Access to [4,3,1]-Bridged Carbocycles via Rhodium(III)-Catalyzed C−H Activation of 2-Arylindoles and Annulation with Quinone Monoacetals

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ABSTRACT: Reported herein is the Rh(III)-catalyzed annulation of N-unprotected 2-arylindoles with quinone monoacetals for the straightforward synthesis of [4,3,1]-bridged carbocycles with exclusive C(3) selectivity. Mechanistic studies, particularly deuterium-labeling experiments, suggest that the coupling likely proceeds via two-fold C−H activation with two-fold migratory insertion into the enone moieties.

- Formal [4+5] annulation
- Exclusive C(3) selectivity
- [4,3,1]-Bridged carbocycle synthesis
- Redox neutral & Atom/Step-economic
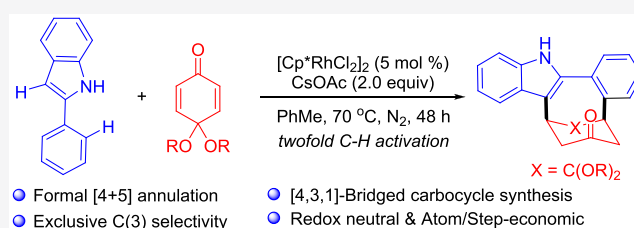
Catalytic C−H functionalization of arenes represents a powerful strategy for construction of value-added organics in a highly step-economic fashion.[1] Among the various transition metals, Cp*Rh(III) complexes[2] play an important role in the synthesis of heterocycles[2,3] as well as carbocycles[4−9] owing to the high efficiency, selectivity, atom/step-economy, and functional group compatibility. Nevertheless, Rh(III)-catalyzed C−H activation−annulation reactions are largely limited to heterocycle synthesis, and access to carbocycles is relatively underexplored. Previously, [3 + 2],[4] [4 + 1],[5] [2 + 2 + 1],[6] [4 + 2],[7] [2 + 2 + 2],[8] and [3 + 3][9] annulations have been developed for the efficient synthesis of five-[4−6] and six-membered[7−9] carbocycles. However, Rh(III)-catalyzed C−H activation has been rarely employed in the synthesis of medium-sized carbocycles.[10] In 2019, we disclosed Mn(I)-catalyzed coupling of 3-alkenyl/allylindoles with propargylic carbonates for the synthesis of fused eight- and four-membered carbocycles,[10a] which occurred via C−H allenylation in tandem with pericyclic reactions (Scheme 1a). During the preparation of this paper, the Reddy group[10b] developed Rh(III)-catalyzed bicyclization of 2-arylimidazo[1,2-a]pyridine with cyclohexenones for the synthesis of [4,3,1]-bridged imidazopyridines (Scheme 1b). Despite the progress, straightforward and atom-economic construction of medium-sized carbocycles from readily available starting materials remains in great demand.

The NH group in unprotected indoles has been recently employed as a nucleophilic directing group in Cp*Rh(III)-catalyzed C−H activation−annulation reactions, which allowed direct access to structurally diverse fused indoles.[11−15] In particular, [4 + 2][11−14] and [4 + 1][13d,15] annulations of 2-arylindoles with diverse unsaturated molecules such as carbene precursors,[11] alkynes,[12] alkenes,[13] and ketenes[14] have been extensively explored, in which 2-arylindoles served as a four-atom synthon with participation of the indole NH or the C(3)−H. To the best of our knowledge, NH indoles have not been applied for in synthesis of medium-sized rings. In 2017, Xu and co-workers[16] documented a formal two-fold Michael addition of benzamides to quinone monoacetal for synthesis of [4,3,1]-heterocycles. Inspired by the high reactivity of 2-arylindoles and the unique reactivity of quinone monoacetal, we reasoned that a formal [4 + 5] annulation reaction may occur between a 2-arylindoles and quinone monoacetals. Despite the design, the following challenges need to be addressed. (1) The reaction may stop at the C−H alkylation stage[17] or proceed with subsequent aromatization, as has been observed in our previous study.[18] (2) Both the C(3) and NH of indoles may participate in formal Michael addition, leading to carbo/heterocyclic products.[12−15] This issue is likely addressable if the C(3)−H is activated via C−Rh formation. We now report Rh(III)-catalyzed synthesis of [4,3,1]-carbocycles[19] via a dual C−H activation process (Scheme 1c).

Initially, the reaction of 2-phenylindole **1a** and quinone monoacetal **2a** was explored to determine the reaction parameters (Table 1). A coupling did occur with [Cp*RhCl₂]₂ (4.0 mol %) as a catalyst in the presence of a stoichiometric amount of CsOAc (2.0 equiv) at 80 °C in PhCF₃, affording the desired [4,3,1]carbocycle **3aa** in 69% NMR yield (entry 1). Evaluation of metal catalysts indicated that [Cp*RhCl₂]₂ was optimal (Table 1, entries 1−3), whereas [Cp*IrCl₂]₂ and

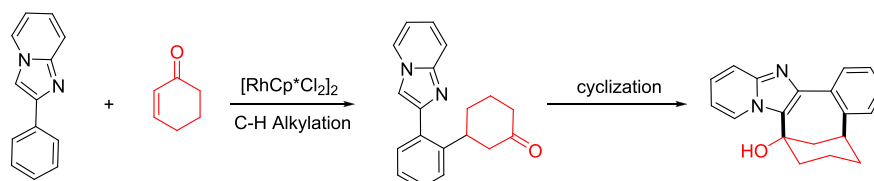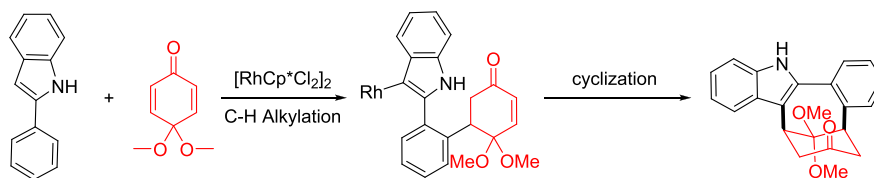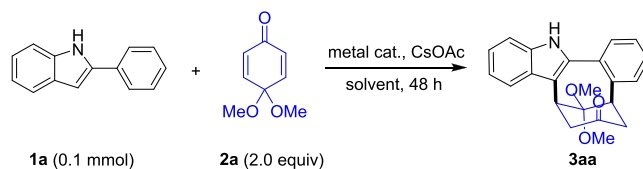**Scheme 1. Synthesis of Medium-Sized Carbocycles via C−H Activation**

a) Mn(I) Catalyzed C-H Activation/Pericyclic Reactions
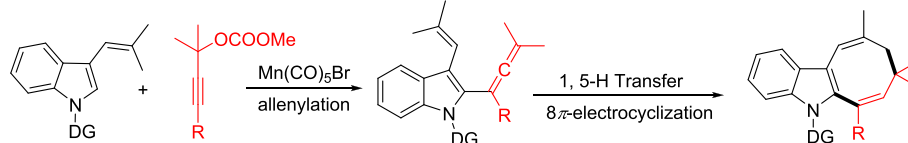
b) Rh(III)-catalyzed C-H Activation/ Friedel-Crafts Cyclization

