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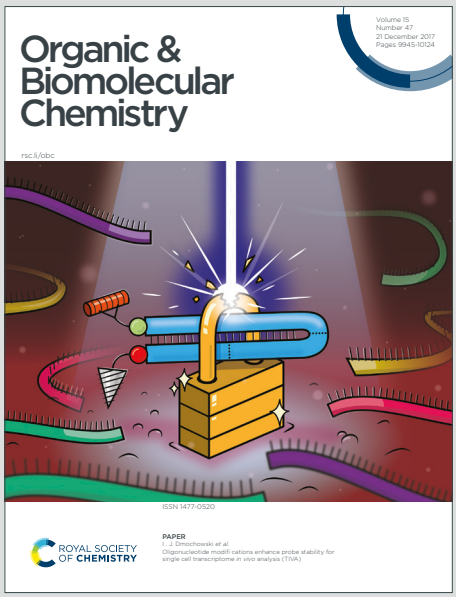

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PAPER

Palladium-catalyzed dearomative allylation of indoles with cyclopropyl acetylenes: access to indolenine derivatives

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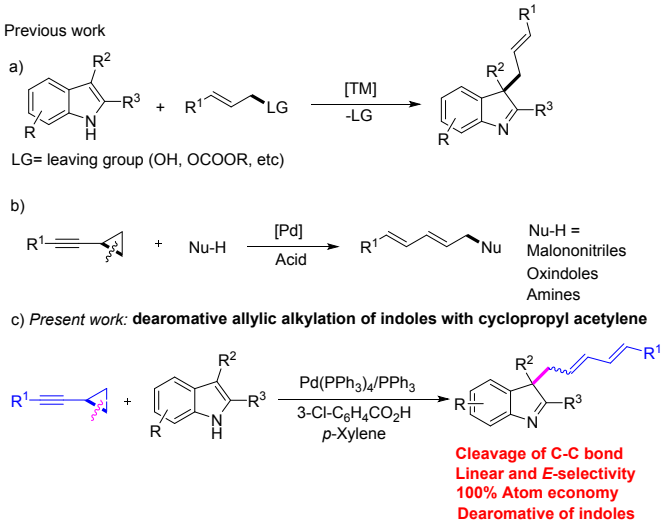
A palladium-catalyzed redox-neutral allylic alkylation of indoles with cyclopropyl acetylenes has been disclosed. Various 1,3-diene indolenine framework bearing a quaternary stereocenter at the C3 position were synthesized straightforwardly in good to excellent yields with high regio- and stereoselectivities. The reaction could be further expanded to the dearomatization of naphthols to synthesize functionalized cyclohexadienones with 1,3-diene motifs. The reaction exhibited high atom economy and good functional group tolerance.

Introduction

Indolenines are privileged heterocyclic motifs frequently appearing as a structural core in a large family of alkaloids and bioactive pharmaceuticals, which display significant physiological activity such as anticancer, antibacterial, and antifungal properties.[1] Additionally, they also provide an attractive platform for structure-activity relationship studies and lead compound discovery in drug development.[2] As many indolenine-containing alkaloids possess C3 quaternary stereocenters, it is of great significance to develop catalytic methods to build these centers. The palladium-catalyzed dearomative allylation of 3-substituted 1H-indoles represents an efficient method to achieve this goal (Scheme 1, (a)).[3] Elegant examples have been reported by Tamaru,[4] Trost,[5] Rawal,[6] You,[7] and other groups.[8] In spite of these advances, most of the allylation partners for the dearomatization of 3-substituted 1H-indoles have been limited to allylic alcohols and carbonates. Some unavoidable limitations of the method still exist with respect to the formation of stoichiometric valueless byproducts and prefunctionalization of substrates.

Recently, the transition-metal-catalyzed redox-neutral allylic alkylation of internal or terminal alkynes in the presence of metal with acid catalyst as the co-catalyst has been described with excellent atom efficiency.[9] A series of N-, O- and C-nucleophiles with these alkynes have been reported to establish linear or branched allylated compounds in the presence of palladium or rhodium catalysts.[10]All the same, the catalytic synthesis of versatile 1,3-diene motifs remains scared.[11] Yao and Lin have developed an elegant palladium-catalyzed redox-neutral allylic alkylation with unactivated skipped enynes to access a wide array of 1,3-dienes.[12] Yamamoto first reported cyclopropyl phenyl acetylene could provide a general system for building 1,3-dienes by C-C bond cleavage of cyclopropane (Scheme 1, (b)).[13,14] Our group recently reported a palladium-catalyzed allylic alkylation of oxindoles with cyclopropyl acetylenes for the synthesis of 1,3-diene oxindole frameworks.[15] As part of our ongoing studies of allylation reaction of alkynes,[16] we report herein a palladium-catalyzed dearomatization of indoles with cyclopropyl acetylenes for the synthesis of indolenines with 1,3-diene motifs in high regio-, and stereoselectivities (Scheme 1, (c)).



Scheme 1 Allylic alkylation reactions of indoles

Results and discussion

First of all, 2,3-dimethylindole (**1a**) and cyclopropyl phenyl acetylene (**2a**) were selected as model substrates to optimize the reaction conditions. To our delight, the reaction of **1a** with **2a** in the presence of 10 mol% of $Pd(PPh_3)_4$ as a catalyst, 20 mol% of PPh_3 as a ligand and 30 mol% of benzoic acid as the additive in 1.2 mL of anhydrous *p*-xylene at 100 °C under argon for 12 h, led to the corresponding dearomative allylic alkylation **3aa** and **3aa'** in 70% total yield and 7.2:1 stereoselectivity (*E*/*Z*) (Table 1, entry 1). The yield and stereoselectivity decreased slightly in the absence of the

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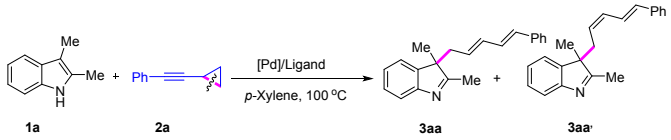
PPh_3 ligand (entry 2). Changing the palladium catalysts to $Pd(dba)_2$ gave similar results (entry 3). Additional studies indicated that $Pd(OAc)_2$, $PdCl_2$ and $Pd(PPh_3)Cl_2$ were poor catalysts for this reaction (entries 4-6). Examination of various ligands revealed that PPh_3 was still the best ligand for this transformation, dppe, dppb, Xantphos, and PCy_3 exhibited reduced yield of **3aa** (entries 7-10)**.** We thus chose PPh_3 as the ligand for further optimization. Screening of acids showed that 3-chlorobenzoic acids could enhance the yield to 80% with a 7.3:1 stereoselectivity (entry 11). Other acids such as 3-F-$C_6H_4CO_2H$, 4-Me-$C_6H_4CO_2H$, and CH_3CO_2H showed inferior performance with respect to both product yields and ratios of **3aa/3aa'** (entries 12-14). Moreover, the concentration of the reaction solution was further screened, lowering the reaction concentration to 0.1 mmol allowed for the preparation of **3aa** in 90% yield and 7.6:1 *E/Z* selectivity (entry 15), while enhancing the concentration provided a diminished yield (entry 16). Additionally, both the yield and ratio could be slightly affected by the reaction temperature. When the reaction was performed at 80 °C, the yield decreased to 66%, but the *E/Z* selectivity was higher (entry 17). However, when the reaction temperature was increased to 120 °C, though the yield was comparable, the selectivity was decreased to 6.5:1 (entry 18). In conclusion, we had screened out the best conditions for the model reaction to be **1a** (0.2 mmol), **2a** (0.4 mmol), 10 mol% $Pd(PPh_3)_4$, 20 mol% PPh_3, 30 mol% 3-Cl-$C_6H_4CO_2H$ in 2.0 mL *p*-xylene at 100 °C for 12 h (Table 1, entry 15).

