3H), 7.28−7.27 (m, 2H), 7.21−7.18 (m, 2H), 7.09−7.07 (m, 1H), 5.40 (s, 2H), 4.29 (q, 1H, J = 7.0 Hz), 1.40 (d, 3H, J = 7.0 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 201.5, 146.5, 146.4, 142.2, 137.4, 136.4, 132.5, 129.3, 128.4, 127.2, 127.1, 126.9, 124.2, 123.4, 122.6, 119.6, 112.0, 109.5, 54.6, 50.9, 20.0. HRMS (MALDI-TOF, M + H) calcd for $C_{23}H_{19}N_2O$ 339.1492, found 339.1487.

*2-Benzyl-6-(3-methoxyphenyl)-2,6-dihydro-2-aza-dibenzo[cd,h]-azulen-7-one (**11j**).* *Route A.* A reaction tube was charged with **8** (33 mg, 0.1 mmol), Xphos precat. (3.7 mg, 0.005 mmol), 3-bromoanisole (14 μL, 0.2 mmol), and NaOt-Bu (11 mg, 0.11 mmol). The tube was evacuated and backfilled with argon (3 times), and then dry 1,4-dioxane (1 mL) was added. The reaction mixture was sparged with argon and then heated to 60 °C for 1 h.

Route B. A reaction tube was charged with **7a** (40 mg, 0.1 mmol), Xphos precat. (3.7 mg, 0.005 mmol), 3-bromoanisole (14 μL, 0.2 mmol), and NaOt-Bu (21.4 mg, 0.22 mmol). The tube was evacuated and backfilled with argon (3 times), and then dry 1,4-dioxane (1 mL) was added. The reaction mixture was sparged with argon and then heated to 60 °C for 2 h.

Route C. A reaction tube was charged with **7b** (36 mg, 0.1 mmol), Xphos precat. (3.7 mg, 0.005 mmol). and NaOt-Bu (21.4 mg, 0.12 mmol). The tube was evacuated and backfilled with argon (3 times) and then dry 1,4-dioxane (1 mL). The reaction mixture was sparged with argon and then heated to 60 °C for 1 h. Then, 3-bromoanisole (14 μL, 0.2 mmol) was added, and the mixture was heated for an additional 1 h.

After cooling, the reaction mixtures were quenched with saturated NH_4Cl and extracted with EtOAc. The organic layers were combined, washed with brine, dried over anhydrous Na_2SO_4, filtered, and evaporated. Purification by chromatography (SiO_2, 5−25% EtOAc in cyclohexane) gave **11j** (94%, 64% and 98% for routes A, B, and C, respectively) as a yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.66 (d, J = 8.0 Hz, 1H), 7.59 (s, 1H), 7.46 (dd, J = 8.0 and 1.5 Hz, 1H), 7.37−7.26 (m, 6H), 7.21−7.17 (m, 2H), 7.09−7.05 (m, 2H), 7.00 (t, J = 8.0 Hz, 1H), 6.58 (dd, J = 8.0 and 2.5 Hz, 1H), 6.54 (d, J = 8.0 Hz, 1H), 6.49 (s, 1H), 5.55 (s, 1H), 5.41 (dd, J = 15.5 and 7.5 Hz, 2H), 3.59 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 200.7, 159.7, 141.1, 137.6, 137.3, 136.8, 131.5, 131.1, 130.8, 129.5, 129.3, 129.2, 128.2, 127.5, 127.2, 125.5, 124.7, 124.0, 123.8, 121.7, 120.5, 115.7, 113.8, 112.5, 109.5, 67.4, 55.2, 50.7. HRMS (MALDI-TOF, M + Na) calcd for $C_{30}H_{23}NNaO_2$ 452.1621, found 452.1623.

*2-Benzyl-6-pyridin-3-yl-2,6-dihydro-2-aza-dibenzo[cd,h]azulen-7-one (**11k**).* ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.31 (dd, J = 4.8 and 1.6 Hz, 1H), 8.25 (d, J = 2.0 Hz, 1H); 7.68 (d, J = 8.0 Hz, 1H), 7.61 (s, 1H), 7.46 (dd, J = 8.0 and 1.2 Hz, 1H), 7.38−7.26 (m, 7H), 7.22−7.18 (m, 2H), 7.09 (ddd, J = 8.0, 8.0, and 1.2 Hz, 1H), 7.05−7.01 (m, 2H), 5.59 (s, 1H), 5.46−5.38 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 199.6, 149.6, 148.5, 137.5, 137.1, 136.6, 135.7, 135.0, 131.5, 130.6, 129.3, 128.3, 127.8, 127.2, 125.7, 124.4, 124.2, 123.9, 123.5, 121.3, 115.5, 109.9, 64.7, 50.8. HRMS (MALDI-TOF, M + H) calcd for $C_{28}H_{21}N_2O$ 401.1648, found 401.1644.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Supporting Information, including NMR spectra of the compounds, is provided. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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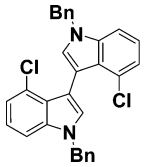
(14) Indoles **3a−c** were unstable at room temperature, even under an inert atmosphere, and therefore were stored at 0 °C for short periods of time.

(15) This reaction required anhydrous conditions to avoid bis-indole formation due to the poor stability of **5** under usual aqueous Suzuki−Miyaura conditions.



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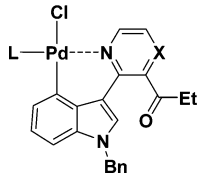
(21) A plausible intermediate formed during attempted intramolecular α-arylations of **10h−i**:



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