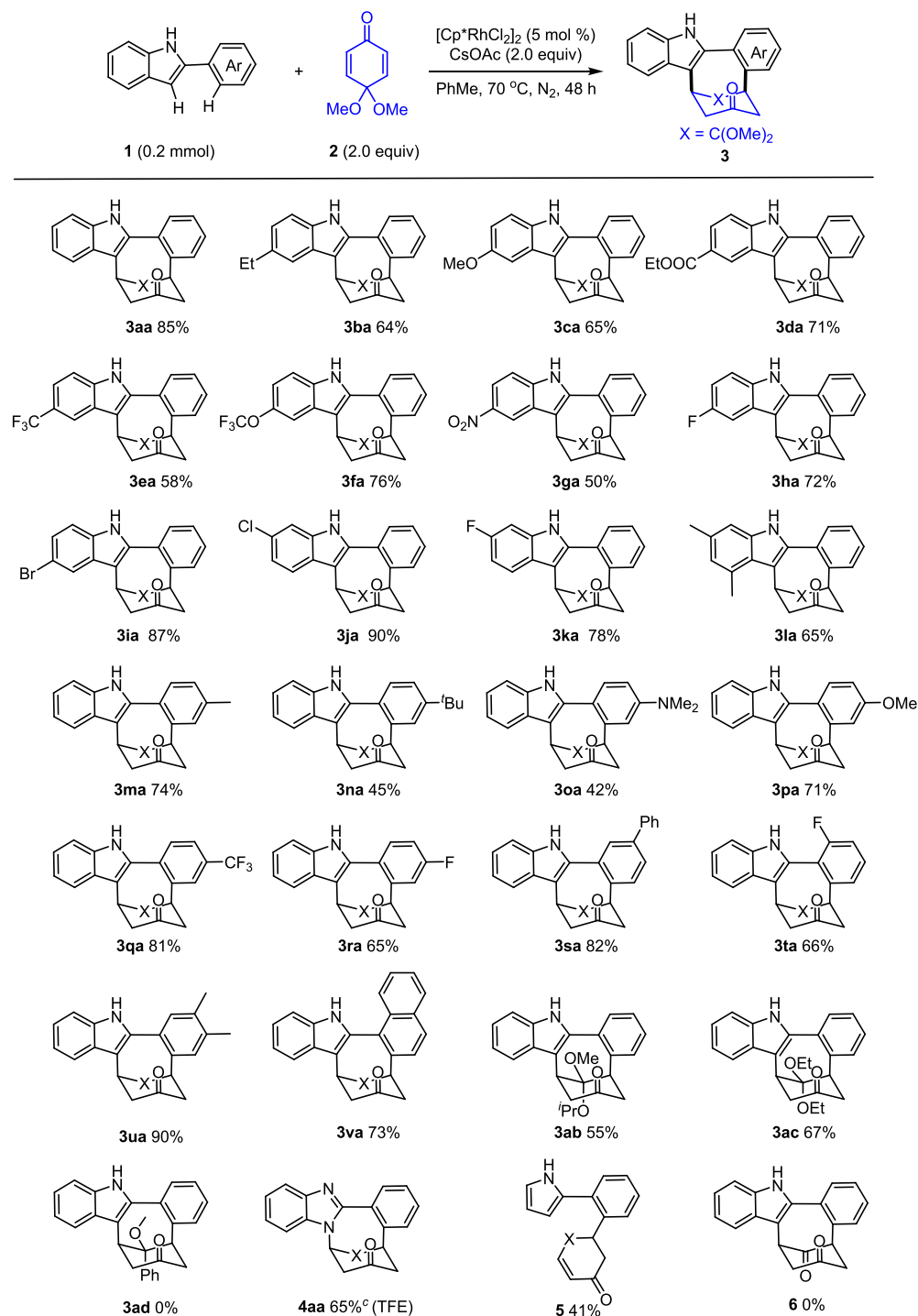c) This work: Rh(III)-catalyzed Twofold C-H Activation with Twofold Migratory Insertion

Table 1. Optimization Studies for the Synthesis of a [4,3,1]Carbocycle[a]

entry	catalyst (mol %)	base (equiv)	solvent	T (°C)	yield (%)[b]
1	[Cp*RhCl$_2$]$_2$ (4)	CsOAc (2.0)	PhCF$_3$	80	69
2	Cp*(CO)CoI$_2$ (8)	CsOAc (2.0)	PhCF$_3$	80	0
3	[Cp*IrCl$_2$]$_2$ (4)	CsOAc (2.0)	PhCF$_3$	80	15
4	[Cp*RhCl$_2$]$_2$ (4)	CsOAc (2.0)	PhCl	80	74
5	[Cp*RhCl$_2$]$_2$ (4)	CsOAc (2.0)	DCE	80	18
6	[Cp*RhCl$_2$]$_2$ (4)	CsOAc (2.0)	MeOH	80	<5
7	[Cp*RhCl$_2$]$_2$ (4)	CsOAc (2.0)	CH$_3$CN	80	39
8	[Cp*RhCl$_2$]$_2$ (4)	CsOAc (2.0)	THF	80	43
9	[Cp*RhCl$_2$]$_2$ (4)	CsOAc (2.0)	TFE	80	0
10	[Cp*RhCl$_2$]$_2$ (4)	CsOAc (2.0)	PhMe	80	75
11	[Cp*RhCl$_2$]$_2$ (4)	CsOAc (2.0)	MTBE	80	14
12	[Cp*RhCl$_2$]$_2$ (4)	CsOAc (2.0)	PhMe	80	71[c]
13	[Cp*RhCl$_2$]$_2$ (4)	CsOAc (2.0)	PhMe	90	54
14	[Cp*RhCl$_2$]$_2$ (4)	CsOAc (2.0)	PhMe	70	80
15	[Cp*RhCl$_2$]$_2$ (4)	CsOAc (2.0)	PhMe	60	trace
16	[Cp*RhCl$_2$]$_2$ (4)	NaOAc (2.0)	PhMe	70	48
17	[Cp*RhCl$_2$]$_2$ (4)	KOAc (2.0)	PhMe	70	55
18	[Cp*RhCl$_2$]$_2$ (4)	CsOAc (1.0)	PhMe	70	69
19	[Cp*RhCl$_2$]$_2$ (4)	CsOAc (0.3)	PhMe	70	54
20	**[Cp*RhCl$_2$]$_2$ (5)**	**CsOAc (2.0)**	**PhMe**	**70**	**87 (85[d])**

[a]Reaction conditions A: **1a** (0.1 mmol), **2a** (0.2 mmol), Rh(III) catalyst, and base in a solvent (2 mL) under N$_2$ for 48 h. [b]Yields were determined by ^{1}H NMR spectroscopy using 1,3,5-trimethoxybenzene as an internal standard. [c]Under air atmosphere. [d]Isolated yield after column chromatography on a 0.2 mmol scale.

Cp*(CO)CoI$_2$ showed poor or no activity. Screening of the solvents revealed that aromatic solvents seemed to be more suitable, and an improved yield was achieved when toluene was used (entries 4−11). Slightly lower yield was observed when the reaction carried out under air atmosphere (Table 1, entry 12). The NMR yield of **3aa** was improved to 80% when the

temperature was decreased to 70 °C (Table 1, entry 14). NaOAc and KOAc are almost as effective as CsOAc (entries 16 and 17), and catalytic amounts of CsOAc give marginally lower yields than superstoichiometric amounts (entries 18 and 19). Increasing the catalyst loading to 5 mol % resulted in formation of **3aa** in 87% NMR yield (85% isolated yield).

## Scheme 2. Scope of the Synthesis of Bridged Carbocycles[a,b]

With the optimal conditions in hand, the scope and generality of this coupling system was next investigated (Scheme 2). Introduction of various electron-donating (alkyl and alkoxy), electron-withdrawing (ester, CF$_3$, OCF$_3$, and NO$_2$), and halogen (F, Cl, and Br) groups into the 5- and 6-positions of the indole ring was fully tolerated, and the corresponding products were isolated in 64–90% yields (3aa–3ka). 4,6-Dimethyl-2-phenylindole was also applicable, such as in the isolation of product 3la in 65% yield. In contrast, no

reactivity was observed for 7-methyl-2-phenylindole, possibly due to steric hindrance around the NH directing group. The scope with respect to the substituent in the 2-phenyl group also proved to be broad. Thus, various para- (Me, ^{t}Bu, NMe$_2$, OMe, CF$_3$, and halogens) and meta-substituted indoles coupled with consistently good efficiency, affording products 3ma–3sa in 42–74% yields. The structure of 3ma was confirmed by X-ray crystallography (CCDC 1888533). Indoles bearing an ortho- and disubstituted arene ring were also