Table 1 Optimization of reaction conditions[a]



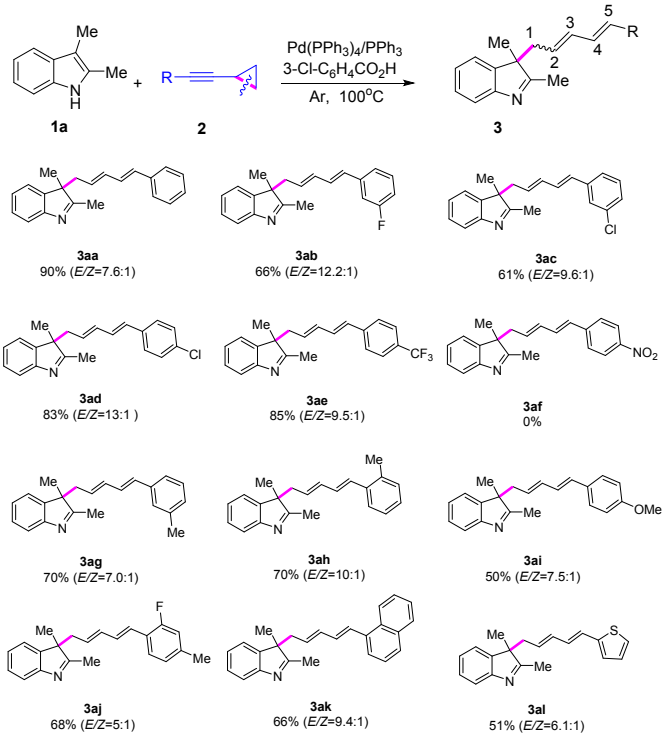
1a 2a 3aa 3aa'

Entry	Catalyst	Ligand	Additive	Yield[b]	**3aa**: **3aa'**[c]
1	$Pd(PPh_3)_4$	PPh_3	$C_6H_5CO_2H$	70%	7.2:1
2	$Pd(PPh_3)_4$	/	$C_6H_5CO_2H$	61%	6.8:1
3	$Pd(dba)_2$	PPh_3	$C_6H_5CO_2H$	62%	7.8:1
4	$Pd(OAc)_2$	PPh_3	$C_6H_5CO_2H$	12%	/
5	$Pd(PPh_3)Cl_2$	PPh_3	$C_6H_5CO_2H$	trace	/
6	$PdCl_2$	PPh_3	$C_6H_5CO_2H$	8%	/
7	$Pd(PPh_3)_4$	dppe	$C_6H_5CO_2H$	50%	5.5:1
8	$Pd(PPh_3)_4$	dppb	$C_6H_5CO_2H$	10%	/
9	$Pd(PPh_3)_4$	Xantphos	$C_6H_5CO_2H$	52%	4.2:1
10	$Pd(PPh_3)_4$	PCy_3	$C_6H_5CO_2H$	30%	5.2:1
11	$Pd(PPh_3)_4$	PPh_3	3-Cl-$C_6H_4CO_2H$	80%	7.3:1
12	$Pd(PPh_3)_4$	PPh_3	3-F-$C_6H_4CO_2H$	33%	3.6:1
13	$Pd(PPh_3)_4$	PPh_3	4-Me-$C_6H_4CO_2H$	56%	5.5:1
14	$Pd(PPh_3)_4$	PPh_3	CH_3CO_2H	44%	4.3:1
15[d]	$Pd(PPh_3)_4$	PPh_3	3-Cl-$C_6H_4CO_2H$	90%	7.6:1
16[e]	$Pd(PPh_3)_4$	PPh_3	3-Cl-$C_6H_4CO_2H$	75%	7.3:1
17[f]	$Pd(PPh_3)_4$	PPh_3	3-Cl-$C_6H_4CO_2H$	66%	9.0:1
18[g]	$Pd(PPh_3)_4$	PPh_3	3-Cl-$C_6H_4CO_2H$	88%	6.5:1

[a] Reaction conditions: **1a** (0.2 mmol), **2a** (0.4 mmol), 10 mol% Pd catalyst, 20 mol% PPh_3, 30 mol% $C_6H_5CO_2H$ in 1.2 mL *p*-xylene at 100 °C for 12 h under an Ar atmosphere. [b] Isolated yields and the yields are reported as a mixture of **3aa** (*E*) and **3aa'** (*Z*) isomers. [c] The ratios were determined by ^1H NMR. [d] In 2 mL *p*-xylene. [e] In 0.6 mL *p*-xylene. [f] At 80 °C. [g] At 120 °C.

With the optimized conditions in hand, we extended the cyclopropylacetylene with different substituents. A series of reaction results are shown in Table 2. Generally, this palladium-catalyzed dearomatization is general for a range of substrates. Regardless of the electronic characteristic of the substrate, the reactions worked well over different substituents affording the corresponding linear allylic products in high regio- and stereoselectivities (**3aa-3al**). Generally, the electron-withdrawing substituents (−Cl, −CF_3) on the phenyl gave better yields and ratios than the ones with electron-donating groups (**3ad**, **3ae** vs **3ai**). However, the strong electron-withdrawing group -NO_2 was found to be incompatible in the reaction (**3af**). By changing the phenyl group to naphthyl or thienyl, the reaction proceeded smoothly to deliver **3ak** and **3al** in 66% and 51% yields.

Table 2 Scope of cyclopropyl acetylene substrates **2** [a,b]

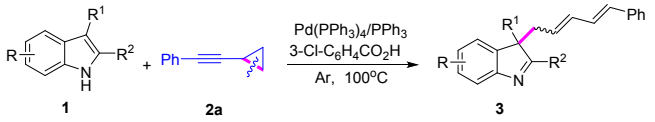


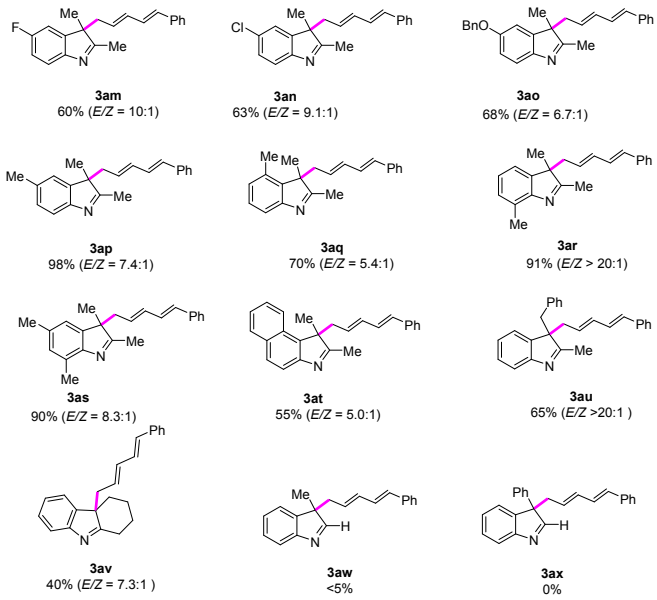
[a] Reaction conditions: **1a** (0.2 mmol), **2** (0.4 mmol), 10 mol% $Pd(PPh_3)_4$, 20 mol% PPh_3, 30 mol% 3-Cl-$C_6H_4CO_2H$ in 2.0 mL *p*-xylene at 100 °C for 12 h under an Ar atmosphere. [b] Isolated yields and the yields are reported as a mixture of *E* and *Z* isomers at C3-allylation of indoles. The ratios of *2E/2Z* were determined by ^1H NMR.

