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Formation of Cyclohepta[*b*]indole Scaffolds via Heck Cyclization: A Strategy for Structural Analogues of Ervatamine Group of Indole Alkaloid

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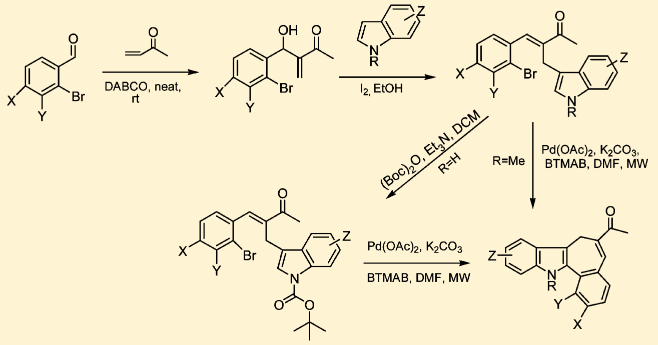
S *Supporting Information*

ABSTRACT: Ervatamine, silicine, methuenine, etc., are naturally occurring alkaloids that exhibit antimicrobial, anticancer, and anti-HIV activities. Indole fused with a seven-membered carbocyclic ring is a commonly observed structural feature among this series of bioactive compounds. This work describes a strategic approach for the synthesis of cyclohepta[*b*]indole structural scaffolds. The synthetic strategy consists of a solvent-free Baylis–Hillman reaction of 2-bromobenzaldehydes, followed by iodine-catalyzed C-alkylation of indole with the Baylis–Hillman adducts. Finally, intramolecular Heck coupling reaction using Pd(OAc)$_2$ as catalyst in the presence of benzyltrimethylammonium bromide under microwave condition produced the desired cyclohepta[*b*]indole derivatives.



INTRODUCTION

Alkaloids containing an indole moiety, such as prenylated indoles, bis-indoles, carbazoles, indoloquinoline, and cyclohepta[*b*]indole, are found to exhibit significant biological activities.[1] For example, ervatamine, silicine, methuenine, ervitsine, actinophyllic acid, caulersin, caulerpin, affinine, and vellosimine are naturally occurring alkaloids that contain an indole nucleus fused with a seven- or eight-membered carbocyclic ring with varying functionality (Figure 1). These compounds have proven as anticancer, antidepressant, anti-HIV, antimicrobial, antileishmanial, and potential therapeutic agents for the treatment of cardiovascular disease.[2] Synthesis of such skeletal analogues can provide a useful lead for the development of new molecular target. Particularly, the synthesis of cyclohepta[*b*]indoles can offer a effective pathway for a large number of polycyclic indole derivatives containing aromatic/nonaromatic rings fused to the [6,7] or [4,5] side of the cyclohepta[*b*]indole substructure.

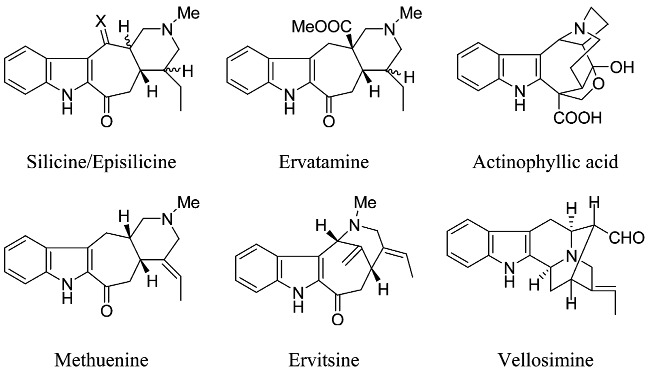

Silicine/Episilicine
Ervatamine
Actinophyllic acid
Methuenine
Ervitsine
Vellosimine

Figure 1. Natural alkaloids containing an indole substructure fused with seven- or eight-membered carbocyclic ring.

Driver et al.[3] recently reported cascade reactions of β,β-disubstituted styryl azides to selectively produce 2,3-disubstituted indoles fused to seven-membered carbocyclic rings. Synthesis of thieno- and benzocyclohepta[*b*]indole derivatives, starting from 7,8,9,10-tetrahydrocyclohepta[*b*]indole-6(5*H*)-one, has been reported elsewhere.[4] Formation of hexahydrocyclohepta[*b*]indole was also observed via a rearrangement reaction during synthesis of 2,3-disubstituted indoles from phenylhydrazine.[5] Recently, a synthetic pathway for structural analogues of bis-indole alkaloids such as caulerpin has been reported.[6] Although a number of approaches for the total synthesis of the aforesaid alkaloids have been revealed,[7] synthesis of these scaffolds necessitates a generalized and viable procedure. In this paper, we are reporting a new synthetic approach for some cyclohepta[*b*]indoles that are structurally analogous to many natural alkaloids (Scheme 1). The key reaction of this multistep process is the intramolecular Heck-type coupling.[8] The precursor halo-indoles were synthesized from the corresponding Baylis–Hilmann adducts via an iodine catalyzed C-alkylation reaction.

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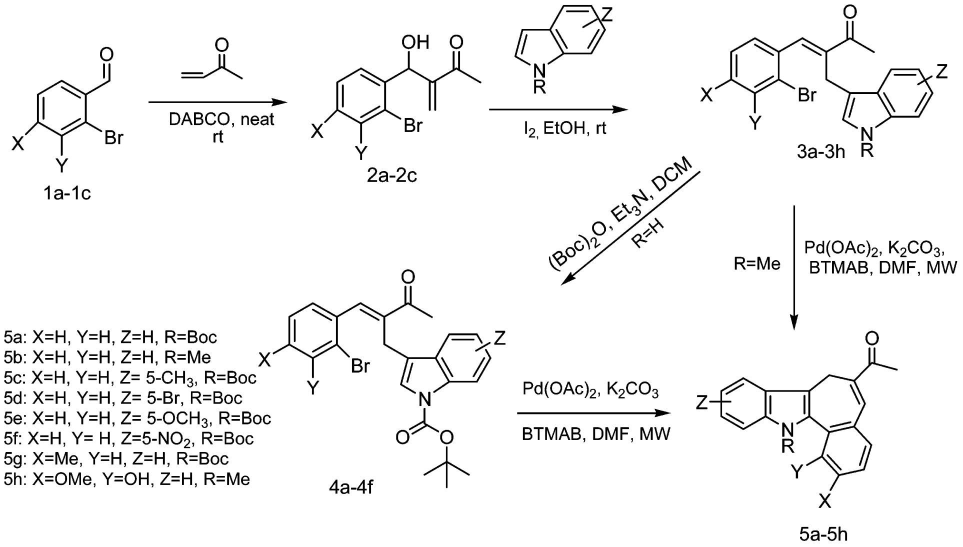
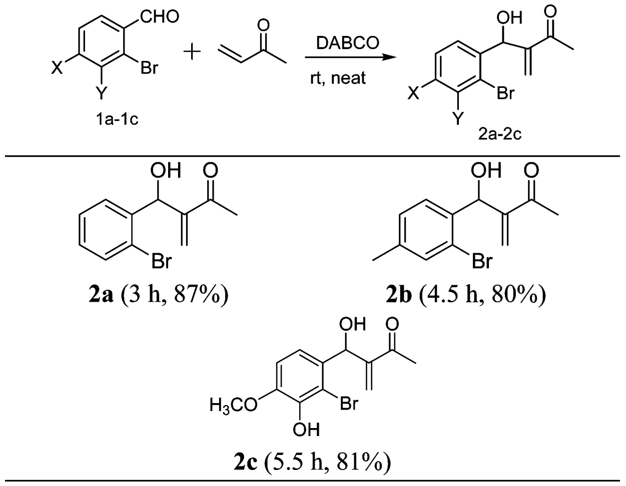
Scheme 1. Synthetic Pathway for Molecular Scaffolds of Cyclohepta[*b*]indoles



■ RESULTS AND DISCUSSION

The Baylis−Hillman reaction,[9] also known as the Morita−Baylis−Hillman reaction, is an important, atom economy, carbon−carbon bond formation organic reaction. The resulted product is an allylic alcohol that offers the prospect of generating the desired functionality during organic synthesis. The initial step of our synthesis is the Baylis−Hillman reaction of substituted 2-bromo benzaldehydes with methyl vinyl ketone (MVK) in the presence 1,4-diazabicyclo[2,2,2]octane (DABCO) as catalyst. The corresponding functionalized allylic alcohols are listed in Table 1. A solvent-free approach was introduced for the formation of the Baylis−Hillman adducts by treating equimolar quantities of aldehydes and MVK in the presence of DABCO (20 mol %) at room temperature.[10] The neat synthesis was found to be comparable for these substrates over the existing solution-based methods in terms of reaction time and yield.