Scheme 3. Key Mechanistic Findings

(a) Control experiments
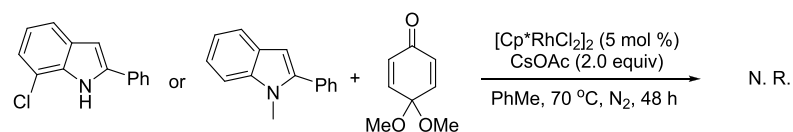
(b) H/D exchange
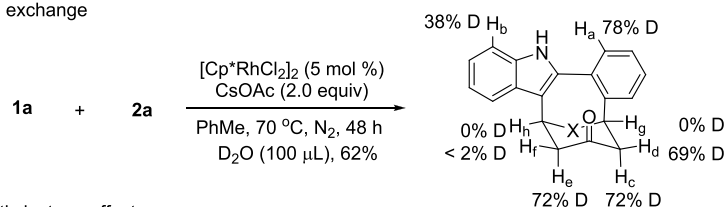
(c) Kinetic isotope effect
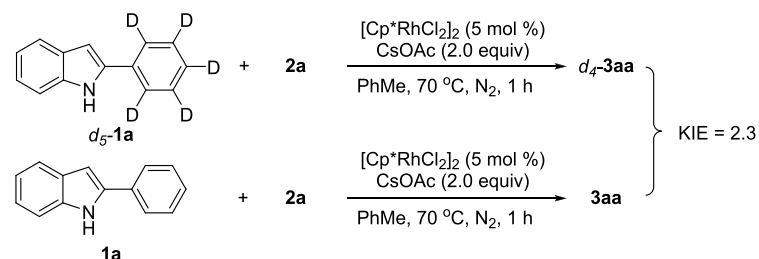
(d) Competition experiment
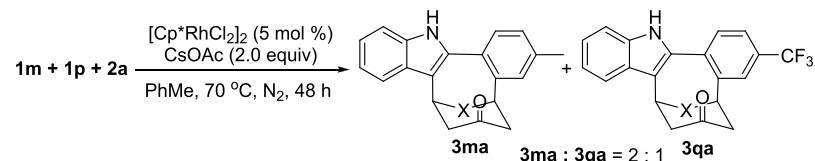
Scheme 4. Proposed Mechanism
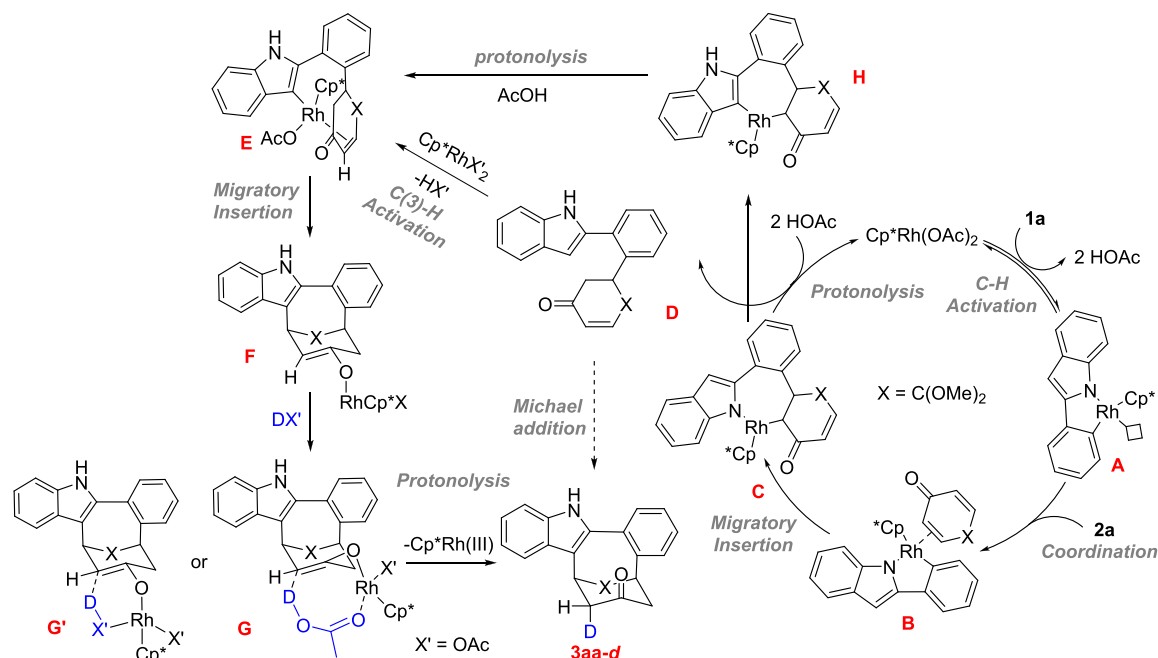
applicable (**3ta**, **3ua**). Extension of the phenyl group to a naphthalene ring was successful, such as in the isolation of **3va** in 73% yield. In addition to the dimethyl acetal, a mixed acetal and a diethyl acetal also reacted smoothly, affording the

corresponding products **3ab** and **3ac** in 55 and 67% yields, respectively. In addition to indoles, 2-phenylbenzimidazole also coupled with **2a** to afford the corresponding [4,3,1] heterocycle **4aa** in 65% yield under modified reaction

conditions. The reaction of 2-phenyl-1H-pyrrole only generated the C−H alkylation product **5** in 41% yield under the standard conditions, which may provide mechanistic insight. The acetal moiety seems to be crucial in this reaction because no reactivity was detected for 1-methoxy-[1,1′-biphenyl]-4(1H)-one (product **3ad**) or a simple benzoquinone (product **6**).

Several derivatization reactions have been conducted for product **3aa** to demonstrate the synthetic utility of the coupling system (Scheme S1). Gram-scale synthesis of **3aa** was performed under a reduced catalyst loading, and **3aa** was isolated in 89% yield (1.24 g). The ketone motif was readily converted to olefin **7** via a Wittig reaction in 87% yield. In addition, **3aa** underwent smooth hydrolysis (product **6**) when treated with a catalytic amount of TsOH in THF/H_2O.

A series of experiments were conducted to gain mechanistic insight into this coupling system (Scheme 3). 7-Chloro-2-phenylindole and 1-methyl-2-phenylindole both failed to undergo any coupling under the standard conditions (Scheme 3a), suggesting the significance of the NH coordination toward C−H functionalization. A deuterium-labeling experiment was performed for the coupling of indole **1a** and **2a** with D_2O being the deuterium source, from which **3aa**-d_n was isolated in 62% yield. ^{1}H NMR analysis of this product revealed 78% deuteration at the *ortho* position (H$_a$) of the product (Scheme 3b), which implies reversibility of the C(phenyl)−H activation. Furthermore, a comparable extent of deuteration was observed at the diastereotopic H$_c$ and H$_d$ positions, which may be ascribed to keto−enol tautomerization as in a Michael addition reaction.[20] In sharp contrast, a high level of deuteration was only observed at the H$_e$ position (72% D) that is *trans* to the indolyl substituent. This argues against a keto−enol tautomerization pathway in this (second) cyclization process because the H$_f$ is essentially undeuterated. Instead, it is more likely that this second C−C bond formation occurs via a C(3)−Rh migratory insertion pathway (vide infra). To further understand the C−H activtion process, kinetic isotope effect has been measured based on parallel reactions, and a large KIE value (k_H/k_D = 2.3) was obtained (Scheme 3c), indicating that cleavage of the C(pheyl)−H bond is likely involved in the turnover-limiting step. In addition, a competition experiment suggested that this C−H functionalization was kinetically favored for a electron-rich arene (Scheme 3d).

On the basis of our mechanistic studies and previous reports,[10−18] a plausible catalytic cycle is proposed in Scheme 4. Starting from an active [Cp*Rh(OAc)$_2$] species generated by anion exchange, cyclorhodation of 2-phenylindole **1a** gives a five-membered rhodacycle **A**. Subsequent coordination of quinone monoacetal **2a** generates a Rh(III) olefin complex **B**. Migratory insertion of the Rh−C(aryl) bond into the olefin unit affords a seven-membered rhodacycle **C**, which is proposed to undergo protonolysis to afford an alkylated intermediate **D** together with regeneration of the Rh(III) catalyst. The alkylated intermediate **D** might undergo rapid H/D exchange at the more acidic α position, or the Rh−C in intermediate **C** likely undergoes epimerization prior to protonolysis. The C(3)−H bond of **D** is then proposed to undergo electrophilic C−H activation possibly with the assistance of a proximal olefin/acetal group to generate a Rh(III) indolyl intermediate **E**, which then undergoes migratory 1,4-insertion into the conjugated ketone unit to produce the Rh(III) alkoxy intermediate **F**. Carboxylate-assisted protonolysis of the Rh−O bond via intermediate **G** or

G′ furnishes product **3aa**, and this protonolysis allowed diastereospecific deuterium incorporation in the presence of a deuterium source. The alternative intramolecular Michael addition of C(3) to the enone seems less likely based on our deuterium-labeling studies. At this stage, we cannot rule out the pathway of rollover (N to C(3)) C−H activation of intermediate **C** to Rh(III) indolyl **H**, followed by protonolysis of the Rh−C alkyl bond, which also gives intermediate **E**.

In summary, we have developed a Rh(III)-catalyzed annulative coupling between 2-arylindoles and quinone monoacetals via two-fold C−H activation/formal Michael addition. This coupling allowed direct access to [4,3,1]-bridged carbocycles with exclusive C(3) selectivity under redox-neutral conditions. Mechanistic studies, particularly H/D exchange experiments, suggest that the C(3) annulation likely proceeds via dual C−H activation−migratory insertion pathway. Further applications of other reactive enones to access biologically relevant bridged cycles are currently underway in our laboratory.

■ EXPERIMENTAL SECTION

General Information. Reaction temperatures are reported as the temperature of the oil bath. All chemicals were obtained from commercial sources and were used as received unless otherwise noted. 2-Arylindoles[14] and quinone monoacetals[16] were prepared following literature procedures. Chemical shifts (δ) of the ^{1}H and ^{13}C{^{1}H} NMR spectra are given in parts per million relative to TMS. The following abbreviations were used to describe multiplicity of peaks: br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublets of doublet, dt = doublets of triplet, td = triplets of doublet. HRMS data were obtained in ESI mode with a TOF mass analyzer. Column chromatography was performed on silica gel (300−400 mesh) using ethyl acetate (EA)/petroleum ether (PE). Pressure vessels were from Synthware.