To further explore the scope and potential utility of this method, we elected to examine reactions of substituted indoles, and the results are summarized in Table 3. The substituted group on the phenyl ring of indole was first examined (Table 3). In general, differently substituted indoles reacted well with cyclopropyl phenyl acetylene **2a** to produce **3** in high yields with excellent regio-, and stereoselectivities. Halogen groups (−Cl, −F), methyl, and BnO-groups installed at the C5-position of indoles provided **3am-3ap** in 60−98% yields. C4-Me substituted indole could also afforded indolenine **3aq** in 70% yield. In addition, 7-methyl- and 5,7-dimethyl-substituted indoles and 1,2-dimethyl-3H-benzo[e]indole could furnish **3ar**−**3at** in 55−91% yields. Substitution at the C3-position of the indole frame was then evaluated. By changing the

C3-methyl group to a benzyl group, **3au** was obtained in 65% yields. Moreover, 1,2,3,4-tetrahydrocarbazole was well accommodated, affording the desired 1,3-dienes product **3av** in 40% yield and 7.3:1 stereoselectivity. Disappointingly, 3-methylindole and 3-phenylindole were found to be incompatible in the reaction and gave none product under the standard conditions.

Table 3 Scope of indole substrates **1** [a,b]

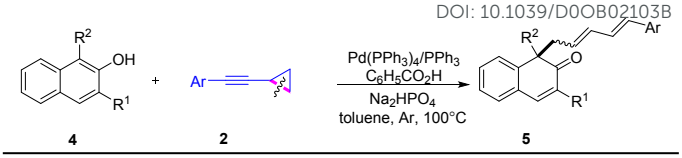


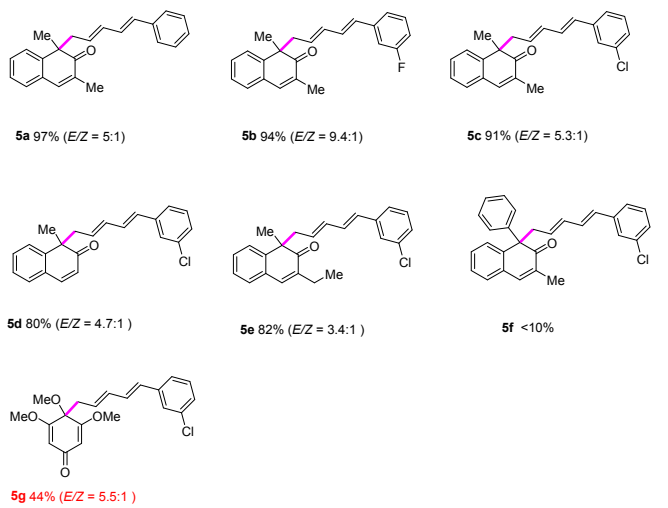


[a] Reaction conditions: **1** (0.2 mmol), **2a** (0.4 mmol), 10 mol% $Pd(PPh_3)_4$, 20 mol% PPh_3, 30 mol% 3-Cl-$C_6H_4CO_2H$ in 2.0 mL *p*-xylene at 100 °C for 12 h under an Ar atmosphere. [b] Isolated yields and the yields are reported as a mixture of *E* and *Z* isomers at 2-position.

Phenolic compounds constitute one of the most fundamental synthetic materials for organic synthesis.[17] The catalytic dearomatization reaction of phenol derivatives has become an effective way to construct highly functional cyclic enones, which are widely embedded in biologically active molecules.[18] To further explore the scope and potential utility of the dearomative allylic alkylation reaction, we examined the reactions of substituted phenols with a slightly changed conditions, and the results are summarized in Table 4. The cyclohexadienones **5a–c** bearing 1,3-diene motifs could be easily accessed through the addition of *β*-naphthol to cyclopropyl acetylene substrates in excellent yields with high regio-, and stereoselectivities. By changing the C3-methyl group to H or ethyl group, **5d** and **5e** were obtained in 80% and 82% yields, respectively. However, 1-phenyl substituted *β*-naphthol was found to be incompatible in the reaction and gave trace product under the reaction conditions. Besides the *β*-naphthol, 3,4,5-trimethoxyphenol can also be used as a substrate to afford the desired 1,3-diene product **5g** in 44% yield and 5.5:1 stereoselectivity.

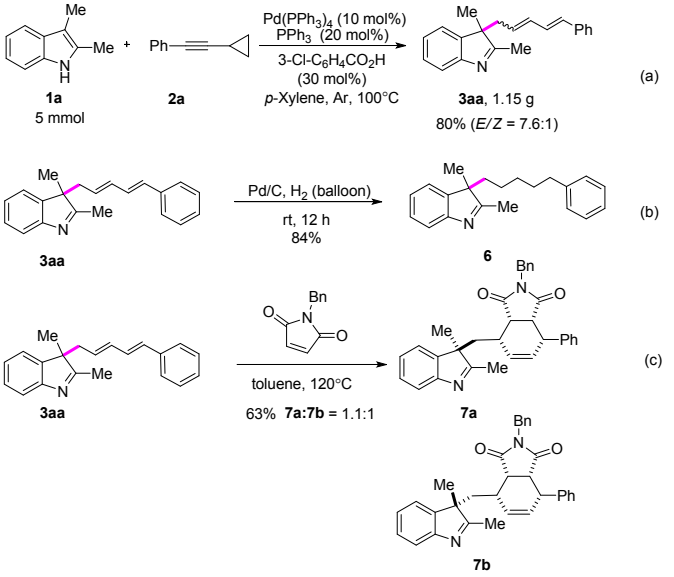
Table 4 Scope of phenol substrates **4** [a,b]





[a] Reaction conditions: **1** (0.2 mmol), **2a** (0.4 mmol), $C_6H_4CO_2H$ (30 mol %), 10 mol%, $Pd(PPh_3)_4$ catalyst, 20 mol% PPh_3, Na_2HPO_4 (0.4 mmol) in 2.0 mL toluene at 100 °C for 12 h under an Ar atmosphere. [b] Isolated yields and the yields are reported as a mixture of *E* and *Z* isomers.

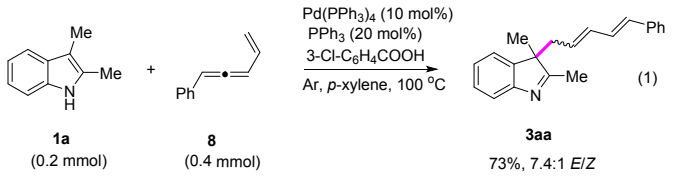
To further test the effectiveness of the reaction, we investigated the reaction of a scaled-up reaction (Scheme 2, (a)). Under the optimal conditions, **3aa** could also be isolated in 80% yield on a 5.0 mmol scale. Subsequently, the transformation reaction of the 1,3-diene product was explored. As shown in Scheme 2, Pd/C-catalyzed hydrogenation of **3aa** in

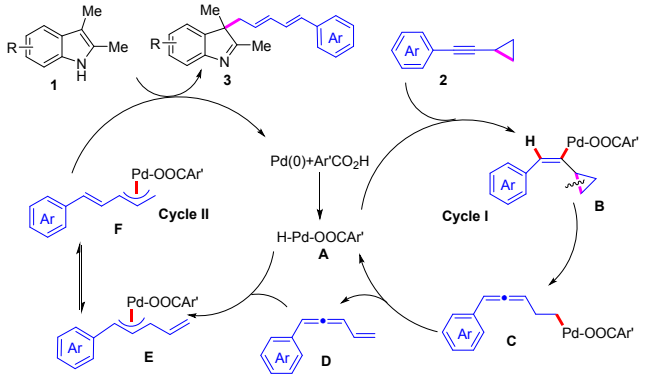


Scheme 2 Scaled-up reaction and synthetic transformations of **3aa**

ethanol readily afforded product **6** in 84% yield (Scheme 2, (b)). While, the Diels-Alder reaction of **3aa** with *N*-benzylmaleimide produced polycyclic compounds **7a** and **7b** in 63% combined yield with a ratio of 1.1:1 (Scheme 2, (c), the ratio was determined by ^{1}H NMR).