Table 1. Suitable Baylis−Hillman Adduct Synthesis under Neat Conditions[a,b]



[a]Reaction conditions: aldehyde (3 mmol), methyl vinyl ketone (3 mmol), DABCO (20 mol %), rt, 3−5.5 h. [b]Isolated yields.

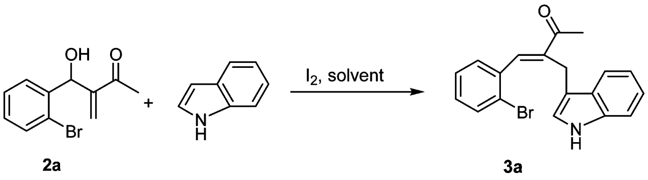
Numerous strategies have been successfully employed for the syntheses of biologically important molecules and natural products via Baylis−Hillman adduct transformation.[9] Perhaps most transformations were performed using Baylis−Hillman acetates as substrates rather than the Baylis−Hillman adducts itself. The direct use of Baylis−Hillman alcohols in organic synthesis without acetylation has been a challenge because the direct substitution of the hydroxyl group of Baylis−Hillman adducts is usually difficult. Yadav et al. first reported the allylic substitution of Baylis−Hillman acetates with indoles.[11] They reported the use of indium tribromide catalyst under reflux conditions for the C-alkylation step. Later, a method for C-alkylation of indoles with Baylis−Hillman alcohols[12] has been reported using 30 mol % of iodine as catalyst in acetonitrile. The regioselective and enantioselective nucleophilic substitution of cyclic Morita−Baylis−Hillman alcohols with indoles was reported elsewhere by the use of a chiral catalyst.[13]

The C-alkylation of indole with the Baylis−Hillman alcohols (**2a**−**2c**) was carried out using iodine as catalyst. To find a better reaction condition, the process was examined under different reaction conditions. Screenings of the reactivity of Baylis−Hillman alcohol (**2a**) with unsubstituted indole in the presence of iodine are summarized in Table 2. The reaction was carried out using different solvents in the presence of varying amounts of iodine. Finally, the use of ethanol and 20 mol % of I_2 at room temperature was found to be the best reaction condition (Table 2, entry 2).

After establishing the optimum reaction conditions for C-alkylation of indole with Baylis−Hilman alcohol, the process was extended to a number of substrates. The results are summarized in Table 3. The crystal structure of compound **3d** is shown in Figure S1 (of the Supporting Information).

For the final step in Scheme 1, our choice was the intramolecular Heck reaction, the palladium-catalyzed carbon−carbon bond forming coupling of an aryl or alkenyl halide with an alkene in the same molecule.[8] Palladium-mediated cross-coupling reactions for the synthesis of heterocyclic compounds have been reported by several groups.[14] Though the palladium-catalyzed chemical transformations of a Baylis−Hillman adduct have been studied,[15] few literatures disclosed the intramolecular Heck coupling of a Baylis−Hillman adduct.[16,17] The intramolecular Heck coupling strategy was

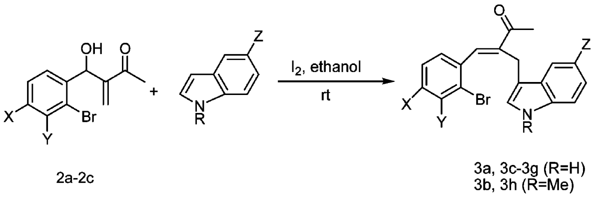
Table 2. Screening Studies of C-Alkylation of Indole with Baylis–Hillman Alcohol 2a[a]

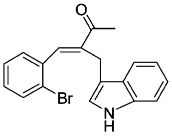


entry	solvent	iodine (mol %)	time (h)	yield (%)[b]
1	CH_3CN	20	5.0	71
2	EtOH	20	3.0	86
3	MeOH	20	4.5	50
4	EtOAc	20	4.5	41
5	THF	20		no reaction
6	toluene	20		no reaction
7	EtOH	10	6	77

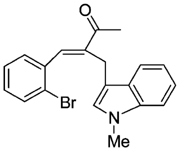
[a]Reaction conditions: **2a** (1.16 mmol), indole (1.2 mmol), solvent (2 mL), rt. [b]Isolated yield.

Table 3. I_2-Catalyzed C-Alkylation of Indole with Baylis–Hillman Adduct[a,b]

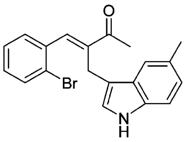




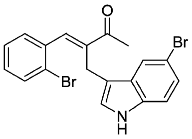
3a (3 h, 86%)



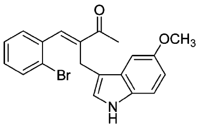
3b (3 h, 78%)



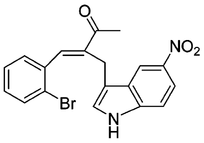
3c (3.5 h, 76%)



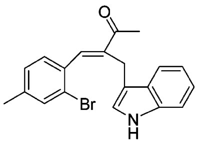
3d (3.5 h, 80%)



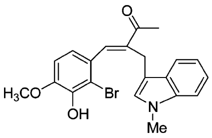
3e (3.5 h, 87%)



3f (4 h. 79%)



3g (3 h, 85%)



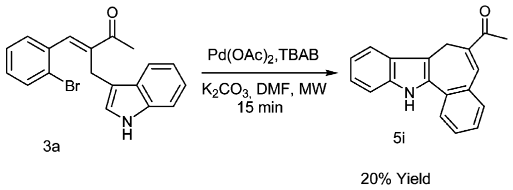
3h (3 h, 80%)

[a]Reaction conditions: **2a**–**2c** (1.16 mmol), indoles (1.2 mmol), I_2 (20 mol %), EtOH (2 mL), rt. [b]Isolated yield

suitably reported by Kim and co-workers during synthesis of pentacyclic benzoazepino[2,1-*a*]isoindole compounds and 7*H*-benzo[3,4]azepino[1,2-*α*,]indole-6-carboxylic acid derivatives.[16] Syntheses of benzazepines using a polymeric support[17a] and constrained scaffolds using aza Baylis–Hillman reaction[17b] were also reported via similar methods.