General Procedure for Synthesis of a [4,3,1]-Carbocycle (Conditions A). A pressure tube was charged with a magnetic stir bar, [RhCp*Cl$_2$]$_2$ (5 mol %), CsOAc (2.0 equiv), 2-arylindoles (**1**, 0.2 mmol), quinone monoacetals (**2**, 0.4 mmol), and PhMe (4.0 mL). The tube was sealed, and the reaction mixture was stirred under N$_2$ at 70 °C in an oil bath for 48 h. After the reaction was completed, the volatiles were removed under reduced pressure and the residue was purified by silica gel chromatography using PE/EA to afford product **3**.

15,15-Dimethoxy-5,8,9,14-tetrahydro-5,9-methanobenzo[8,9]-cyclonona[1,2-b]indol-7(6H)-one 3aa: white solid, mp 200−202 °C, 58.9 mg, 85% yield. The eluent used was petroleum ether/ethyl acetate (5:1): ^{1}H NMR (600 MHz, CDCl$_3$) δ 8.51 (s, 1H), 7.55 (d, J = 7.8 Hz, 1H), 7.43 (d, J = 7.9 Hz, 1H), 7.23−7.20 (m, 2H), 7.20−7.11 (m, 3H), 7.08 (t, J = 7.4 Hz, 1H), 4.17−4.16 (m, 1H), 3.87−3.81 (m, 1H), 3.46 (s, 3H), 3.07−2.99 (m, 4H), 2.92 (dd, J = 15.3, 9.5 Hz, 1H), 2.69 (d, J = 15.7 Hz, 1H), 2.49 (dd, J = 15.6, 4.0 Hz, 1H); ^{13}C{^{1}H} NMR (150 MHz, CDCl$_3$) δ 209.0, 137.9, 136.6, 132.0, 131.0, 129.3, 128.7, 127.7, 127.4, 124.7, 119.9, 118.2, 111.9, 111.0, 99.5, 50.4, 49.0, 48.7, 44.8, 43.0, 38.3; HRMS (ESI) calcd for C$_{22}$H$_{21}$NNaO$_3^+$ 370.1414, found 370.1418.

11-Ethyl-15,15-dimethoxy-5,8,9,14-tetrahydro-5,9-methanobenzo[8,9]cyclonona[1,2-b]indol-7(6H)-one 3ba: white solid, mp 205−207 °C, 48.3 mg, 64% yield. The eluent used was petroleum ether/ethyl acetate (5:1): ^{1}H NMR (600 MHz, CDCl$_3$) δ 8.28 (s, 1H), 7.60 (d, J = 7.9 Hz, 1H), 7.33−7.28 (m, 1H), 7.24 (t, J = 4.9 Hz, 2H), 7.27−7.24 (m, 2H), 7.22−7.19 (m, 2H), 7.07 (dd, J = 8.2, 1.2 Hz, 1H), 4.18−4.12 (m, 1H), 3.84 (ddd, J = 9.4, 4.5, 2.9 Hz, 1H), 3.48 (s, 3H), 3.06−2.99 (m, 4H), 2.90 (dd, J = 15.3, 9.5 Hz, 1H), 2.76−2.68 (m, 3H), 2.50 (dd, J = 14.8, 4.1 Hz, 1H), 1.29 (t, J = 7.6 Hz, 3H); ^{13}C{^{1}H} NMR (150 MHz, CDCl$_3$) δ 208.6, 138.0, 136.1, 135.1, 132.0, 131.1, 129.5, 129.0, 127.6, 127.4, 124.5, 124.0, 116.8, 111.9, 110.8, 99.5, 50.3, 49.0, 48.7, 44.6, 42.8, 38.2, 29.1, 16.5; HRMS (ESI) calcd for C$_{24}$H$_{26}$NO$_3^+$ 376.1907, found 376.1902.

11,15,15-Trimethoxy-5,8,9,14-tetrahydro-5,9-methanobenzo[8,9]cyclonona[1,2-b]indol-7(6H)-one 3ca: white solid, 49.1 mg, mp 213-215 °C, 65% yield. The eluent used was petroleum ether/ethyl acetate (4:1): ^{1}H NMR (600 MHz, CDCl$_3$) δ 8.33 (s, 1H), 7.56 (d, J = 7.9 Hz, 1H), 7.28−7.25 (m, 1H), 7.21−7.17 (m, 3H), 6.88−6.81 (m, 2H), 4.10 (dd, J = 4.0, 2.5 Hz, 1H), 3.89−3.82 (m, 4H), 3.48 (s, 3H), 3.07−2.99 (m, 4H), 2.92 (dd, J = 15.2, 9.5 Hz, 1H), 2.68 (d, J = 15.6 Hz, 1H), 2.49 (dd, J = 15.2, 4.0 Hz, 1H); ^{13}C{^{1}H} NMR (150 MHz, CDCl$_3$) δ 208.8, 154.4, 137.8, 132.0, 131.8, 129.4, 129.1, 127.6, 127.4, 124.5, 113.4, 111.8, 111.6, 100.3, 99.5, 56.0, 50.3, 49.0, 48.7, 44.7, 42.7, 38.3; HRMS (ESI) calcd for C$_{23}$H$_{23}$NNaO$_4$$^+$ 400.1519, found 400.1509.

Ethyl-15,15-dimethoxy-7-oxo-5,6,7,8,9,14-hexahydro-5,9-methanobenzo[8,9]cyclonona[1,2-b]indole-11-carboxylate 3da: white solid, mp 242−244 °C, 59.3 mg, 71% yield. The eluent used was petroleum ether/ethyl acetate (5:1): ^{1}H NMR (600 MHz, CDCl$_3$) δ 8.81 (s, 1H), 8.20 (s, 1H), 7.81 (dd, J = 8.5, 1.3 Hz, 1H), 7.51 (d, J = 6.9 Hz, 1H), 7.20−7.12 (m, 4H), 4.42 (q, J = 7.1 Hz, 2H), 4.27−4.21 (m, 1H), 3.91 (dt, J = 9.2, 3.2 Hz, 1H), 3.51 (s, 3H), 3.12 (dd, J = 15.1, 6.2 Hz, 1H), 3.07−2.99 (m, 4H), 2.67 (d, J = 15.2 Hz, 1H), 2.47 (dd, J = 15.2, 1.9 Hz, 1H), 1.43 (t, J = 7.1 Hz, 3H); ^{13}C{^{1}H} NMR (150 MHz, CDCl$_3$) δ 209.2, 167.6, 139.1, 137.9, 132.4, 132.2, 128.7, 128.2, 127.4, 124.7, 124.6, 122.2, 120.8, 112.6, 110.5, 99.2, 60.7, 50.7, 49.0, 48.7, 45.3, 43.5, 38.5, 14.5; HRMS (ESI) calcd for C$_{25}$H$_{25}$NNaO$_5$$^+$ 442.1625, found 442.1620.

15,15-Dimethoxy-11-(trifluoromethyl)-5,8,9,14-tetrahydro-5,9-methanobenzo[8,9]cyclonona[1,2-b]indol-7(6H)-one 3ea: white solid, mp 199−201 °C, 48.5 mg, 58% yield. The eluent used was petroleum ether/ethyl acetate (4:1): ^{1}H NMR (600 MHz, DMSO-d$_6$) δ 11.50 (s, 1H), 7.99 (d, J = 7.9 Hz, 1H), 7.87 (d, J = 1.6 Hz, 1H), 7.45−7.37 (m, 3H), 7.35−7.29 (m, 2H), 4.28−4.19 (m, 1H), 4.05 (dd, J = 6.2, 2.9 Hz, 1H), 3.50 (s, 3H), 3.11−2.95 (m, 5H), 2.62−2.51 (m, 1H), 2.32 (d, J = 14.8 Hz, 1H), 2.19 (d, J = 14.8 Hz, 1H); ^{13}C{^{1}H} NMR (150 MHz, DMSO-d$_6$) δ 208.5, 139.4, 137.4, 133.9, 130.3, 129.3 (q, J = 3.4 Hz), 128.4, 127.6 (q, J = 31.9 Hz), 126.4, 124.7 (q, J = 270.0 Hz), 124.2 (q, J = 3.0 Hz), 123.9, 119.9, 119.0, 113.6, 111.9, 99.0, 49.3, 48.7, 48.7, 45.4, 43.7, 38.6; HRMS (ESI) calcd for C$_{23}$H$_{21}$F$_3$NO$_3$$^+$ 416.1468, found 416.1460.