In order to explore the mechanism of this reaction, we synthesized penta-1,2,4-trien-1-ylbenzene **8** and used it to react with indole **1a** (eqn, (1)). Under the optimized reaction conditions, the reaction proceeded smoothly to afford dearomative alkylation product **3aa** in 73 % yield and 7.4:1 *E/Z* selectivity, suggesting that the cyclopropyl acetylene is capable of undergoing C–C activation to allene through β-C-elimination. On the basis of previous reports,[10,13] a reasonable mechanism for the dearomative allylic alkylation reaction can be envisioned (Scheme 3). The palladium (0) complex is able to undergo oxidative addition to $ArCO_2H$ acid to generate a hydridopalladium complex **A**, which then reacts with alkynes to form vinyl palladium intermediate **B**. The resulting vinylpalladium species would produce active alkylpalladium(II) intermediate **C** via *β*-**C** elimination. *β*-H elimination of alkylpalladium(II) species **C** produces the vinyl allene **D**. Next, hydropalladation of vinyl allene intermediate **D** delivers the π-allylpalladium species **E** (Cycle II), which delivers intermediate **F** through π−σ−π isomerization. Finally, the palladium-allyl species **F** is captured by the indole nucleophile **1** to afford the desired product **3** and regenerated intermediate **A** to achieve the catalytic cycle.[19,20]





Scheme 3 A proposed mechanism for the allylic alkylation reaction.

Conclusions

In conclusion, we have developed a palladium-catalyzed allylic alkylation of indoles with cyclopropyl acetylene for the synthesis of indolenine frameworks bearing a quaternary stereocenter at the C3 position with high regio-, and stereoselectivities under mild conditions. Moreover, the reaction could be further expanded to the dearomatization of naphthols to synthesize functionalized cyclohexadienones with 1,3-diene motifs. This methodology was found to be advantageous in terms of substrate scope and functional group tolerance and shows high atom economy.

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Experimental section

Materials and methods

The glassware required before the experiment was heated in an oven for 2 hours, and reactions and operations involving organometallic or moisture-sensitive compounds were performed under dry argon. *p*-xylene was freshly distilled over Na and stored under nitrogen. Unless otherwise stated, commercial reagents were used without further purification. ^{1}H and ^{13}C spectra were recorded on a Bruker AVANCE III 500 MHz instrument with $CDCl_3$ as the solvent and TMS as the internal standard. Melting points (m.p.) were recorded on an SGW Melting Point X-4 instrument. HRMS was recorded on an Agilent 6210 TOF LC/MS mass spectrometer. Column chromatography was performed on silica gel (200-300 mesh).

General procedure for the synthesis of alkynes

CuI (76 mg, 0.4 mmol, 4.0 mol%), $(PPh_3)_2PdCl_2$ (142 mg, 0.2 mmol, 2.0 mol%), PPh_3 (106 mg, 0.4 mmol, 4.0 mol%), and NEt_3 (30 mL) were placed in a round-bottomed flask equipped with a magnetic stirring bar. After addition of the iodobenzene (10.0 mmol, 1.1 mL, 1.0 eq), the mixture was stirred at room temperature for 30 min, and cyclopropylacetylene (10.0 mmol, 0.8 mL, 1.0 eq) was then added. The reaction mixture was stirred at the same temperature for 16 h, saturated NH_4Cl solution was added. The mixture was extracted with ethyl acetate and the combined organic layers were dried with $MgSO_4$ and concentrated under vacuum. The residue was purified by flash chromatography to give the product **2a** (1.36 g, 96 %).

General procedure for the synthesis of substituted indoles

Phenylhydrazine hydrochloride (723 mg, 5 mmol, 1.0 eq) was dissolved in a glacial acetic acid (5 mL) solution in a three-necked flask containing magnetons. The reaction was carried out at 50 °C for 30 min, and then 2-butanone (10 mmol, 1.0 mL, 2.0 eq) was added dropwise. The mixture was refluxed for 3 hours and then cooled to room temperature. Part of the acetic acid was removed by rotary evaporation. Then extracted three times with EtOAc, washed with saturated NaCl solution and water. The combined organic layers were dried over Na_2SO_4 and concentrated under vacuum, and purified by column to give the product **1a** (645 mg, 89 %).

General procedure for the synthesis of substituted *β*-naphthols

To a dry round bottom flask was added 1-bromo-2-naphthol (2.23 g, 10 mmol) and a solution of dichloromethane (50 mL), followed by 1.9 mL (1.1 eq) of diisopropylethylamine. The mixture was cooled to 0 °C in an ice water bath, and 0.9 mL (1.1 eq) of MOMCl (chloromethyl methyl ether) was slowly added. The mixture was warmed to room temperature and stirred overnight. The reaction was quenched by methanol followed by water, and extracted with dichloromethane. The combined organic layers were dried over Na_2SO_4 and concentrated under vacuum, and purified by column chromatography (Neutral Al_2O_3, PE/EtOAc = 60/1) to afford 1-

bromo-2-(methoxymethoxy)naphthalene (2.63 g, 97%) as a colorless oil.

In a sealed three neck flask filled with nitrogen was added 1-bromo-2-(methoxymethoxy)naphthalene (2.0 g, 7.5 mmol) and THF (50 mL). The reaction was cooled to -78 °C and slowly added *n*-BuLi (5.2 mL, 1.1 eq, 1.6 M in *n*-hexane). After the solution reacted at -78 °C for 1 h, iodomethane (1.2 mL, 2.5 eq) was slowly added and warmed to room temperature for 1 h. Saturated NH_4Cl solution was added. The mixture was extracted with ethyl acetate and the combined organic layers were dried with $MgSO_4$ and concentrated under vacuum. The residue was purified by flash chromatography by column chromatography (Neutral Al_2O_3, PE/EtOAc = 80/1) to afford 2-(methoxymethoxy)-1-methylnaphthalene (1.3 g, 86%) as a colourless oil.

Under the protection of nitrogen, 2-(methoxymethoxy)-1-methylnaphthalene (1.0 g, 5 mmol) was dissolved in ether (20 mL) and cooled to 0 °C. *n*-BuLi (4.6 mL, 1.5 eq, 1.6 M in *n*-hexane) was slowly added to the solution, and warmed to room temperature. After stirred at this temperature for one hour, methyl iodide (0.93 mL, 3.0 eq) was added. The reaction mixture was stirred at the same temperature for 16 h, saturated NH_4Cl solution was added. The mixture was extracted with ethyl acetate and the combined organic layers were dried with $MgSO_4$ and concentrated under vacuum. Methanol (20 mL) was added to above mixture and placed in an oil bath at 50 °C, concentrated hydrochloric acid (36 % - 38 %, 5 drops) was added dropwise. The reaction was carried out at 50 °C for 1 h and quenched with water. The mixture was extracted with ethyl acetate and the combined organic layers were dried with $MgSO_4$ and concentrated under vacuum. Purified by column chromatography (SiO_2, PE/EtOAc = 100/1) to give 1,3-dimethyl-2-naphthol (674 mg, 78 %) as a white solid.