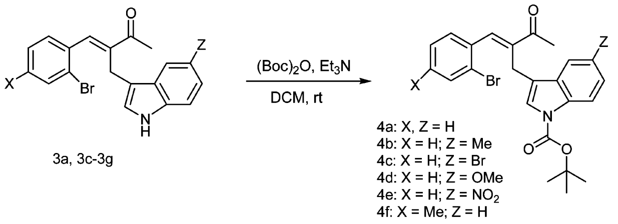
The final step of the synthesis is the intramolecular Heck coupling[8] of compound **3** to obtain the desired cyclohepta[*b*]-indole structure. To achieve the Heck cyclization, we desired to attempt the phosphine-free route using tetrabutyl ammonium salts under Jeffery conditions.[18] Rate enhancement in the activity of palladium catalysts in the presence of tetraalkyl ammonium salts was also observed by several other researchers.[19] Initially, the cyclization reaction was carried out by using $Pd(OAc)_2$ as catalyst in the presence of TBAB under microwave irradiation. To carry out the reaction, a homogeneous paste of the bromo-compound (0.175 mmol), $Pd(OAc)_2$ (10 mol %), TBAB (0.175 mmol), and K_2CO_3 (0.35 mmol) was prepared with a few drops of DMF and was placed under microwave irradiation at a total power of 420 W with the temperature reached up to 100 °C for 15 min. However, the attempt to cyclize compound **3a** resulted in very low product yield (Scheme 2: **5i**, 20%).

Scheme 2. Heck Cyclization of Indole with Free N–H is Found to be a Low Yield Reaction



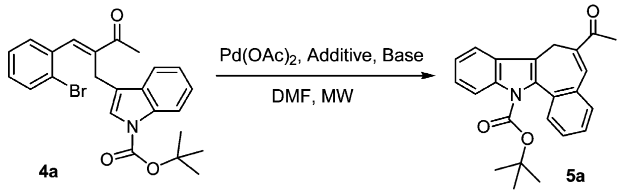
Then, the N–H bond of compound **3a** was protected using ditertiarybutyl dicarbonate in the presence of triethylamine in dichloromethane (Scheme 3).[20] When the cyclization reaction was carried out using Boc-proteted bromo-indole **4a**, the reaction yield was improved to 64% (Table 4, entry 1). The crystal structure of compound **4c** is shown in Figure S2 (of the Supporting Information).

Scheme 3. Synthesis of *N*-Boc-Protected Indole Derivatives for Heck Cyclization



Because the reaction yield was moderate, the reaction was further examined using different additives such as cetyltrimethylammonium bromide (CTAB), PPh_3, and benzyltrimethylammonium bromide (BTMAB) in DMF under microwave irradiation. The results are summarized in Table 4. Use of CTAB and PPh_3 was not found fruitful in comparison to TBAB. However, the use of BTMAB could drive the reaction with promising yield. When the reaction was examined with 5 mol % of the catalyst, the yield was found to increase significantly. Further lowering the catalyst amount could not improve the reaction yield (Table 4, entry 9). Finally, the use of 1 equiv of BTMAB with 2 equiv of K_2CO_3 base in the presence

Table 4. Optimization of Intramolecular Heck Cyclization of 4a to Synthesize Compound 5a



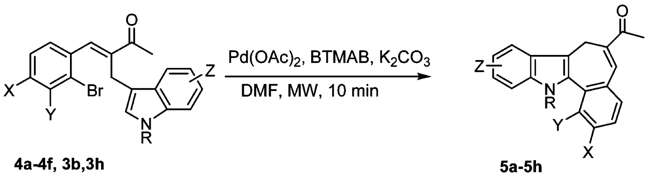
entry	catalyst	additive	base	time (min)	isolated yield (%)
1	$Pd(OAc)_2$ (10 mol %)	TBAB (1.0 equiv)	K_2CO_3 (2.0 equiv)	10.0	64
2	$Pd(OAc)_2$ (10 mol %)	TBAB (1.0 equiv)	K_2CO_3 (2.0 equiv)	15.0	60
3	$Pd(OAc)_2$ (10 mol %)	CTAB (1.0 equiv)	K_2CO_3 (2.0 equiv)	15.0	58
4	$Pd(OAc)_2$ (10 mol %)	Ph_3P (1.0 equiv)	K_2CO_3 (2.0 equiv)	20.0	34
5	$Pd(OAc)_2$ (10 mol %)	BTMAB (1.0 equiv)	K_2CO_3 (2.0 equiv)	10.0	69
6	$Pd(OAc)_2$ (10 mol %)	BTMAB (1.0 equiv)	Et_3N (2.0 equiv)	10.0	20
7	$Pd(OAc)_2$ (10 mol %)	BTMAB (1.0 equiv)	$NaHCO_3$ (2.0 equiv)	10.0	41
8	$Pd(OAc)_2$ (5 mol %)	BTMAB (1.0 equiv)	K_2CO_3 (2.0 equiv)	10.0	78
9	$Pd(OAc)_2$ (3 mol %)	BTMAB (1.0 equiv)	K_2CO_3 (2.0 equiv)	10.0	72

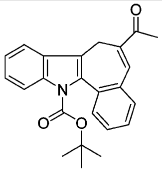
of 5 mol % $Pd(OAc)_2$ (Table 4, entry 8) was found to be the best choice.

Then, the reaction was further extended under the optimized conditions to a number of substrates to provide benzocyclohepta[*b*]indoles. The results are summarized in Table 5. The *N*-methylated compounds **3b** and **3h** also effectively underwent the cyclization reaction to yield the desired product.

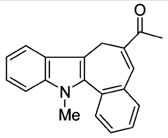
The crystal structure of compound **5d** is shown in Figure S3 (of the Supporting Information). Single crystals of *C*-alkylated indole product **3d** were grown from $CHCl_3$ after column chromatography purification. X-ray data were collected and refined in the $P2_1/c$ monoclinic space group. The asymmetric unit contains a single molecule. Single-crystal X-ray parameters for all structures are tabulated in Table 6. The presence of strong donor N−H in the indole ring and C═O from the acetyl group engaged in N−H···O hydrogen bonding with the symmetry related molecule as dimer (Figure 2a). The halogen atom (Br) is weakly connected to the π-cloud of the indole ring and acetyl carbonyl groups of the second molecule. This interaction is supported by weak C−H···O interaction fulfilling the three-dimensional packing of molecules. Protection of N−H by a Boc functionality blocked the N−H···O dimer formation in structure **4c**; rather, the acetyl group plays the role of C−H···O hydrogen bonded homodimer formation to the symmetry related molecule (Figure 2b). Only one molecule is found in the asymmetric unit in the $P2_1/n$ monoclinic space group for the structure of the molecule **4c**. Strong π···π interactions between the indole ring and the hanging phenyl ring of the next molecule, supported by C−H···Br and C−H···O weak interactions, lead to the 3D structure of **4c**. In structure **5d**, the C−H···O hydrogen bonded homodimer formation is shifted to the protecting Boc group. The ester C═O and C−H from the hanging isobutyl group are engaged in C−H···O hydrogen bonding (Figure 2c). Two molecules are found as symmetry independent molecules in the $Pca2_1$ orthorhombic space group. 3D molecular packing in **5d** is supported by the acetyl group involved in weak C−H···O bonding. Because of the absence of strong hydrogen bonding functional groups, solvent inclusion is avoided in all three structures. A structural correlation based on hydrogen bonding preferences in **3d**, **4c**, and **5d** dictates the shifting of N−H···O dimeric hydrogen bonds to the weaker acetyl C−H···O dimer. In the final

Table 5. Synthesis of Benzocyclohepta[*b*]indoles[a,b]

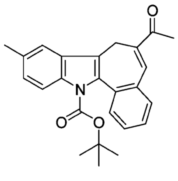




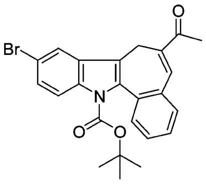
5a (78%)



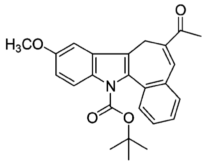
5b (75%)



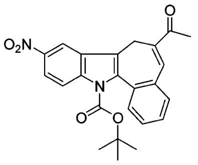
5c (71%)