15,15-Dimethoxy-11-(trifluoromethoxy)-5,8,9,14-tetrahydro-5,9-methanobenzo[8,9]cyclonona[1,2-b]indol-7(6H)-one 3fa: white solid, mp 215−217 °C, 65.4 mg, 76% yield. The eluent used was petroleum ether/ethyl acetate (5:1): ^{1}H NMR (600 MHz, CDCl$_3$) δ 8.57 (s, 1H), 7.46 (d, J = 7.6 Hz, 1H), 7.25 (br s, 2H), 7.18−7.11 (m, 4H), 6.97 (d, J = 8.6 Hz, 1H), 4.16−4.09 (m, 1H), 3.91−3.90 (m, 1H), 3.51 (s, 3H), 3.11 (dd, J = 15.0, 6.2 Hz, 1H), 3.08−3.01 (m, 4H), 2.62 (d, J = 15.0 Hz, 1H), 2.52−2.43 (m, 1H); ^{13}C{^{1}H} NMR (150 MHz, CDCl$_3$) δ 209.3, 143.2 (q, J = 1.6 Hz), 137.8, 134.7, 132.9, 132.2, 128.7 (two signals overlapped), 128.3, 127.4, 124.6, 120.8 (q, J = 255.5 Hz), 117.2, 111.6 (two signals overlapped), 110.5, 99.1, 50.8, 49.0, 48.7, 45.3, 43.3, 38.6; HRMS (ESI) calcd for C$_{23}$H$_{20}$F$_3$NNaO$_4$$^+$ 454.1237, found 454.1224.

15,15-Dimethoxy-11-nitro-5,8,9,14-tetrahydro-5,9-methanobenzo[8,9]cyclonona[1,2-b]indol-7(6H)-one 3ga: yellow solid, mp 237−239 °C, 39.1 mg, 50% yield. The eluent used was petroleum ether/ethyl acetate (4:1): ^{1}H NMR (600 MHz, DMSO-d$_6$) δ 11.99 (s, 1H), 8.66 (d, J = 1.7 Hz, 1H), 8.07 (dd, J = 8.9, 1.9 Hz, 1H), 7.98 (d, J = 7.9 Hz, 1H), 7.54 (d, J = 8.9 Hz, 1H), 7.43−7.39 (m, 2H), 7.33 (t, J = 7.3 Hz, 1H), 4.41−4.32 (m, 1H), 4.04 (d, J = 9.1 Hz, 1H), 3.48 (s, 3H), 3.08 (dd, J = 14.8, 6.1 Hz, 1H), 3.01 (dd, J = 15.0, 9.3 Hz, 1H), 2.95 (s, 1H), 2.30 (d, J = 14.9 Hz, 1H), 2.16 (d, J = 15.1 Hz, 1H); ^{13}C{^{1}H} NMR (150 MHz, DMSO-d$_6$) δ 208.1, 140.8, 139.7, 138.6, 134.8, 132.5, 128.5, 128.3, 127.6, 127.2, 125.6, 118.0, 115.6, 113.5, 111.5, 98.6, 49.7, 48.3, 48.2, 45.3, 43.6, 37.8; HRMS (ESI) calcd for C$_{22}$H$_{20}$N$_2$NaO$_5$$^+$ 415.1264, found 415.1268.

11-Fluoro-15,15-dimethoxy-5,8,9,14-tetrahydro-5,9-methanobenzo[8,9]cyclonona[1,2-b]indol-7(6H)-one 3ha: white solid, mp 225−227 °C, 52.5 mg, 72% yield. The eluent used was petroleum ether/ethyl acetate (3:1): ^{1}H NMR (600 MHz, CDCl$_3$) δ 8.48 (s, 1H), 7.47 (br s, 1H), 7.16 (br s, 3H), 7.09−7.01 (m, 2H), 6.84 (t, J = 8.3 Hz, 1H), 4.08 (br s, 1H), 3.88 (d, J = 8.8 Hz, 1H),

3.48 (s, 3H), 3.09−2.96 (m, 5H), 2.63 (d, J = 15.1 Hz, 1H), 2.47 (d, J = 14.2 Hz, 1H); ^{13}C{^{1}H} NMR (150 MHz, CDCl$_3$) δ 209.2, 158.0 (d, J = 235.5 Hz), 137.8, 133.0, 132.7, 132.1, 128.9, 128.0, 127.4, 124.6, 111.7 (d, J = 9.7 Hz), 111.6 (d, J = 26.2 Hz), 103.0 (d, J = 23.7 Hz), 99.2, 50.6, 49.0, 48.6, 45.1, 43.1, 38.5; HRMS (ESI) calcd for C$_{22}$H$_{20}$FNNaO$_3$$^+$ 388.1319, found 388.1312.

11-Bromo-15,15-dimethoxy-5,8,9,14-tetrahydro-5,9-methanobenzo[8,9]cyclonona[1,2-b]indol-7(6H)-one 3ia: white solid, mp 253−255 °C, 74.4 mg, 87% yield. The eluent used was petroleum ether/ethyl acetate (5:1): ^{1}H NMR (600 MHz, CDCl$_3$) δ 8.50 (s, 1H), 7.52 (d, J = 1.4 Hz, 1H), 7.46 (d, J = 7.2 Hz, 1H), 7.21−7.13 (m, 4H), 7.02 (d, J = 8.5 Hz, 1H), 4.12−4.08 (m, 1H), 3.89 (dt, J = 9.3, 3.2 Hz, 1H), 3.48 (s, 3H), 3.12−3.06 (m, 1H), 3.06−2.99 (m, 4H), 2.63 (d, J = 15.0 Hz, 1H), 2.45 (ddd, J = 15.2, 3.5, 1.6 Hz, 1H); ^{13}C{^{1}H} NMR (150 MHz, CDCl$_3$) δ 209.2, 137.8, 135.1, 132.2, 132.1, 130.2, 128.7, 128.2, 127.4, 126.1, 124.6, 120.5, 113.1, 112.4, 110.9, 99.1, 50.6, 49.0, 48.6, 45.2, 43.3, 38.5; HRMS (ESI) calcd for C$_{22}$H$_{20}$BrNNaO$_3$$^+$ 448.0519, found 448.0511.

12-Chloro-15,15-dimethoxy-5,8,9,14-tetrahydro-5,9-methanobenzo[8,9]cyclonona[1,2-b]indol-7(6H)-one 3ja: white solid, mp 266−268 °C, 68.4 mg, 90% yield. The eluent used was petroleum ether/ethyl acetate (4:1): ^{1}H NMR (600 MHz, CDCl$_3$) δ 8.45 (s, 1H), 7.45 (d, J = 7.5 Hz, 1H), 7.31 (d, J = 8.4 Hz, 1H), 7.15 (dq, J = 8.8, 4.6 Hz, 4H), 7.04 (dd, J = 8.4, 1.7 Hz, 1H), 4.17−4.10 (m, 1H), 3.89 (dt, J = 9.2, 3.3 Hz, 1H), 3.52−3.48 (m, 3H), 3.10−2.97 (m, 5H), 2.63 (d, J = 15.1 Hz, 1H), 2.51−2.45 (m, 1H); ^{13}C{^{1}H} NMR (150 MHz, CDCl$_3$) δ 209.2, 137.7, 136.8, 132.1, 131.7, 129.1, 128.8, 128.0, 127.4, 127.1, 124.5, 120.7, 118.9, 111.5, 110.9, 99.2, 50.6, 49.0, 48.6, 45.1, 43.3, 38.5; HRMS (ESI) calcd for C$_{22}$H$_{20}$ClNNaO$_3$$^+$ 404.1024, found 404.1018.

12-Fluoro-15,15-dimethoxy-5,8,9,14-tetrahydro-5,9-methanobenzo[8,9]cyclonona[1,2-b]indol-7(6H)-one 3ka: white solid, mp 234−236 °C, 56.7 mg, 78% yield. The eluent used was petroleum ether/ethyl acetate (4:1): ^{1}H NMR (600 MHz, CDCl$_3$) δ 8.51 (s, 1H), 7.40 (d, J = 7.7 Hz, 1H), 7.29 (dd, J = 8.6, 5.1 Hz, 1H), 7.15−7.11 (m, 2H), 7.10−7.06 (m, 1H), 6.85−6.75 (m, 2H), 4.17−4.10 (m, 1H), 3.88 (dt, J = 9.2, 3.2 Hz, 1H), 3.49 (s, 3H), 3.10 (dd, J = 15.0, 6.2 Hz, 1H), 3.07−2.98 (m, 4H), 2.65 (d, J = 15.0 Hz, 1H), 2.53−2.44 (m, 1H); ^{13}C{^{1}H} NMR (150 MHz, CDCl$_3$) δ 209.6, 160.7 (d, J = 239.0 Hz), 137.3, 136.6 (d, J = 12.8 Hz), 132.0, 131.4 (d, J = 3.4 Hz), 128.9, 127.7, 127.4, 125.0, 124.4, 118.8 (d, J = 10.3 Hz), 111.3, 108.6 (d, J = 24.7 Hz), 99.2, 97.3 (d, J = 26.2 Hz), 50.6, 49.0, 48.6, 45.2, 43.3, 38.6; HRMS (ESI) calcd for C$_{22}$H$_{20}$FNNaO$_3$$^+$ 388.1319, found 388.1310.