General procedure for the palladium-catalyzed allylation of indoles with cyclopropyl acetylene derivatives

To the solution of 2,3-dimethylindole **1a** (29.0 mg, 0.20 mmol, 1.0 eq), cyclopropyl phenyl acetylene **2a** (56.0 mg, 0.4 mmol, 2.0 eq), $Pd(PPh_3)_4$ (23.0 mg, 0.02 mmol, 10 mol%), PPh_3 (10.0 mg, 0.04 mmol, 20 mol%) and 3-Cl-$C_6H_4CO_2H$ (9.0 mg, 0.06 mmol, 30 mol%) in a sealed tube was added 2.0 mL dry *p*-xylene. The reaction mixture was vigorously stirred at 100 °C for 12 h under an Ar atmosphere. After cooling to room temperature, the mixture was transferred in vacuo and concentrated. The residue was purified by silica gel column chromatography PE/EtOAc （50: 1 to 10: 1) to obtain a mixture of stereoisomers of compound **3**, and the *E/Z* ratio was determined by ^{1}H NMR. The mixture of stereoisomers was separated by a second flash column (PE/EtOAc = 10:1) to afford the major stereoisomer **3aa** (53.8 mg, 90%).

General procedure for the palladium-catalyzed allylation of β-naphthols with cyclopropyl acetylene derivatives

To the solution of 1,3-dimethyl-2-naphthol (34.0 mg, 0.20 mmol, 1.0 eq), cyclopropyl phenyl acetylene **2a** (56.0 mg, 0.4 mmol, 2.0 eq), $Pd(PPh_3)_4$ (23.0 mg, 0.02 mmol, 10 mol%), PPh_3 (10.0 mg, 0.04 mmol, 20 mol%), Na_2HPO_4 (57.0 mg, 0.4 mmol, 2.0 eq) and 3-Cl-$C_6H_4CO_2H$ (9.0 mg, 0.06 mmol, 30 mol%) in a sealed tube was added 2.0 mL dry toluene. The reaction mixture was vigorously stirred at 100 °C for 12 h under an Ar atmosphere. After cooling to room temperature, the mixture was transferred in vacuo and concentrated. The residue was purified by silica gel column chromatography PE/EtOAc (360:1 to 300:1) to obtain a mixture of stereoisomers of compound **5**, and the *E/Z* ratio was determined by ^{1}H NMR. The mixture of stereoisomers was separated by a second flash column (PE/EtOAc = 300:1) to afford the major stereoisomer **5a** (61.0 mg , 97%).

General procedure for the synthesis of 6

To the solution of **3aa** (57.4 mg, 0.2 mmol), 10% Pd/C(10 % mmol) in a sealed tube was added 2.0 mL MeOH. The reaction mixture was vigorously stirred at room temperature under a balloon of H_2 overnight. The mixture was transferred in vacuo and concentrated. The residue was purified by silica gel column chromatography PE/EtOAc (40: 1 to 20: 1) to obtain compound **6** (48.9 mg, 84%).

General procedure for the synthesis of 7a and 7b

To the solution of **3aa** (86.1 mg, 0.3 mmol, 1.0 eq), *N*-benzylmaleimide (62 mg, 0.33 mmol, 1.1 eq) in a sealed tube was added 3.0 mL dry toluene and the reaction mixture was stirred at 120 °C for 12 h. After cooling to room temperature, the mixture was transferred in vacuo and concentrated. The residue was purified by silica gel column chromatography PE/EtOAc (10: 1 to 4: 1) to obtain compound **7a** and **7b** (89.7 mg, 63%).

2,3-Dimethyl-3-((2E,4E)-5-phenylpenta-2,4-dien-1-yl)-3H-indole (3aa). Total isolated yield: 90%, 53.8 mg, 0.19 mmol, *2E/2Z* = 7.6:1. **3aa**, yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.57 (d, *J* = 7.7 Hz, 1H), 7.36-7.27 (m, 6H), 7.25-7.17 (m, 2H), 6.55 (dd, *J* = 15.6, 10.4 Hz, 1H), 6.39 (d, *J* = 15.7 Hz, 1H), 6.14 (dd, *J* = 15.0, 10.4 Hz, 1H), 5.20 (dt, *J* = 15.0, 7.4 Hz, 1H), 2.74 (dd, *J* = 14.3, 6.2 Hz, 1H), 2.50 (dd, *J* = 14.2, 8.3 Hz, 1H), 2.30 (s, 3H), 1.35 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 186.65, 143.34, 137.18, 133.64, 131.42, 128.51, 128.48, 128.27, 127.80, 127.35, 126.19, 125.09, 121.84, 119.89, 57.70, 40.24, 21.75, 15.90 ppm. HRMS (ESI) m/z calcd for $[C_{21}H_{21}N+H]^+$ 288.1747, found 288.1744.

3-((2E,4E)-5-(3-Fluorophenyl)penta-2,4-dien-1-yl)-2,3-dimethyl-3H-indole (3ab). Total isolated yield: 66%, 40.5 mg, 0.13 mmol, *2E/2Z* = 12.2:1. **3ab**, yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54 (d, *J* = 7.7 Hz, 1H), 7.36-7.26 (m, 2H), 7.24-7.17 (m, 2H), 7.04 (d, *J* = 7.8 Hz, 1H), 6.98 (dt, *J* = 10.3, 2.0 Hz, 1H), 6.86 (td, *J* = 8.6, 2.8 Hz, 1H), 6.50 (dd, *J* = 15.6, 10.4 Hz, 1H), 6.31 (d, *J* = 15.7 Hz, 1H), 6.10 (dd, *J* = 15.0, 10.4 Hz, 1H), 5.19 (dt, *J* = 15.0, 7.5 Hz, 1H), 2.77-2.68 (m, 1H), 2.53-2.45 (m, 1H), 2.27 (s, 3H), 1.33 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 186.35, 163.99, 162.04, 154.24, 143.28, 139.55 (d, *J* = 7.8 Hz), 133.10, 129.98 (q, *J* = 29.9 Hz), 129.74, 129.48, 127.78, 125.04, 122.02 (d, *J* = 2.9 Hz), 121.76, 119.91, 114.06 (d, *J* = 21.5 Hz), 112.46(d, *J* = 21.8 Hz), 57.64, 40.20, 21.76, 15.94 ppm. HRMS (ESI) m/z calcd for $[C_{21}H_{20}FN+H]^+$ 306.1658, found 306.1660.

3-((2E,4E)-5-(3-Chlorophenyl)penta-2,4-dien-1-yl)-2,3-dimethyl-3H-indole (3ac). Total isolated yield: 61%, 39.2 mg, 0.12 mmol, *2E/2Z* = 9.6:1. **3ac**, yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54 (d, *J* = 7.7 Hz, 1H), 7.34-7.26 (m, 3H), 7.23-7.11 (m, 5H), 6.51 (dd, *J* = 15.6, 10.4 Hz, 1H), 6.28 (d, *J* = 15.7 Hz, 1H), 6.10 (dd, *J* = 15.0, 10.4 Hz, 1H), 5.24-5.15 (m, 1H), 2.77-2.68 (m, 1H), 2.53-2.44 (m, 1H), 2.27 (s, 3H), 1.33 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 154.19, 139.06, 134.41, 133.08, 129.83, 129.77, 129.66, 129.57, 127.78, 127.15, 125.98, 125.03, 124.28, 121.75, 119.90, 57.62,

40.17, 21.74, 15.92 ppm. HRMS (ESI) m/z calcd for $[C_{21}H_{20}ClN+H]^+$ 322.1363, found 322.1357.