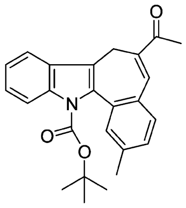
5d (76%)



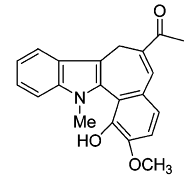
5e (77%)



5f (74%)



5g (72%)

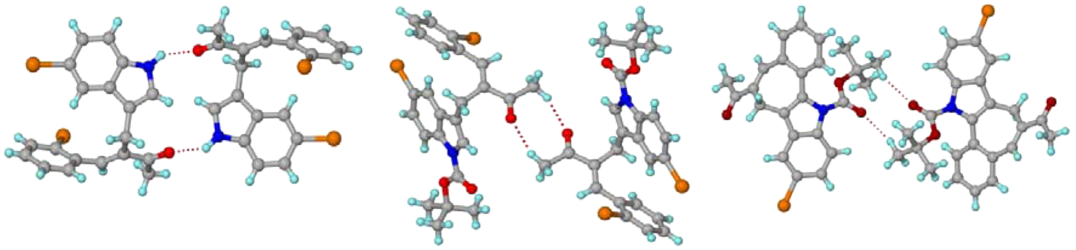


5h (70%)

[a]Reaction conditions: **4a−4f**, **3b**, **3h** (0.175 mmol), BTMAB (0.175 mmol), K_2CO_3 (0.35 mmol), $Pd(OAc)_2$ (5 mol %). [b]Isolated yield.

Table 6. Single-Crystal Data Parameters

parameter	compound **3d**	compound **4c**	compound **5d**
chemical formula	$C_{19}H_{15}Br_2NO$	$C_{24}H_{23}Br_2NO_3$	$C_{24}H_{22}BrNO_3$
formula weight	433.14	533.25	452.34
crystal system	monoclinic	monoclinic	orthorhombic
space group	$P2_1/n$	$P2_1/n$	$Pca2_1$
T/K	296	100	296
a/Å	9.6427(10)	13.2694(7)	16.9222(14)
b/Å	19.228(2)	11.5931(6)	10.4851(8)
c/Å	9.9157(11)	15.3462(8)	23.796(2)
α/deg	90	90	90
β/deg	110.877(5)	108.069(3)	90
γ/deg	90	90	90
Z	4	4	8
V/Å^3	1717.8(3)	2244.3(2)	4222.1(6)
D_{calc}/g cm^{-3}	1.675	1.578	1.423
μ/mm^{-1}	4.722	3.637	1.972
reflns collected	11491	20103	16635
unique reflns	2661	4181	5373
range h	−10 to 11	−17 to 13	−12 to 20
range k	−18 to 23	−14 to 15	−9 to 12
range h	−12 to 10	−19 to 20	−20 to 28
R1 [$I > 2(I)$]	0.0337	0.0490	0.0549
wR2 (all)	0.0946	0.1445	0.1556
goodness-of-fit	1.170	1.058	1.071
instrument	Bruker APEX-II CCD	Bruker APEX-II CCD	Bruker APEX-II CCD



(a) The N-H···O hydrogen bonded homodimer in 3d

(b) The acetyl C-H···O hydrogen bonded homodimer 4c

(c) The ester C-H···O hydrogen bonded homodimer 5d

Figure 2. (a) The N−H···O hydrogen bonded homodimer formation in structure **3d**, which was found to be absent in structure **4c**. (b) Because of Boc protection, preferential formation of acetyl C−H···O dimers in structure **4c**. (c) Preferential formation of Boc ester C−H···O dimers in structure **5d**.

product, the bulkiness prevents acetyl C−H···O dimer formation; rather, the Boc ester is preferred. Br is weakly interacted to C−H and π rings of nearby molecules. Due to the absence of strong hydrogen bonding functional groups, the structures are mostly closed packed, leaving no space for solvent inclusion.

■ CONCLUSION

A new approach has been developed for the synthesis of molecular scaffolds of indole rings fused with seven-membered carbocyclic skeletons. These molecular frameworks are commonly found in many naturally occurring alkaloids such as ervatamine, silicine, methuenine, etc. The synthesis was achieved in sequential steps consisting of Baylis−Hillman reaction, I_2-catalyzed C-alkylation of indole, and a phosphine-free Heck cross-coupling reaction using $Pd(OAc)_2$ as catalyst in the presence of benzyltrimethylammonium bromide. Baylis−Hilmann adducts that can be transformed into carbocycle fused indole analogues have shown tremendous opportunity to construct a library of compounds with desired properties.

■ EXPERIMENTAL SECTION

General Information. Microwave reactions were carried out using an Anton Paar Multiwave PRO microwave reactor having an internal temperature sensing probe. Chemical shifts are given in δ units relative to the tetramethylsilane (TMS) signal as an internal reference. TLC was performed using a 0.2 mm thick precoated TLC plate (Merck, GF-254). Chromatographic purification was performed using flash chromatography over a hand-packed column containing silica gel (230−400 mesh).

X-ray Crystallography. X-ray data reduction was performed using Bruker SAINT software.[21] Intensities for absorption were corrected using SADABS. Structures were solved and refined using SHELXL-2008[22] with anisotropic displacement parameters for non-H atoms. Hydrogen atoms on O and N were experimentally located in all crystal structures. All C−H atoms were fixed geometrically using the HFIX command in SHELX-TL. X-Seed was used to prepare figures and packing diagrams. A check of the final CIF file using PLATON[23] did not show any missed symmetry. Crystallographic cif files (CCDC Nos. 1023198−1023200) are available at www.ccdc.cam.ac.uk/. Molecular diagrams and hydrogen bonded pictures are prepared in the X-Seed program.[24] ORTEPs are generated in the XP module of the SHELXTL program.

General Procedure for the Synthesis of Baylis−Hillman Adducts (2a−2c). Equimolar quantities of the aldehyde (3 mmol) and olefin (3 mmol) were stirred in the presence of DABCO (20 mol %) at room temperature under neat conditions. After completion of the reaction (TLC), the reaction mixture was diluted with ethyl acetate (20 mL) and washed with water (3 × 10 mL). The organic layer was dried over Na_2SO_4, concentrated, and purified by column chromatography using a mixture of petroleum ether and ethyl acetate as eluent.

*3-[(2-Bromo-phenyl)(hydroxy)methyl]but-3-en-2-one (**2a**).* Colorless liquid (0.665 g, 87% yield); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.56−7.51 (m, 2H), 7.37 (t, J = 7.5 Hz, 1H), 7.17 (t, J = 7.8 Hz, 1H), 6.17 (s, 1H), 5.94 (s, 1H), 5.65 (s, 1H), 3.70 (br, 1H), 2.38 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 200.4, 148.7, 140.2, 132.6, 129.1, 128.3, 127.7, 127.6, 122.8, 70.6, 26.3; IR (neat) ν_{max} (cm^{-1}) 3415, 1677, 1467, 1437, 1365, 1118, 1021, 755; m/z (GC-MS): 255 [M$^+$].

*3-[(2-Bromo-4-methylphenyl)(hydroxy)methyl]but-3-en-2-one (**2b**).* Colorless liquid (0.645 g, 80% yield); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.18 (d, J = 7.8 Hz, 1H), 7.12 (s, 1H), 6.92 (d, J = 7.8 Hz, 1H), 5.99 (s, 1H), 5.72 (s, 1H), 5.55 (s, 1H), 3.96 (s, 1H), 2.37 (s, 3H), 2.30 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 199.1, 148.8, 138.5, 137.2, 132.4, 127.8, 127.5, 126.3, 122.2, 69.5, 25.8, 20.1; IR (neat) ν_{max} (cm^{-1}) 3425, 1669, 1477, 1279, 1178, 1041, 785; m/z (GC-MS): 268 [M$^+$]; Anal. Calcd (%) for $C_{12}H_{13}BrO_2$: C, 53.55; H, 4.87; Found: C, 53.69; H, 4.71.