15,15-Dimethoxy-10,12-dimethyl-5,8,9,14-tetrahydro-5,9-methanobenzo[8,9]cyclonona[1,2-b]indol-7(6H)-one 3la: white solid, mp 227−229 °C, 51.0 mg, 65% yield. The eluent used was petroleum ether/ethyl acetate (5:1): ^{1}H NMR (600 MHz, CDCl$_3$) δ 8.26 (s, 1H), 7.52 (d, J = 7.9 Hz, 1H), 7.28−7.24 (m, 1H), 7.19−7.15 (m, 2H), 6.93 (s, 1H), 6.66 (s, 1H), 4.54−4.48 (m, 1H), 3.90−3.82 (m, 1H), 3.46 (s, 3H), 3.09 (s, 3H), 3.03 (dd, J = 15.0, 6.9 Hz, 1H), 2.94 (dd, J = 14.5, 9.4 Hz, 1H), 2.67−2.57 (m, 4H), 2.46 (ddd, J = 14.9, 4.0, 1.4 Hz, 1H), 2.37 (s, 3H); ^{13}C{^{1}H} NMR (150 MHz, CDCl$_3$) δ 209.1, 137.7, 137.3, 133.2, 131.9, 129.8, 129.7, 129.6, 127.4, 124.9, 124.6, 124.5, 113.4, 109.0, 99.6, 50.2, 49.0, 48.4, 45.3, 45.2, 39.6, 21.4, 20.4; HRMS (ESI) calcd for C$_{24}$H$_{25}$NNaO$_3$$^+$ 398.1727, found 398.1720.

15,15-Dimethoxy-3-methyl-5,8,9,14-tetrahydro-5,9-methanobenzo[8,9]cyclonona[1,2-b]indol-7(6H)-one 3ma: white solid, 53.6 mg, mp 231−233 °C, 74% yield. The eluent used was petroleum ether/ethyl acetate (3:1): ^{1}H NMR (600 MHz, CDCl$_3$) δ 8.37 (s, 1H), 7.46−7.42 (m, 2H), 7.28 (d, J = 8.1 Hz, 1H), 7.17 (t, J = 7.6 Hz, 1H), 7.11−7.06 (m, 2H), 7.12−7.04 (m, 2H), 7.00 (s, 1H), 4.16 (dt, J = 6.4, 2.2 Hz, 1H), 3.85−3.78 (m, 1H), 3.48 (s, 3H), 3.08−3.00 (m, 4H), 2.92 (dd, J = 15.2, 9.4 Hz, 1H), 2.67 (d, J = 15.7 Hz, 1H), 2.48 (ddd, J = 15.2, 4.3, 1.2 Hz, 1H), 2.32 (s, 3H); ^{13}C{^{1}H} NMR (150 MHz, CDCl3) δ 208.9, 137.8, 137.6, 136.4, 132.8, 131.2, 128.8, 128.1, 126.5, 124.5, 123.1, 119.9, 118.1, 111.2, 110.9, 99.5, 50.2, 49.0, 48.6, 44.9, 43.1, 38.3, 20.9; HRMS (ESI) calcd for C$_{23}$H$_{23}$NNaO$_3$$^+$ 384.1570, found 384.1567.

3-(tert-Butyl)-15,15-dimethoxy-5,8,9,14-tetrahydro-5,9-methanobenzo[8,9]cyclonona[1,2-b]indol-7(6H)-one **3na:** white solid, mp 221–223 °C, 36.2 mg, 45% yield. The eluent used was petroleum ether/ethyl acetate (4:1): ^{1}H NMR (600 MHz, CDCl$_3$) δ 8.41 (s, 1H), 7.52 (d, *J* = 8.3 Hz, 1H), 7.44 (d, *J* = 7.9 Hz, 1H), 7.31 (d, *J* = 7.9 Hz, 2H), 7.21–7.15 (m, 2H), 7.10 (t, *J* = 7.4 Hz, 1H), 4.16 (d, *J* = 6.5 Hz, 1H), 3.85 (d, *J* = 9.0 Hz, 1H), 3.48 (s, 3H), 3.07–2.99 (m, 4H), 2.92 (d, *J* = 9.4 Hz, 1H), 2.67 (d, *J* = 15.7 Hz, 1H), 2.50 (d, *J* = 3.9 Hz, 1H), 1.33 (s, 9H); ^{13}C{^{1}H} NMR (150 MHz, CDCl$_3$) δ 208.8, 150.9, 137.6, 136.4, 131.2, 130.0, 129.1, 128.8, 126.4, 124.4, 123.1, 119.9, 118.1, 111.3, 110.9, 99.6, 50.7, 48.9, 48.6, 45.0, 43.0, 38.3, 34.5, 31.2; HRMS (ESI) calcd for C$_{26}$H$_{29}$NNaO$_3^+$ 426.2040, found 426.2030.

3-(Dimethylamino)-15,15-dimethoxy-5,8,9,14-tetrahydro-5,9-methanobenzo[8,9]cyclonona[1,2-b]indol-7(6H)-one **3oa:** white solid, mp 218–220 °C, 33.0 mg, 42% yield. The eluent used was petroleum ether/ethyl acetate (2:1): ^{1}H NMR (600 MHz, CDCl$_3$) δ 8.24 (s, 1H), 7.47 (d, *J* = 8.7 Hz, 1H), 7.40 (d, *J* = 7.8 Hz, 1H), 7.30 (d, *J* = 8.0 Hz, 1H), 7.15 (t, *J* = 7.5 Hz, 1H), 7.08 (t, *J* = 7.4 Hz, 1H), 6.65 (dd, *J* = 8.7, 2.6 Hz, 1H), 6.52 (d, *J* = 2.6 Hz, 1H), 4.12–4.11 (m, 1H), 3.77 (ddd, *J* = 9.1, 4.6, 2.8 Hz, 1H), 3.47 (s, 3H), 3.09 (s, 3H), 3.02–2.97 (m, 7H), 2.89 (dd, *J* = 13.1, 7.4 Hz, 1H), 2.68 (d, *J* = 15.9 Hz, 1H), 2.53 (dd, *J* = 15.2, 4.7 Hz, 1H); ^{13}C{^{1}H} NMR (150 MHz, CDCl$_3$) δ 208.9, 149.8, 139.3, 136.3, 132.0, 129.2, 125.8, 122.3, 119.7, 117.6, 115.2, 111.0, 110.5, 109.0, 99.8, 50.8, 49.1, 48.6, 44.9, 43.1, 40.3, 38.1; HRMS (ESI) calcd for C$_{24}$H$_{26}$N$_2$NaO$_3^+$ 413.1836, found 413.1827.

3,15,15-Trimethoxy-5,8,9,14-tetrahydro-5,9-methanobenzo[8,9]cyclonona[1,2-b]indol-7(6H)-one **3pa:** white solid, mp 130–132 °C, 53.6 mg, 71% yield. The eluent used was petroleum ether/ethyl acetate (2:1): ^{1}H NMR (600 MHz, CDCl$_3$) δ 8.19 (s, 1H), 7.46 (d, *J* = 8.7 Hz, 1H), 7.36 (d, *J* = 7.8 Hz, 1H), 7.24 (d, *J* = 8.0 Hz, 1H), 7.11 (t, *J* = 7.5 Hz, 1H), 7.03 (t, *J* = 7.4 Hz, 1H), 6.77 (dd, *J* = 8.7, 2.6 Hz, 1H), 6.69 (d, *J* = 2.5 Hz, 1H), 4.08–4.07 (m, 1H), 3.78–3.71 (m, 4H), 3.41 (s, 3H), 3.01 (s, 3H), 2.95 (dd, *J* = 15.6, 6.6 Hz, 1H), 2.84 (dd, *J* = 15.2, 9.6 Hz, 1H), 2.61 (d, *J* = 15.7 Hz, 1H), 2.43 (dd, *J* = 14.9, 4.0 Hz, 1H); ^{13}C{^{1}H} NMR (150 MHz, CDCl$_3$) δ 208.6, 159.0, 139.7, 136.4, 131.1, 128.9, 126.0, 122.9, 122.2, 119.9, 118.0, 117.9, 112.2, 110.7, 110.4, 99.5, 55.3, 50.4, 49.1, 48.6, 44.7, 43.0, 38.2; HRMS (ESI) calcd for C$_{23}$H$_{23}$NNaO$_4^+$ 400.1519, found 400.1511.