3-((2E,4E)-5-(4-Chlorophenyl)penta-2,4-dien-1-yl)-2,3-dimethyl-3H-indole (3ad). Total isolated yield: 83%, 53.3 mg, 0.17 mmol, *2E/2Z* = 13:1. **3ad**, yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.55 (d, *J* = 7.7 Hz, 1H), 7.35-7.26 (m, 2H), 7.24-7.18 (m, 5H), 6.48 (dd, *J* = 15.6, 10.4 Hz, 1H), 6.30 (d, *J* = 15.7 Hz, 1H), 6.10 (dd, *J* = 15.0, 10.4 Hz, 1H), 5.18 (dt, *J* = 14.9, 7.4 Hz, 1H), 2.72 (dd, *J* = 14.2, 6.6 Hz, 1H), 2.49 (dd, *J* = 14.2, 8.3 Hz, 1H), 2.28 (s, 3H), 1.33 (s, 3H).^{13}C NMR (126 MHz, $CDCl_3$) δ 186.35, 154.20, 143.28, 135.67, 133.20, 132.78, 129.94, 129.02 (d, *J* = 7.4 Hz), 128.61, 127.75, 127.28, 125.02, 121.74, 119.86, 57.62, 40.17, 21.73, 15.88 ppm. HRMS (ESI) m/z calcd for $[C_{21}H_{20}ClN+H]^+$ 322.1363, found 322.1356.

2,3-Dimethyl-3-((2E,4E)-5-(4-(trifluoromethyl)phenyl)penta-2,4-dien-1-yl)-3H-indole (3ae). Total isolated yield: 85%, 60.3 mg, 0.17 mmol, *2E/2Z* = 9.5:1. **3ae**, yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.55 (d, *J* = 7.7 Hz, 1H), 7.49 (d, *J* = 8.3 Hz, 2H), 7.38-7.27 (m, 4H), 7.21 (td, *J* = 7.4, 0.9 Hz, 1H), 6.57 (dd, *J* = 15.7, 10.4 Hz, 1H), 6.36 (d, *J* = 15.7 Hz, 1H), 6.12 (dd, *J* = 15.0, 10.5 Hz, 1H), 5.21 (dt, *J* = 15.0, 7.5 Hz, 1H), 2.74 (dd, *J* = 14.3, 6.5 Hz, 1H), 2.51 (dd, *J* = 14.5, 8.4 Hz, 1H), 2.27 (s, 3H), 1.33 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 186.31, 154.24, 143.23, 140.65, 132.99, 130.88, 130.31, 129.70, 129.03, 128.77, 127.82, 126.20, 125.3 (q, *J* = 3.9 Hz), 125.08, 124.20 (q, *J* = 268.8 Hz), 121.74, 119.93, 57.65, 40.21, 21.81, 15.92 ppm. HRMS (ESI) m/z calcd for $[C_{22}H_{20}F_3N+H]^+$ 356.1626, found 356.1621.

2,3-Dimethyl-3-((2E,4E)-5-(m-tolyl)penta-2,4-dien-1-yl)-3H-indole (3ag). Total isolated yield: 70%, 42.1 mg, 0.14 mmol, *2E/2Z* =7.0:1. **3ag**, yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56 (d, *J* = 7.7 Hz, 1H), 7.36-7.27 (m, 2H), 7.24-7.09 (m, 4H), 7.01 (d, *J* = 7.4 Hz, 1H), 6.54 (dd, *J* = 15.6, 10.4 Hz, 1H), 6.35 (d, *J* = 15.7 Hz, 1H), 6.13 (dd, *J* = 15.0, 10.4 Hz, 1H), 5.22-5.14 (m, 1H), 2.75-2.69 (m, 1H), 2.51-2.45 (m, 1H), 2.31 (s, 3H), 2.28 (s, 3H), 1.33 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 186.43, 154.19, 143.34, 137.92, 137.04, 133.58, 131.42, 128.34, 128.25, 128.12, 128.06, 127.68, 126.78, 124.95, 123.35, 121.76, 119.82, 57.61, 40.16, 21.68, 21.28, 15.91 ppm. HRMS (ESI) m/z calcd for $[C_{22}H_{23}N+H]^+$ 302.1909, found 302.1917.

2,3-Dimethyl-3-((2E,4E)-5-(o-tolyl)penta-2,4-dien-1-yl)-3H-indole (3ah). Total isolated yield: 70%, 42.2 mg, 0.14 mmol, *2E/2Z* =10.0:1. **3ah**, yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56 (d, *J* = 7.7 Hz, 1H), 7.42-7.27 (m, 3H), 7.22 (td, *J* = 7.4, 0.9 Hz, 1H), 7.15-7.08 (m, 3H), 6.61 (d, *J* = 15.5 Hz, 1H), 6.46 (dd, *J* = 15.5, 10.3 Hz, 1H), 6.18 (dd, *J* = 15.0, 10.4 Hz, 1H), 5.23-5.15 (m, 1H), 2.77-2.69 (m, 1H), 2.53-2.45 (m, 1H), 2.32 (s, 3H), 2.29 (s, 3H), 1.34 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 186.46, 154.21, 143.35, 135.91, 135.28, 133.89, 130.26, 129.50, 128.90, 128.14, 127.71, 127.21, 125.98, 124.97, 124.85, 121.79, 119.85, 57.64, 40.19, 21.72, 19.72, 15.94 ppm. HRMS (ESI) m/z calcd for $[C_{22}H_{23}N+H]^+$ 302.1909, found 302.1904.

3-((2E,4E)-5-(4-Methoxyphenyl)penta-2,4-dien-1-yl)-2,3-dimethyl-3H-indole (3ai) Total isolated yield: 50%, 31.8 mg, 0.1 mmol, *2E/2Z* =7.5:1. **3ai**, yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54 (d, *J* = 7.7 Hz, 1H), 7.35-7.27 (m, 2H), 7.26-7.18 (m, 3H), 6.83-6.78 (m, 2H), 6.41 (dd, *J* = 15.6, 10.2 Hz, 1H), 6.32 (d, *J* = 15.7 Hz, 1H), 6.10 (dd, *J* = 15.0, 10.1 Hz, 1H), 5.13 (dt, *J* = 14.9, 7.4 Hz, 1H), 3.77 (s, 3H), 2.74-2.67 (m, 1H), 2.49-2.42 (m, 1H), 2.27 (s, 3H), 1.32 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 186.54, 159.01, 154.22, 143.42, 133.72, 130.87, 129.94, 127.67, 127.33, 127.03, 126.47, 124.94, 121.79, 119.82, 113.94, 57.67, 55.17, 40.20, 21.70, 15.95 ppm. HRMS (ESI) m/z calcd for $[C_{22}H_{23}NO+H]^+$ 318.1858, found 318.1851.

3-((2E,4E)-5-(2-Fluoro-4-methylphenyl)penta-2,4-dien-1-yl)-2,3-dimethyl-3H-indole (3aj). Total isolated yield: 68%, 43.4 mg, 0.14 mmol, *2E/2Z* =5:1. **3aj**, yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54 (d, *J* = 7.7 Hz, 1H), 7.34-7.18 (m, 4H), 6.82 (dd, *J* = 19.6, 9.9 Hz, 2H), 6.55 (d, *J* = 15.8 Hz, 1H), 6.53-6.46 (m, 1H), 6.13 (dd, *J* = 15.1, 9.5 Hz, 1H), 5.20-5.12 (m, 1H), 2.75-2.68 (m, 1H), 2.48 (dd, *J* = 14.3, 8.3 Hz, 1H), 2.29 (s, 3H), 2.27 (s, 3H), 1.32 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 186.46, 160.93, 158.95, 154.21, 143.34, 139.10(d, *J* = 8.2 Hz), 133.84, 129.7(d, *J* = 4.8 Hz), 129.66, 128.54, 127.72, 126.46(d, *J* = 4.2 Hz), 125.00, 124.82, 124.8(d, *J* = 2.9 Hz), 123.58(d, *J* = 3.3 Hz), 122.05, 121.96, 121.76, 119.85, 116.18, 116.00, 57.64, 40.19, 21.75, 21.02, 15.92 ppm. HRMS (ESI) m/z calcd for $[C_{22}H_2FN+H]^+$ 320.1815, found 320.1813.