*3-[(2-Bromo-3-hydroxy-4-methoxyphenyl)(hydroxyl)methyl]but-3-en-2-one (**2c**).* White crystals (0.731 g, 81% yield); mp 118−120 °C; ^{1}H NMR (300 MHz, $CDCl_3$, DMSO-d_6) δ 6.89 (d, J = 8.4 Hz, 1H), 6.76 (d, J = 8.7 Hz, 1H), 6.08 (s, 1H), 5.83 (s, 1H), 5.70 (s, 1H), 4.95 (br s, 1H), 3.79 (s, 3H), 2.27 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, DMSO-d_6) δ 198.2, 149.5, 146.3, 142.7, 133.6, 125.1, 117.4, 109.7, 108.9, 68.3, 55.4, 25.7; IR (neat) ν_{max} (cm^{-1}) 3452, 1654, 1485, 1269, 1118, 1033, 790; m/z (GC-MS) 301 [M$^+$]; Anal. Calcd (%) for $C_{12}H_{13}BrO_4$: C, 47.86; H, 4.35; Found: C, 47.76; H, 4.45.

General Procedure for C-Alkylation of Indole with Baylis−Hilmann Adducts *(*3a−3h*)*. To a stirred solution of Baylis−Hilmann adduct (1.16 mmol) in ethanol (2 mL) was added indole (1.2 mmol) and iodine (20 mol %). The mixture was stirred to completion as monitored by TLC. After completion of the reaction, it was quenched with a saturated solution of sodium thiosulfate and extracted with ethyl acetate. The organic layer was separated, dried over anhydrous Na_2SO_4, and concentrated to give the crude product. The product was purified by column chromatography using a mixture of petroleum ether and ethyl acetate as eluent.

*4-(2-Bromophenyl)-3-[(1H-indol-3-yl)methyl]but-3-en-2-one (**3a**).* Brown liquid (0.352 g, 86% yield); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.01 (br s, 1H), 7.72 (s, 1H), 7.65 (d, J = 9.0 Hz, 1H), 7.46 (d, J = 7.8 Hz, 1H), 7.35−7.32 (m, 2H), 7.21−7.08 (m, 4H), 6.83 (s, 1H), 3.87 (s, 2H), 2.47 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 200.8, 141.1, 139.3, 136.5, 135.7, 132.8, 130.4, 130.3, 128.0, 127.6, 124.5, 122.3, 122.1, 119.3, 118.8, 113.4, 111.5, 26.7, 22.9; IR (neat) ν_{max} (cm^{-1}) 3406, 1667, 1620, 1457, 1431, 1353, 1216, 1024, 747; m/z (GC-MS) 355 [M$^+$]; Anal. Calcd (%) for $C_{19}H_{16}BrNO$: C, 64.42; H, 4.55; N, 3.95; Found: C, 64.25; H, 4.70; N, 4.09.

*4-(2-Bromophenyl)-3-[(1-methyl-1H-indol-3-yl)methyl]but-3-en-2-one (**3b**).* Yellow liquid (0.323 g, 76% yield); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.71 (s, 1H), 7.65 (d, J = 9.3 Hz, 1H), 7.43−7.35 (m, 2H), 7.24−7.06 (m, 5H), 6.71 (s, 1H), 3.82 (s, 2H), 3.70(s, 3H), 2.47 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 200.2, 141.3, 138.8, 137.1, 135.8, 132.8, 130.4, 130.1, 127.8, 127.5, 126.8, 124.5, 121.7, 119.0, 118.8, 112.2, 109.2, 32.7, 26.7, 22.6; IR (neat) ν_{max} (cm^{-1}) 1671, 1615, 1465, 1431, 1373, 1329, 1215, 1025, 753; m/z (GC-MS) 367 [M$^+$]; Anal. Calcd (%) for $C_{20}H_{18}BrNO$: C, 65.23; H, 4.93; N, 3.80; Found: C, 65.35; H, 5.02; N, 3.70.

*4-(2-Bromophenyl)-3-[(5-methyl-1H-indol-3-yl)methyl]but-3-en-2-one (**3c**).* Light brown crystals (0.319 g, 75% yield); mp 121−123 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.01 (br s, 1H), 7.74 (s, 1H), 7.68 (d, J = 6.0 Hz, 1H), 7.42 (d, J = 6.9 Hz, 1H), 7.23−7.19 (m, 4H), 7.03 (d, J = 8.4 Hz, 1H), 6.81(s, 1H), 3.88 (s, 2H), 2.48 (s, 3H), 2.43 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 200.3, 141.1, 138.7, 135.7, 134.5, 132.7, 130.3, 129.9, 128.4, 127.4, 127.1, 124.4, 123.6, 122.1, 118.4, 113.1, 110.7, 26.6, 22.5, 21.4; IR (neat) ν_{max} (cm^{-1}) 3402, 1666, 1624, 1462, 1431, 1350, 1219, 1026, 756; m/z (GC-MS) 366.9 [M$^+$]. Anal. Calcd (%) for $C_{20}H_{18}BrNO$: C, 65.23; H, 4.93; N, 3.80; Found: C, 65.14; H, 4.86; N, 3.92.

*4-(2-Bromophenyl)3-[(5-bromo-1H-indol-3-yl)methyl]but-3-en-2-one (**3d**).* White crystals (0.395 g, 79% yield); mp 124−126 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.14 (br s, 1H), 7.71 (s, 1H), 7.68 (d, J = 7.2 Hz, 1H), 7.41 (s, 1H), 7.34−7.15 (m, 5H), 6.86 (s, 1H), 3.80 (s, 2H), 2.49 (s, 3H).^{13}C NMR (75 MHz, $CDCl_3$) δ 200.1, 141.1, 139.5, 135.7, 134.8, 132.9, 130.3, 130.2, 128.7, 127.5, 124.8, 124.3, 123.5, 121.5, 113.5, 112.6, 112.5, 26.6, 22.1. IR (neat) ν_{max} (cm^{-1}) 3371, 1666, 1624, 1458, 1435, 1381, 1219, 1029, 756; m/z (GC-MS) 432 [M$^+$]. Anal. Calcd (%) for $C_{19}H_{15}Br_2NO$: C, 52.69; H, 3.49; N, 3.23; Found: C, 52.58; H, 3.41; N, 3.29.

*4-(2-Bromophenyl)-3-[(5-methoxy-1H-indol-3-yl)methyl]but-3-en-2-one (**3e**).* Yellow liquid (0.382 g, 86% yield); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.97 (s, 1H), 7.72 (s, 1H), 7.65 (d, J = 7.5 Hz, 1H), 7.40 (d, J = 7.2 Hz, 1H), 7.23−7.17 (m, 3H), 6.86−6.82(m, 3H), 3.85 (s, 2H), 3.80 (s, 3H), 2.49 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 200.3, 153.5, 140.9, 138.6, 135.4, 132.5, 131.3, 130.0, 129.8, 127.2, 127.0, 124.2, 122.8, 112.8, 112.0, 111.8, 100.1, 55.5, 26.3, 22.4; IR (neat) ν_{max} (cm^{-1}) 3394, 1666, 1620, 1485, 1435, 1392, 1215, 1107, 750; m/z (GC-MS) 383 [M$^+$]; Anal. Calcd (%) for $C_{20}H_{18}BrNO_2$: C, 65.51; H, 4.72; N, 3.65; Found: C, 65.35; H, 4.88; N, 3.79.