15,15-Dimethoxy-3-(trifluoromethyl)-5,8,9,14-tetrahydro-5,9-methanobenzo[8,9]cyclonona[1,2-b]indol-7(6H)-one **3qa:** white solid, mp 233–235 °C, 67.3 mg, 81% yield. The eluent used was petroleum ether/ethyl acetate (4:1): ^{1}H NMR (600 MHz, acetone-*d$_6$*) δ 10.65 (s, 1H), 8.12 (d, *J* = 8.3 Hz, 1H), 7.73 (s, 1H), 7.66–7.62 (m, 2H), 7.43 (d, *J* = 8.1 Hz, 1H), 7.21 (t, *J* = 7.5 Hz, 1H), 7.09 (t, *J* = 7.5 Hz, 1H), 4.36–4.30 (m, 1H), 4.22 (dt, *J* = 9.2, 3.1 Hz, 1H), 3.53 (s, 3H), 3.13 (dd, *J* = 15.0, 6.2 Hz, 1H), 3.07–2.99 (m, 4H), 2.50 (dd, *J* = 15.0, 1.9 Hz, 1H), 2.34 (ddd, *J* = 15.3, 3.2, 1.8 Hz, 1H); ^{13}C{^{1}H} NMR (150 MHz, acetone) δ 207.4, 140.3, 138.3, 138.2, 134.7, 131.0, 129.8 (q, *J* = 3.8 Hz), 129.4, 129.0 (q, *J* = 32.1 Hz), 126.5, 126.2, 125.3 (q, *J* = 270.0 Hz), 124.7 (q, *J* = 3.8 Hz), 124.5, 124.4, 120.6, 119.4, 114.8, 112.3, 112.2, 99.9, 50.7, 48.9, 48.8, 45.6, 43.8, 39.5; HRMS (ESI) calcd for C$_{23}$H$_{20}$F$_3$NNaO$_3^+$ 438.1287, found 438.1283.

3-Fluoro-15,15-dimethoxy-5,8,9,14-tetrahydro-5,9-methanobenzo[8,9]cyclonona[1,2-b]indol-7(6H)-one **3ra:** white solid, mp 243–245 °C, 47.3 mg, 65% yield. The eluent used was petroleum ether/ethyl acetate (4:1): ^{1}H NMR (600 MHz, acetone-*d$_6$*) δ 10.45 (s, 1H), 7.96 (dd, *J* = 8.8, 5.6 Hz, 1H), 7.56 (d, *J* = 7.9 Hz, 1H), 7.38 (d, *J* = 8.1 Hz, 1H), 7.20 (dd, *J* = 9.8, 2.7 Hz, 1H), 7.18–7.09 (m, 2H), 7.05 (t, *J* = 7.5 Hz, 1H), 4.29–4.23 (m, 1H), 4.05 (dt, *J* = 9.2, 3.2 Hz, 1H), 3.51 (s, 3H), 3.08 (dd, *J* = 15.1, 6.2 Hz, 1H), 3.04 (s, 3H), 2.97 (dd, *J* = 9.8, 5.5 Hz, 1H), 2.86–2.79 (m, 1H), 2.50 (d, *J* = 15.1 Hz, 1H), 2.36–2.30 (m, 1H); ^{13}C{^{1}H} NMR (150 MHz, acetone-*d$_6$*) δ 207.5, 162.5 (d, *J* = 245.7 Hz), 142.2 (d, *J* = 7.1 Hz), 138.0, 131.6, 129.7, 127.9 (d, *J* = 8.2 Hz), 127.5 (d, *J* = 3.1 Hz), 123.7, 120.3, 119.5 (d, *J* = 21.8 Hz), 119.0, 114.6 (d, *J* = 21.2 Hz), 112.3, 112.0, 100.0, 50.7, 49.0, 48.7, 45.6, 44.0, 39.3; HRMS (ESI) calcd for C$_{22}$H$_{20}$FNNaO$_3^+$ 388.1319, found 388.1316.

15,15-Dimethoxy-2-phenyl-5,8,9,14-tetrahydro-5,9-methanobenzo[8,9]cyclonona[1,2-b]indol-7(6H)-one **3sa:** white solid, mp 215–217 °C, 69.0 mg, 82% yield. The eluent used was petroleum ether/ethyl acetate (3:1): ^{1}H NMR (600 MHz, CDCl$_3$) δ 8.47 (s, 1H), 7.78 (d, *J* = 1.4 Hz, 1H), 7.63 (d, *J* = 7.2 Hz, 2H), 7.50–7.46 (m, 3H), 7.43 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.39 (t, *J* = 7.4 Hz, 1H), 7.35 (d, *J* = 8.1 Hz, 1H), 7.27 (s, 1H), 7.22 (t, *J* = 7.5 Hz, 1H), 7.12 (t, *J* = 7.5 Hz, 1H), 4.20 (dd, *J* = 4.1, 2.5 Hz, 1H), 3.94–3.87 (m, 1H), 3.50 (s, 3H), 3.12–3.02 (m, 4H), 2.95 (dd, *J* = 15.3, 9.5 Hz, 1H), 2.69 (d, *J* = 15.6 Hz, 1H), 2.51 (dd, *J* = 15.3, 4.3 Hz, 1H); ^{13}C{^{1}H} NMR (150 MHz, CDCl$_3$) δ 208.6, 140.6, 136.9, 136.6, 132.6, 130.9, 129.6, 128.9, 128.8, 127.6, 127.2, 126.5, 123.6, 120.1, 118.4, 112.4, 111.0, 99.5, 49.9, 49.1, 48.7, 44.7, 43.0, 38.4; HRMS (ESI) calcd for C$_{28}$H$_{25}$NNaO$_3^+$ 446.1727, found 446.1719.

1-Fluoro-15,15-dimethoxy-5,8,9,14-tetrahydro-5,9-methanobenzo[8,9]cyclonona[1,2-b]indol-7(6H)-one **3ta:** white solid, mp 207–209 °C, 48.0 mg, 66% yield. The eluent used was petroleum ether/ethyl acetate (4:1): ^{1}H NMR (600 MHz, CDCl$_3$) δ 8.47 (s, 1H), 7.78 (d, *J* = 1.4 Hz, 1H), 7.63 (d, *J* = 7.2 Hz, 2H), 7.48 (dd, *J* = 13.5, 7.4 Hz, 3H), 7.43 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.39 (t, *J* = 7.4 Hz, 1H), 7.35 (d, *J* = 8.1 Hz, 1H), 7.27 (s, 1H), 7.22 (t, *J* = 7.5 Hz, 1H), 7.12 (t, *J* = 7.5 Hz, 1H), 4.20 (dd, *J* = 4.1, 2.5 Hz, 1H), 3.94–3.87 (m, 1H), 3.50 (s, 3H), 3.12–3.02 (m, 4H), 2.95 (dd, *J* = 15.3, 9.5 Hz, 1H), 2.69 (d, *J* = 15.6 Hz, 1H), 2.51 (dd, *J* = 15.3, 4.3 Hz, 1H); ^{13}C{^{1}H} NMR (150 MHz, CDCl$_3$) δ 208.0, 160.4 (d, *J* = 245.3 Hz), 140.6, 136.1 (d, *J* = 3.5 Hz), 128.3, 128.2 (d, *J* = 2.4 Hz), 127.2, 127.0 (d, *J* = 3.8 Hz), 123.7, 120.0, 118.4, 118.0 (d, *J* = 7.4 Hz), 115.7 (d, *J* = 27.7 Hz), 113.2, 111.2, 99.2, 50.5, 50.0, 48.7, 44.0, 42.8, 38.2; HRMS (ESI) calcd for C$_{22}$H$_{20}$FNNaO$_3^+$ 388.1319, found 388.1314.

15,15-Dimethoxy-2,3-dimethyl-5,8,9,14-tetrahydro-5,9-methanobenzo[8,9]cyclonona[1,2-b]indol-7(6H)-one **3ua:** white solid, mp 225–226 °C, 67.4 mg, 90% yield. The eluent used was petroleum ether/ethyl acetate (8:1): ^{1}H NMR (600 MHz, CDCl$_3$) δ 8.37 (s, 1H), 7.42 (d, *J* = 7.9 Hz, 1H), 7.33 (s, 1H), 7.30 (d, *J* = 8.0 Hz, 1H), 7.16 (t, *J* = 7.4 Hz, 1H), 7.09 (t, *J* = 7.8 Hz, 1H), 6.94 (s, 1H), 4.18–4.13 (m, 1H), 3.84–3.77 (m, 1H), 3.48 (s, 3H), 3.09–3.01 (m, 4H), 2.93 (dd, *J* = 15.0, 9.4 Hz, 1H), 2.65 (d, *J* = 15.5 Hz, 1H), 2.51–2.43 (m, 1H), 2.26 (s, 3H), 2.24 (s, 3H); ^{13}C{^{1}H} NMR (150 MHz, CDCl$_3$) δ 209.0, 136.4, 135.5, 135.4, 133.5, 131.3, 128.8, 126.6, 125.8, 123.0, 119.8, 118.0, 111.1, 110.8, 99.5, 49.7, 49.0, 48.5, 45.3, 43.2, 38.4, 19.5, 19.3; HRMS (ESI) calcd for C$_{24}$H$_{25}$NNaO$_3^+$ 398.1727, found 398.1720.