2,3-Dimethyl-3-((2E,4E)-5-(naphthalen-2-yl)penta-2,4-dien-1-yl)-3H-indole (3ak). Total isolated yield: 66%, 44.5 mg, 0.13 mmol, *2E/2Z* =9.4:1. **3ak**, yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.09 (d, *J* = 8.1 Hz, 1H), 7.85-7.80 (m, 1H), 7.73 (d, *J* = 8.2 Hz, 1H), 7.56 (dd, *J* = 7.4, 2.8 Hz, 2H), 7.51-7.45 (m, 2H), 7.44-7.38 (m, 1H), 7.37-7.29 (m, 2H), 7.23 (td, *J* = 7.4, 0.9 Hz, 1H), 7.17 (d, *J* = 15.4 Hz, 1H), 6.61 (dd, *J* = 15.3, 10.5 Hz, 1H), 6.29 (dd, *J* = 14.9, 10.6 Hz, 1H), 5.24 (dt, *J* = 15.0, 7.4 Hz, 1H), 2.80-2.73 (m, 1H), 2.57-2.49 (m, 1H), 2.31 (s, 3H), 1.36 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 186.49, 154.24, 143.36, 134.43, 133.82, 133.65, 131.23, 130.99, 128.68, 128.52, 127.99, 127.77, 127.74, 125.89, 125.64, 125.53, 125.03, 123.46, 123.09, 121.81, 119.91, 57.67, 40.23, 21.78, 15.99 ppm. HRMS (ESI) m/z calcd for $[C_{25}H_{23}N+H]^+$ 338.1909, found 338.1899.

2,3-Dimethyl-3-((2E,4E)-5-(thiophen-3-yl)penta-2,4-dien-1-yl)-3H-indole (3al). Total isolated yield: 51%, 29.4 mg, 0.1 mmol, *2E/2Z* =6.1:1. **3al**, yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56 (d, *J* = 7.7 Hz, 1H), 7.35-7.27 (m, 2H), 7.21 (t, *J* = 7.4 Hz, 1H), 7.10 (d, *J* = 5.0 Hz, 1H), 6.94-6.88 (m, 2H), 6.51 (d, *J* = 15.5 Hz, 1H), 6.35 (dd, *J* = 15.4, 10.4 Hz, 1H), 6.06 (dd, *J* = 15.0, 10.4 Hz, 1H), 5.17 (dt, *J* = 15.0, 7.5 Hz, 1H), 2.71 (dd, *J* = 14.3, 6.6 Hz, 1H), 2.46 (dd, *J* = 14.2, 8.3 Hz, 1H), 2.28 (s, 3H), 1.33 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 186.37, 154.18, 143.31, 142.53, 133.01, 128.18 (d, *J* = 3.6 Hz), 127.71, 127.37, 125.46, 124.97, 124.25, 124.07, 121.75, 119.84, 57.59, 40.15, 21.65, 15.87 ppm. HRMS (ESI) m/z calcd for $[C_{19}H_{19}NS+H]^+$ 294.1316, found 294.1310.

5-Fluoro-2,3-dimethyl-3-((2E,4E)-5-phenylpenta-2,4-dien-1-yl)-3H-indole (3am). Total isolated yield: 60%, 36.8 mg, 0.12 mmol, *2E/2Z* =10.0:1. **3am**, yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47 (dd, *J* = 8.2, 4.6 Hz, 1H), 7.35-7.25 (m, 4H), 7.22-7.16 (m, 1H), 7.04-6.97 (m, 2H), 6.54 (dd, *J* = 15.7, 10.3 Hz, 1H), 6.39 (d, *J* = 15.7 Hz, 1H), 6.13 (dd, *J* = 15.0, 10.4 Hz, 1H), 5.17 (dt, *J* = 15.0, 7.5 Hz, 1H), 2.73-2.65 (m, 1H), 2.54-2.46 (m, 1H), 2.27 (s, 3H), 1.33 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 186.28, 162.06, 160.12, 150.23, 145.46, 145.40, 137.11, 133.93, 131.71, 128.55, 128.31, 127.66, 127.44, 126.24, 120.54, 120.47, 114.44, 114.25, 109.67, 109.48, 58.30, 40.16, 21.71, 15.96 ppm. HRMS (ESI) m/z calcd for $[C_{21}H_{20}FN+H]^+$ 306.1653, found 306.1649.

5-Chloro-2,3-dimethyl-3-((2E,4E)-5-phenylpenta-2,4-dien-1-yl)-3H-indole (3an). Total isolated yield: 63%, 40.4 mg, 0.13 mmol, *2E/2Z* =9.1:1. **3an**, yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45 (d, *J* = 8.2 Hz, 1H), 7.33-7.26 (m, 6H), 7.20 (tt, *J* = 6.5, 1.3 Hz, 1H), 6.54 (dd, *J* = 15.6, 10.3 Hz, 1H), 6.40 (d, *J* = 15.7 Hz, 1H), 6.14 (dd, *J* = 15.0, 10.4 Hz, 1H), 5.15 (dt, *J* = 15.0, 7.5 Hz, 1H), 2.74-2.67 (m, 1H), 2.50 (dd, *J* = 14.3, 8.2 Hz, 1H), 2.27 (s, 3H), 1.33 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 187.01, 152.79, 145.25, 137.09, 133.96, 131.75, 130.90, 128.53, 128.27, 127.97, 127.54, 127.44, 126.23, 122.35, 120.76, 58.24, 40.13, 21.69, 16.01 ppm. HRMS (ESI) m/z calcd for $[C_{21}H_{20}ClN+H]^+$ 322.1357, found 322.1366.

5-Benzyloxy-2,3-dimethyl-3-((2E,4E)-5-phenylpenta-2,4-dien-1-yl)-3H-indole (3ao) Total isolated yield: 68%, 54 mg, 0.14 mmol, *2E/2Z* =6.7:1. **3ao**, yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46 (s, 1H), 7.41 (dd, *J* = 10.1, 4.8 Hz, 2H), 7.37-7.27 (m, 5H), 7.21 (t, *J* = 7.2 Hz, 1H), 6.98-6.93 (m, 2H), 6.57 (dd, *J* = 15.6, 10.4 Hz, 1H), 6.41 (d, *J* = 15.7 Hz, 1H), 6.15 (dd, *J* = 15.1, 10.4 Hz, 1H), 5.21 (dt, *J* = 14.9, 7.4 Hz, 1H), 5.10 (s, 2H), 2.69 (dd, *J* = 14.4, 6.7 Hz, 1H),

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2.49 (dd, *J* = 14.4, 8.1 Hz, 1H), 2.27 (s, 3H), 1.33 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 184.43,157.02, 148.19, 145.02, 137.18, 137.00, 133.62, 131.37, 128.52, 128.52, 128.49, 128.30, 127.93, 127.53, 127.32, 126.18, 120.07, 113.28, 109.80, 70.60, 57.83, 40.29, 21.86, 15.82 ppm. HRMS (ESI) m/z calcd for $[C_{28}H_{27}NO+H]^+$ 394.2171, found 394.2180.