*4-(2-Bromophenyl)-3-[(5-nitro-1H-indol-3-yl)methyl]but-3-en-2-one (**3f**).* Light yellow crystals (0.360 g, 78% yield); mp 180−182 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.79 (br s, 1H), 8.22 (s, 1H), 8.07 (d, J = 9.0 Hz, 1H), 7.72 (s, 1H), 7.69 (d, J = 8.7 Hz, 1H), 7.34−7.23 (m, 4H), 7.04 (s, 1H), 3.88 (s, 2H), 2.51 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 199.7, 141.5, 140.9, 140.1, 138.9, 135.5, 133.0, 130.3, 129.8, 127.5, 126.4, 125.3, 124.0, 117.7, 116.5, 116.3, 110.9, 26.3, 21.8; IR (neat) ν_{max} (cm^{-1}) 3359, 1666, 1622, 1518, 1470, 1330, 1217, 1100, 752; m/z (GC-MS) 397 [M$^+$]. Anal. Calcd (%) for $C_{19}H_{15}BrN_2O_3$: C, 57,16; H, 3.79; N, 7.02; Found: C, 57.27; H, 3.68; N, 6.89.

*4-(2-Bromo-4-methylphenyl)-3-[(1H-indol-3-yl)methyl)]-but-3-en-2-one (**3g**).* Yellow liquid (0.358 g, 84% yield); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.12 (br s, 1H), 7.76 (s, 1H), 7.49 (br, 2H), 7.34−7.29 (m, 2H), 7.22−7.08 (m, 2H), 7.01 (d, J = 7.8 Hz, 1H), 6.81 (s, 1H), 3.89 (s, 2H), 2.49 (s, 3H), 2.33 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 200.2, 140.6, 139.0, 136.2, 133.2, 132.5, 129.9, 128.2, 126.9, 124.3, 121.9, 121.8, 119.1, 118.8, 113.8, 111.0, 26.5, 22.6, 20.8; IR (neat) ν_{max} (cm^{-1}) 3407, 1666, 1602, 1483, 1456, 1353, 1221, 1041, 744; m/z (GC-MS) 367 [M$^+$]; Anal. Calcd (%) for $C_{20}H_{18}BrNO$: C, 65.23; H, 4.93; N, 3.80; Found: C, 65.31; H, 5.04; N, 3.64.

*4-(2-Bromo-3-hydroxy-4-methoxyphenyl)-3-[(1-methyl-1H-indol-3-yl)methyl]but-3-en-2-one (**3h**).* White crystalline solid (0.379 g, 79% yield); mp 102−104 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.63 (s, 1H), 7.50 (d, J = 7.8 Hz, 1H), 7.29−7.20 (m, 2H), 7.11 (t, J = 7.5 Hz 1H), 6.99 (d, J = 8.4 Hz, 1H), 6.70 (d, J = 8.7 Hz, 2H), 6.06 (s, 1H), 3.88 (s, 5H), 3.71 (s, 3H), 2.49 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 200.1, 147.1, 143.2, 140.2, 138.9, 137.0, 128.5, 127.3, 126.5, 121.5, 121.4, 118.9, 118.6, 112.4, 110.6, 109.2, 109.0, 56.2, 32.6, 26.4, 22.6; IR (neat) ν_{max} (cm^{-1}) 1662, 1620, 1458, 1415, 1273, 1157, 744; m/z (GC-MS) 413 [M$^+$]. Anal. Calcd (%) for $C_{21}H_{20}BrNO_3$: C, 60.88; H, 4.87; N, 3.38; Found: C, 60.99; H, 4.95; N, 3.27.

General Procedure for Boc-Protection of Indoles (4a−4f). To a stirred solution of C-alkylation products (0.4 mmol) in 1 mL of DCM, di-*tert*-butyl-dicarbonate (0.481 mmol) and triethylamine (1.2 mmol) were added sequentially at room temperature. The completion of the reaction was monitored by TLC. The reaction mixture was extracted with DCM, dried over anhydrous Na_2SO_4, concentrated, and purified by column chromatography using a mixture of petroleum ether and ethyl acetate as eluent.

*3-[2-(2-Bromobenzylidene)-3-oxobutyl]indole-1-carboxylic Acid tert-Butyl Ester (**4a**).* Brown semisolid (0.173 g, 96% yield); ^{1}H NMR (300 MHz, CDCl$_3$) δ 8.06 (s, 1H), 7.78 (s, 1H), 7.65 (d, J = 9.0 Hz, 1H), 7.41 (d, J = 7.5 Hz, 1H), 7.33−7.17 (m, 6H), 3.78 (s, 2H), 2.53 (s, 3H), 1.65 (s, 9H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 199.1, 149.7, 140.3, 140.2, 135.6, 135.5, 132.8, 130.2, 130.0, 127.5, 124.5, 124.2, 122.9, 122.5, 119.6, 119.1, 118.8, 115.2, 83.4, 28.2, 26.3, 22.1 ; IR (neat) ν_{max} (cm^{-1}) 1731, 1674, 1452, 1370, 1256, 1158, 1083, 748; m/z (GC-MS) 453 [M$^+$]; Anal. Calcd (%) for $C_{24}H_{24}BrNO_3$: C, 63.44; H, 5.32; N, 3.08; Found: C, 63.28; H, 5.47; N, 3.23.

*3-[2-(2-Bromobenzylidene)-3-oxobutyl]-5-methylindole-1-carboxylic Acid tert-Butyl Ester (**4b**).* White semisolid (0.177 g, 95% yield); ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.97 (s, 1H), 7.78 (s, 1H), 7.67 (d, J = 7.2 Hz, 1H), 7.38 (d, J = 7.2 Hz, 1H), 7.25−7.12 (m, 5H), 3.78 (s, 2H), 2.54 (s, 3H), 2.42 (s, 3H), 1.66 (s, 9H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 199.3, 149.7, 140.1, 139.9, 135.5, 133.5, 132.7, 131.7, 130.2, 130.1, 129.9, 127.4, 125.6, 124.1, 122.8, 118.8, 118.3, 114.7, 83.2, 28.1, 26.2, 22.0, 21.2; IR (neat) ν_{max} (cm^{-1}) 1739, 1678, 1462, 1377, 1257, 1161, 1084, 756; m/z (GC-MS) 469 [M$^+$]; Anal. Calcd (%) for $C_{25}H_{26}BrNO_3$: C, 64.11; H, 5.60; N, 2.99; Found: C, 64.01; H, 5.75; N, 2.82.

*5-Bromo-3-[2-(2-bromobenzylidene)-3-oxobutyl]indole-1-carboxylic Acid tert-Butyl Ester (**4c**).* White solid (0.203 g, 96% yield) mp 117−119 °C; ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.93 (s, 1H), 7.75 (s, 1H), 7.66 (d, J = 8.4 Hz, 1H), 7.37 (d, J = 9.0 Hz, 1H), 7.29−7.20 (m, 5H), 3.72 (s, 2H), 2.53 (s, 3H), 1.64 (s, 9H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 199.1, 149.2, 140.4, 139.9, 135.4, 134.0, 132.8, 131.7, 130.2, 129.7, 127.4, 127.0, 124.1, 123.9, 121.6, 117.8, 116.5, 115.7, 83.8, 28.0, 26.1, 21.6; IR (neat) ν_{max} (cm^{-1}) 1739, 1674, 1458, 1373, 1261, 1157, 1095, 756; m/z (GC-MS) 531 [M$^+$]; Anal. Calcd (%) for $C_{24}H_{23}Br_2NO_3$: C, 54.06; H, 4.35; N, 2.63; Found: C, 54.21; H, 4.54; N, 2.45.