17,17-Dimethoxy-7,10,11,16-tetrahydro-7,11-methanonaphtho[2',1':8,9]cyclonona[1,2-b]indol-9(8H)-one **3va:** white solid, mp 272–274 °C, 57.9 mg, 73% yield. The eluent used was petroleum ether/ethyl acetate (6:1): ^{1}H NMR (600 MHz, CDCl$_3$) δ 8.55 (d, *J* = 8.5 Hz, 1H), 8.51 (s, 1H), 7.89 (d, *J* = 7.6 Hz, 1H), 7.74 (d, *J* = 8.2 Hz, 1H), 7.57–7.48 (m, 3H), 7.39 (d, *J* = 8.1 Hz, 1H), 7.31 (d, *J* = 8.2 Hz, 1H), 7.27–7.23 (m, 1H), 7.16 (t, *J* = 7.5 Hz, 1H), 4.23 (dd, *J* = 4.8, 2.0 Hz, 1H), 3.75–3.69 (m, 1H), 3.41 (s, 3H), 2.96 (dd, *J* = 17.4, 1.4 Hz, 1H), 2.93–2.87 (m, 1H), 2.81–2.72 (m, 4H), 2.60 (dd, *J* = 15.3, 7.4 Hz, 1H); ^{13}C{^{1}H} NMR (150 MHz, CDCl$_3$) δ 208.0, 137.0, 136.3, 133.8, 130.9, 130.7, 129.2, 128.8, 128.0, 127.9, 126.9, 126.8, 126.0, 125.7, 123.2, 120.0, 119.2, 113.1, 111.0, 101.0, 50.2, 49.2, 49.1, 42.2, 41.9, 38.4; HRMS (ESI) calcd for C$_{26}$H$_{23}$NNaO$_3^+$ 420.1570, found 420.1560.

15-Isopropoxy-15-methoxy-5,8,9,14-tetrahydro-5,9-methanobenzo[8,9]cyclonona[1,2-b]indol-7(6H)-one **3ab:** white solid, mp 220–222 °C, 43.5 mg, 55% yield. The eluent used was petroleum ether/ethyl acetate (4:1): ^{1}H NMR (600 MHz, CDCl$_3$) δ 8.43 (s, 1H), 7.55 (d, *J* = 7.7 Hz, 1H), 7.45 (d, *J* = 7.8 Hz, 1H), 7.29 (d, *J* = 8.0 Hz, 1H), 7.26–7.23 (m, 1H), 7.21–7.15 (m, 3H), 7.10 (t, *J* = 7.4 Hz, 1H), 4.42–4.38 (m, 1H), 4.25–4.18 (m, 1H), 3.94–3.87 (m, 1H), 3.17 (dd, *J* = 15.3, 6.4 Hz, 1H), 3.07 (s, 3H), 2.97 (dd, *J* = 15.0, 9.4 Hz, 1H), 2.64 (d, *J* = 15.4 Hz, 1H), 2.49 (dd, *J* = 15.1, 3.2 Hz, 1H), 1.36–1.32 (m, 6H); ^{13}C{^{1}H} NMR (150 MHz, CDCl$_3$) δ 209.2, 138.7, 136.5, 132.0, 131.1, 129.2, 128.6, 127. 8, 127.2, 124.4, 123.4, 120.0, 118.2, 112.1, 111.0, 100.0, 64.0, 51.4, 49.8, 45.4, 43.6,

39.3, 24.5, 24.4; HRMS (ESI) calcd for $C_{24}H_{25}NNaO_3^+$ 398.1727, found 398.1719.

15,15-Diethoxy-5,8,9,14-tetrahydro-5,9-methanobenzo[8,9]-cyclonona[1,2-b]indol-7(6H)-one **3ac:** yellow oil, 50.5 mg, 67% yield. The eluent used was petroleum ether/ethyl acetate (5:1): ^1H NMR (600 MHz, $CDCl_3$) δ 8.46 (s, 1H), 7.58 (d, *J* = 7.8 Hz, 1H), 7.44 (d, *J* = 7.9 Hz, 1H), 7.33−7.25 (m, 2H), 7.22−7.14 (m, 3H), 7.09 (t, *J* = 7.5 Hz, 1H), 4.14 (dd, *J* = 4.6, 2.2 Hz, 1H), 3.84 (ddd, *J* = 9.3, 5.1, 2.6 Hz, 1H), 3.78 (dq, *J* = 14.2, 7.1 Hz, 1H), 3.70 (dq, *J* = 14.0, 7.0 Hz, 1H), 3.42 (tt, *J* = 14.1, 7.0 Hz, 1H), 3.32−3.25 (m, 1H), 3.00 (dd, *J* = 16.1, 6.7 Hz, 1H), 2.88 (dd, *J* = 15.3, 9.7 Hz, 1H), 2.71 (d, *J* = 16.2 Hz, 1H), 2.52 (dd, *J* = 15.3, 5.2 Hz, 1H), 1.32 (t, *J* = 7.0 Hz, 3H), 0.63 (t, *J* = 7.1 Hz, 3H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 209.1, 138.5, 136.5, 131.9, 131.2, 129.7, 128.9, 127.5, 127.3, 124.6, 123.3, 119.9, 118.5, 112.6, 111.0, 100.0, 99.5, 56.9, 56.5, 51.0, 44.3, 42.8, 39.0, 15.3, 14.8; HRMS (ESI) calcd for $C_{24}H_{25}NNaO_3^+$ 398.1727, found 398.1718.

6,6-dimethoxy-2'-(1H-pyrrol-2-yl)-1,6-dihydro-[1,1'-biphenyl]-3(2H)-one **5:** yellow oil, 24.5 mg, 41% yield. The eluent used was petroleum ether/ethyl acetate (5:1): ^1H NMR (600 MHz, $CDCl_3$) δ 9.46 (s, 1H), 7.58−7.50 (m, 1H), 7.44−7.36 (m, 1H), 7.29−7.24 (m, 2H), 7.00 (d, *J* = 10.4 Hz, 1H), 6.88 (dd, *J* = 4.0, 2.4 Hz, 1H), 6.37−6.26 (m, 2H), 6.15 (d, *J* = 10.4 Hz, 1H), 4.10 (dd, *J* = 10.4, 4.3 Hz, 1H), 3.35 (s, 3H), 3.06 (s, 3H), 2.97 (dd, *J* = 17.1, 10.5 Hz, 1H), 2.53 (dd, *J* = 17.1, 4.3 Hz, 1H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 198.6, 148.6, 135.6, 134.3, 131.4, 131.2, 130.4, 129.7, 127.3, 127.0, 118.6, 109.4, 108.9, 99.1, 51.4, 50.3, 45.2, 43.0; HRMS (ESI) calcd for $C_{18}H_{19}NNaO_3^+$ 320.1257, found 320.1252.

Procedure for [4 + 5] Annulations of 2-Phenyl-1*H*-benzo-[*d*]imidazole with Quinone Monoacetals (Conditions B). A pressure tube was charged with a magnetic stir bar, $[RhCp^*Cl_2]_2$ (5 mol %), CsOAc (2.0 equiv), 2-phenyl-1*H*-benzo[*d*]-imidazole (**1z**, 0.2 mmol), quinone monoacetals (**2a**, 0.4 mmol), and TFE (4.0 mL). The tube was sealed, and the reaction mixture was stirred under N_2 at 70 °C in an oil bath for 48 h. After the reaction was completed, the volatiles were removed under reduced pressure and the residue was purified by silica gel chromatography using PE/EA to afford the product **4aa**.

16,16-Dimethoxy-5,6,8,9-tetrahydro-7H-5,9-methanobenzo[c]-benzo[4,5]imidazo[1,2-a]azonin-7-one **4aa:** white solid, mp 256−258 °C, 45.0 mg, 65% yield. The eluent used was petroleum ether/ethyl acetate (2:1): ^1H NMR (600 MHz, $CDCl_3$) δ 9.09−8.96 (m, 1H), 7.82 (d, *J* = 6.6 Hz, 1H), 7.40−7.37 (m, 2H), 7.35−7.29 (m, 2H), 7.22−7.15 (m, 1H), 5.37−5.19 (m, 1H), 4.12 (dd, *J* = 4.7, 2.7 Hz, 1H), 3.56 (s, 3H), 3.28−3.12 (m, 2H), 3.01 (s, 3H), 2.68 (d, *J* = 15.3 Hz, 1H), 2.52 (dd, *J* = 9.6, 7.3 Hz, 1H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 204.9, 150.4, 136.0, 135.6, 131.8, 131.5, 130.7, 127.5, 123.3, 123.2, 120.1, 108.6, 97.2, 56.5, 49.3, 48.9, 48.6, 46.8, 43.5; HRMS (ESI) calcd for $C_{21}H_{20}N_2NaO_3^+$ 371.1366, found 371.1365.

ASSOCIATED CONTENT

Ⓢ Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.0c00018.

    Experimental procedures and spectral data of new compounds (PDF)

    Crystallographic data of **3ma** (CIF)

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Notes

The authors declare no competing financial interest.

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