*3-[2-(2-Bromobenzylidene)-3-oxobutyl]-5-methoxyindole-1-carboxylic Acid tert-Butyl Ester (**4d**).* Yellow semisolid (0.185 g, 96% yield); ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.98 (s, 1H), 7.77 (s, 1H), 7.63 (d, J = 6.3 Hz, 1H), 7.35 (d, J = 6.3 Hz, 1H), 7.22−7.17 (m, 3H), 6.93 (d, J = 8.7 Hz, 1H), 6.86 (s, 1H), 3.80 (s, 3H), 3.76 (s, 2H), 2.54 (s, 3H), 1.65 (s, 9H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 192.9, 149.4, 143.3, 133.9, 133.8, 129.2, 126.4, 124.5, 123.8, 123.6, 121.1, 117.8, 117.1, 112.1, 109.5, 106.8, 95.2, 76.9, 49.2, 21.8, 19.9, 15.8; IR (neat) ν_{max} (cm^{-1}) 1728, 1674, 1477, 1381, 1257, 1157, 1080, 763; m/z (GC-MS) 485 [M$^+$]; Anal. Calcd (%) for $C_{25}H_{26}BrNO_4$: C, 61.99; H, 5.41; N, 2.89; Found: C, 61.81; H, 5.63; N, 3.08.

*3-[2-(2-Bromobenzylidene)-3-oxobutyl]-5-nitroindole-1-carboxylic Acid tert-Butyl Ester (**4e**).* Yellow semisolid (0.190 g, 96% yield); ^{1}H NMR (300 MHz, CDCl$_3$) δ 8.06−7.97 (m, 3H), 7.66 (s, 1H), 7.54 (d, J = 7.8 Hz, 1H), 7.23−7.12 (m, 4H), 3.72 (s, 2H), 2.47 (s, 3H), 1.60 (s, 9H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 198.3, 148.2, 142.6, 140.4, 139.3, 137.8, 134.8, 132.3, 129.8, 129.3, 129.1, 127.0, 125.5, 123.2, 118.8, 118.7, 114.7, 114.5, 84.2, 27.4, 25.5, 20.8; IR (neat) ν_{max} (cm^{-1}) 1740, 1673, 1520, 1446, 1339, 1258, 1155, 1107, 735; m/z (GC-MS) 500 [M$^+$]; Anal. Calcd (%) for $C_{24}H_{23}BrN_2O_5$: C, 57.73; H, 4.64; N, 5.61; Found: C, 57.53; H, 4.44; N, 5.84.

*3-[2-(2-Bromo-4-methylbenzylidene)-3-oxobutyl]indole-1-carboxylic Acid tert-Butyl Ester (**4f**).* Yellow semisolid (0.177 g, 95% yield); ^{1}H NMR (300 MHz, CDCl$_3$) δ 8.08 (s, 1H), 7.80 (s, 1H), 7.48 (s, 1H), 7.44 (d, J = 7.5 Hz, 1H), 7.31−7.19 (m, 4H), 7.02 (d, J = 7.5 Hz, 1H), 3.79 (s, 2H), 2.53 (s, 3H), 2.32 (s, 3H), 1.66 (s, 9H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 199.3, 149.7, 146.6, 140.7, 140.2, 139.6, 133.2, 132.3, 130.1, 129.6, 128.2, 124.3, 124.1, 122.7, 122.3, 118.9, 118.8, 115.1, 83.4, 28.1, 26.2, 22.1, 20.8; IR (neat) ν_{max} (cm^{-1}) 1732, 1674, 1624, 1454, 1369, 1257, 1157, 1083, 752; m/z (GC-MS) 469 [M$^+$]; Anal. Calcd (%) for $C_{25}H_{26}BrNO_3$: C, 64.11; H, 5.60; N, 2.99; Found: C, 64.28; H, 5.37; N, 2.75.

General Procedure for Intramolecular Heck Coupling (5a−5h). To the mixture of compounds **4a**−**4f**, **3b**, and **3h** (1.0 equiv, 0.175 mmol), 2.0 equiv (0.35 mmol) of K_2CO_3, Pd(OAc)$_2$ (5 mol %), and benzyltrimethylammonium bromide (1.0 equiv, 0.175 mmol), a few drops of DMF were added just to prepare a homogeneous phase. The mixture was placed under microwave irradiation conditions at a total power of 420 W. The color of the reaction mixture changed from brown to reddish within 10 min. The reaction mixture was extracted with diethyl ether, washed with water, dried over anhydrous Na_2SO_4, and concentrated to give the crude product. The crude products were purified by column chromatography using a mixture of petroleum ether and ethyl acetate as eluent to obtain the pure compounds.

*6-Acetyl-7H-benzo[6,7]cyclohepta[1,2-b]indole-12-carboxylic Acid tert-Butyl Ester (**5a**).* Yellow crystal (0.050 g, 78% yield); mp 173−175 °C; ^{1}H NMR (300 MHz, CDCl$_3$) δ 8.13 (d, J = 7.2 Hz, 1H), 7.75 (d, J = 7.2 Hz, 1H), 7.63 (s, 1H), 7.52 (t, J = 7.5 Hz, 2H), 7.42−7.30 (m, 4H), 3.44(br, 2H), 2.48 (s, 3H), 1.38 (s, 9H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 196.7, 150.4, 143.3, 139.1, 138.5, 133.7, 133.3, 132.7, 130.3, 130.2, 128.1, 127.2, 126.6, 126.2, 125.2, 123.1, 119.1, 115.0, 83.6, 27.6, 25.6, 18.3; IR (neat) ν_{max} (cm^{-1}) 1731, 1664, 1455, 1316, 1228, 1152, 752; m/z (GC-MS) 373 [M$^+$]. Anal. Calcd (%) for $C_{24}H_{23}NO_3$: C, 77.19; H, 6.21; N, 3.75; Found: C, 77.12; H, 6.14; N, 3.67.

*1-(12-Methyl-7,12-dihydrobenzo[6,7]cyclohepta[1,2-b]indol-6-yl)-ethanone (**5b**).* Light brown crystals (0.037 g, 75% yield); mp 124−126 °C; ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.82 (d, J = 7.8 Hz, 1H), 7.57 (d, J = 9.0 Hz, 1H), 7.54−7.17 (m, 7H), 3.77 (s, 3H), 3.51 (br s, 2H), 2.43 (s, 3H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 196.9, 144.0,139.8, 138.1, 135.2, 134.7, 131.6, 131.0, 128.9, 127.9, 126.4, 125.6, 122.5, 119.8, 119.0, 117.8, 109.7, 32.5, 25.7, 18.8; IR (neat) ν_{max} (cm^{-1}) 1661, 1618, 1469, 1434, 1358, 1277, 1252, 1206, 1183, 743; m/z (GC-MS) 287 [M$^+$]. Anal. Calcd (%) for $C_{20}H_{17}NO$: C, 83.59; H, 5.96; N, 4.87; Found: C, 83.50; H, 5.87; N, 4.80.

*6-Acetyl-9-methyl-7H-benzo[6,7]cyclohepta[1,2-b]indole-12-carboxylic Acid tert-Butyl Ester (**5c**).* Yellow crystal (0.047 g, 71% yield); mp 214−216 °C; ^{1}H NMR (300 MHz, CDCl$_3$) δ 8.01 (d, J = 8.4 Hz, 1H), 7.65 (s, 1H), 7.55−7.50 (m, 3H), 7.42−7.37 (m, 2H), 7.19 (d, J = 8.4 Hz, 1H), 3.41(br s, 2H), 2.49(s, 6H), 1.39(s, 9H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 196.7, 150.4, 143.3, 139.1, 136.7, 133.7, 133.1, 132.7, 132.5, 130.1, 128.2, 127.1, 126.5, 126.1, 118.9, 114.6, 83.4, 27.6, 25.5, 21.2, 18.1; IR (neat) ν_{max} (cm^{-1}) 1728, 1662, 1454, 1311, 1230, 1157, 767; m/z (GC-MS) 387 [M$^+$]. Anal. Calcd (%) for $C_{25}H_{25}NO_3$: C, 77.49; H, 6.50; N, 3.61; Found: C, 77.59; H, 6.35; N, 3.75.

*6-Acetyl-9-bromo-7H-benzo[6,7]cyclohepta[1,2-b]indole-12-carboxylic Acid tert-Butyl Ester (**5d**).* Yellow crystal (0.059 g, 76% yield); mp 190−192 °C; ^{1}H NMR (300 MHz, CDCl$_3$) δ 8.00 (d, J = 9.0 Hz, 1H), 7.87 (s, 1H), 7.63 (s, 1H), 7.53−7.51 (m, 2H), 7.44−7.41(m, 3H), 3.43(br s, 2H), 2.49(s, 3H), 1.37(s, 9H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 196.5, 150.0, 143.2, 138.9, 137.1, 134.6, 133.4, 132.1, 130.2, 129.7, 127.8, 127.2, 126.6, 125.4, 121.6, 116.4, 116.3, 84.1, 27.5, 25.5, 18.1; IR (neat) ν_{max} (cm^{-1}) 1739, 1658, 1454, 1338, 1284, 1153, 763; m/z (GC-MS) 451 [M$^+$]. Anal. Calcd (%) for $C_{24}H_{22}BrNO_3$: C, 63.73; H, 4.90; N, 3.10; Found: C, 63.63; H, 4.98; N, 3.21.

*6-Acetyl-9-methoxy-7H-benzo[6,7]cyclohepta[1,2-b]indole-12-carboxylic Acid tert-Butyl Ester (**5e**).* Orange crystal (0.053 g, 77% yield); mp 175−178 °C; ^{1}H NMR (300 MHz, CDCl$_3$) δ 8.03 (d, J = 9.0 Hz, 1H), 7.64 (s, 1H), 7.55−7.49 (m, 2H), 7.41(t, J = 7.2 Hz, 2H), 7.18 (s, 1H), 6.98 (d, J = 9.0 Hz, 1H), 3.92(s, 3H), 3.38 (br s, 2H), 2.49 (s, 3H), 1.39 (s, 9H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 196.6, 156.2, 150.3, 143.2, 139.1, 134.2, 133.1, 132.6, 130.2, 130.1, 128.7, 127.1, 126.4, 126.1, 115.9, 114.2, 101.1, 83.4, 55.7, 27.6, 25.4, 18.2; IR (neat) ν_{max} (cm^{-1}) 1724, 1658, 1473, 1319, 1230, 1153, 771; m/z (GC-MS) 403 [M$^+$]. Anal. Calcd (%) for $C_{25}H_{25}NO_4$: C, 74.42; H, 6.25; N, 3.47; Found: C, 74.31; H, 6.14; N, 3.39.

*6-Acetyl-9-nitro-7H-benzo[6,7]cyclohepta[1,2-b]indole-12-carboxylic Acid tert-Butyl Ester (**5f**).* Fine yellow crystal (0.053 g, 74% yield); mp 188−190 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.17 (s, 1H), 8.00, (d, J = 8.7 Hz, 1H), 7.89, (d, J = 7.8 Hz, 1H), 7.73- 7.67 (m, 2H), 7.57−7.44 (m, 3H), 3.58 (s, 2H), 2.45(s, 3H), 1.20 (s, 9H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 197.1, 143.5, 140.1, 139.9, 139.3, 138.6, 136.3, 132.7, 132.5, 130.0, 128.8, 127.2, 126.4, 125.2, 116.8, 115.6, 114.6, 111.3, 78.6, 30.1, 25.3, 17.8; IR (neat) ν_{max} (cm^{-1}) 1728, 1647, 1465, 1334, 1207, 1157, 732; m/z (GC-MS) 418 [M$^+$]. Anal. Calcd (%) for $C_{24}H_{22}N_2O_5$: C, 68.89; H, 5.30; N, 6.69; Found: C, 68.77; H, 5.40; N, 6.78.

*6-Acetyl-2-methyl-7H-benzo[6,7]cyclohepta[1,2-b]indole-12-carboxylic Acid tert-Butyl Ester (**5g**).* Yellow solid (0.048 g, 72% yield); mp 123−126 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.14 (d, J = 7.8 Hz, 1H), 7.77 (d, J = 7.2 Hz, 1H), 7.63 (s, 1H), 7.43−7.31 (m, 4H), 7.21 (d, J = 7.8 Hz, 1H), 3.39 (br s, 2H), 2.48 (s, 3H), 2.46 (s, 3H), 1.37 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 196.7, 150.4, 142.3, 139.2, 138.5, 137.0, 133.7, 132.5, 130.7, 130.5, 130.3, 128.0, 127.3, 126.2, 125.0, 122.9, 119.0, 114.7, 83.3, 27.5, 25.5, 21.4, 18.2; IR (neat) ν_{max} (cm^{-1}) 1735, 1620, 1415, 1253, 1141, 748; m/z (GC-MS) 387 [M$^+$]. Anal. Calcd (%) for $C_{24}H_{25}NO_3$: C, 77.49; H, 6.50; N, 3.61; Found: C, 77.37; H, 6.63; N, 3.56.

*1-(1-Hydroxy-2-methoxy-12-Methyl-7,12-dihydro-benzo[6,7]-cyclohepta[1,2-b]indol-6-yl)-ethanone (**5h**).* Brown solid (0.040 g, 70% yield); mp 149−151 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.81 (d, J = 7.8 Hz, 1H), 7.46 (s, 1H), 7.36 (d, J = 8.1 Hz, 1H), 7.24−7.09 (m, 3H), 7.01 (d, J = 8.4 Hz, 1H), 4.51 (d, J = 14.4 Hz, 1H), 4.03 (s, 3H), 3.67 (s, 3H), 2.62 (d, J = 14.7 Hz, 1H), 2.40 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 196.8, 146.3, 143.9, 142.3, 139.2, 138.2, 131.8, 128.9, 125.4, 122.8, 121.9, 119.2, 118.8, 118.3, 117.3, 109.5, 109.4, 56.2, 32.8, 29.6, 25.5; IR (neat) ν_{max} (cm^{-1}) 1647, 1616, 1543, 1512, 1458, 1338, 1273, 1252, 1152, 744; m/z (GC-MS) 333 [M$^+$]. Anal. Calcd (%) for $C_{21}H_{19}NO_3$: C, 75.66; H, 5.74; N, 4.20; Found: C, 75.78; H, 5.69; N, 4.34.

*1-(7,12-Dihydro-benzo[6,7]cyclohepta[1,2-b]indol-6-yl)-ethanoate (**5i**).* Yellow solid (0.009 g, 20% yield); mp 89−91 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.86 (br s, 1H), 7.94 (s, 1H), 7.83 (d, J = 7.8 Hz, 1H), 7.56−7.27 (m, 7H), 3.57(s, 2H), 2.50 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 196.4, 139.6, 137.3, 136.0, 131.8, 131.0, 130.1, 129.5, 129.4, 127.5, 126.6, 125.4, 124.1, 121.1, 118.9, 113.7, 111.3, 31.2, 25.6; IR (neat) ν_{max} (cm^{-1}) 3284, 1635, 1596, 1493, 1339, 1252, 743; GCMS (m/z) 273[M$^+$]; Anal. Calcd (%) for $C_{19}H_{15}NO$: C, 83.49; H, 5.53; N, 5.12; Found: C, 83.60; H, 5.44; N, 5.08.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^{1}H NMR, ^{13}C NMR, and GC-Mass spectra and crystallographic data. 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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