5-Methyl-2,3-dimethyl-3-((2E,4E)-5-phenylpenta-2,4-dien-1-yl)-3H-indole (3ap). Total isolated yield: 98%, 59 mg, 0.2 mmol, *2E/2Z* =7.4:1. **3ap**, yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44 (d, *J* = 7.8 Hz, 1H), 7.34-7.27 (m, 4H), 7.21-7.17 (m, 1H), 7.16-7.09 (m, 2H), 6.55 (dd, *J* = 15.6, 10.4 Hz, 1H), 6.39 (d, *J* = 15.7 Hz, 1H), 6.15 (dd, *J* = 15.0, 10.4 Hz, 1H), 5.22-5.14 (m, 1H), 2.71 (dd, *J* = 14.8, 6.5 Hz, 1H), 2.49 (dd, *J* = 14.3, 8.3 Hz, 1H), 2.42 (s, 3H), 2.26 (s, 3H), 1.32 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 185.50, 152.13, 143.59, 137.24, 134.76, 133.46, 131.30, 128.62, 128.54, 128.38, 127.35, 126.41, 126.21, 123.72, 122.62, 119.45, 57.52, 40.33, 35.02, 21.96, 21.52, 15.96 ppm. HRMS (ESI) m/z calcd for $[C_{22}H_{23}N+H]^+$ 302.1903, found 302.1906.

2,3,4-Trimethyl-3-((2E,4E)-5-phenylpenta-2,4-dien-1-yl)-3H-indole (3aq). Total isolated yield: 70%, 42.2 mg, 0.14 mmol, *2E/2Z* =5.4;1. **3aq**, yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 (s, 1H), 7.29 (dt, *J* = 11.2, 5.5 Hz, 4H), 7.21-7.15 (m, 2H), 7.04 (d, *J* = 7.5 Hz, 1H), 6.56 (dd, *J* = 15.7, 10.4 Hz, 1H), 6.39 (d, *J* = 15.7 Hz, 1H), 6.15 (dd, *J* = 15.0, 10.4 Hz, 1H), 5.25-5.18 (m, 1H), 2.71 (dd, *J* = 14.2, 6.6 Hz, 1H), 2.47 (dd, *J* = 14.3, 8.3 Hz, 1H), 2.43 (s, 3H), 2.28 (s, 3H), 1.32 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 186.63, 154.42, 140.35, 137.55, 137.14, 133.41, 131.23, 128.52, 128.49, 128.44, 127.25, 126.11, 125.67, 121.36, 120.55, 57.26, 40.20, 21.81, 21.45, 15.86 ppm. HRMS (ESI) m/z calcd for $[C_{22}H_{23}N+H]^+$ 302.1909, found 302.1901.

2,3,7-Trimethyl-3-((2E,4E)-5-phenylpenta-2,4-dien-1-yl)-3H-indole (3ar) Total isolated yield: 91%, 54.8 mg, 0.18 mmol, *2E/2Z* >20:1. **3ar**, yellow solid, m.p.112-114°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 (ddd, *J* = 15.2, 10.9, 4.7 Hz, 4H), 7.23-7.12 (m, 4H), 6.57 (dd, *J* = 15.6, 10.4 Hz, 1H), 6.40 (d, *J* = 15.7 Hz, 1H), 6.16 (dd, *J* = 15.0, 10.4 Hz, 1H), 5.26-5.19 (m, 1H), 2.73 (dd, *J* = 14.3, 6.4 Hz, 1H), 2.62 (s, 3H), 2.50 (dd, *J* = 14.5, 8.0 Hz, 1H), 2.31 (d, *J* = 4.5 Hz, 3H), 1.34 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 185.36, 152.67, 143.24, 137.21, 133.45, 131.25, 129.43, 129.13, 128.58, 128.57, 128.48, 127.29, 126.15, 124.90, 119.20, 57.73, 40.27, 21.95, 16.89, 15.86 ppm. HRMS (ESI) m/z calcd for $[C_{22}H_{23}N+H]^+$ 302.1903, found 302.1902.

2,3,4,6-Tetramethyl-3-((2E,4E)-5-phenylpenta-2,4-dien-1-yl)-3H-indole (3as). Total isolated yield: 90%, 56.7 mg, 0.18 mmol, *2E/2Z* =8.3;1. **3as**, yellow solid, m.p.110-112°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30-7.24 (m, 4H), 7.22-7.16 (m, 2H), 6.80 (d, *J* = 9.5 Hz, 1H), 6.48-6.42 (m, 1H), 6.35 (d, *J* = 15.7 Hz, 1H), 6.13 (dd, *J* = 15.1, 10.2 Hz, 1H), 4.99-4.92 (m, 1H), 3.04 (dd, *J* = 15.0, 6.4 Hz, 1H), 2.63 (dd, *J* = 15.3, 8.1 Hz, 1H), 2.43 (s, 3H), 2.38 (s, 3H), 2.26 (s, 3H), 1.41 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 186.11, 154.91, 137.59, 137.21, 137.04, 132.59, 132.27, 131.09, 128.68, 128.60, 128.45, 128.10, 127.24, 126.12, 118.44, 77.29, 77.03, 76.78, 58.42, 37.98, 21.29, 20.31, 17.77, 15.63 ppm. HRMS (ESI) m/z calcd for $[C_{23}H_{25}N+H]^+$ 316.2060, found 316.2058.

2,3-Dimethyl-3-((2E,4E)-5-phenylpenta-2,4-dien-1-yl)-3H-benzo[*g*]indole (3at). Total isolated yield 55%, 37 mg, 0.11 mmol, *2E/2Z* =5.0;1. **3at**, yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.11-7.94 (m, 2H), 7.91-7.79 (m, 2H), 7.59 (ddd, *J* = 9.5, 7.2, 1.1 Hz, 1H), 7.46 (ddd, *J* = 13.3, 8.0, 0.8 Hz, 1H), 7.32-7.22 (m, 4H), 7.19-7.13 (m, 1H), 6.32 (dt, *J* = 31.5, 12.8 Hz, 2H), 6.05 (dd, *J* = 15.1, 9.9 Hz, 1H), 4.85 (ddd, *J* = 14.8, 8.2, 6.4 Hz, 1H), 3.26 (dd, *J* = 15.3, 6.1 Hz, 1H), 2.84 (dd, *J* = 14.8, 8.5 Hz, 1H), 2.40 (s, 3H), 1.59 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 187.92, 151.77, 137.16, 136.26, 132.88, 132.31, 131.24, 129.74, 129.12, 128.85, 128.44 (d, *J* = 3.0 Hz), 128.17, 127.26, 126.39, 126.13, 124.40, 122.35, 119.89, 59.85, 40.07, 34.97, 22.08, 15.87 ppm. HRMS (ESI) m/z calcd for $[C_{25}H_{23}N+H]^+$ 338.1903, found 338.1899.

3-Benzyl-2-methyl-3-((2E,4E)-5-phenylpenta-2,4-dien-1-yl)-3H-indole (3au). Total isolated yield: 65%, 47.3 mg, 0.13 mmol, *2E/2Z* >20:1. **3au**, yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43 (d, *J* = 7.7 Hz, 1H), 7.32-7.27 (m, 5H), 7.22-7.17 (m, 3H), 7.12-7.08 (m, 3H), 6.79 (dd, *J* = 7.8, 1.6 Hz, 2H), 6.50 (dd, *J* = 15.6, 10.3 Hz, 1H), 6.38 (d, *J* = 15.7 Hz, 1H), 6.17 (dd, *J* = 15.0, 10.3 Hz, 1H), 5.08 (ddd, *J* = 14.9, 8.2, 6.5 Hz, 1H), 3.29 (d, *J* = 13.6 Hz, 1H), 2.97 (d, *J* = 13.6 Hz, 1H), 2.91 (dd, *J* = 15.0, 6.3 Hz, 1H), 2.70 (dd, *J* = 14.3, 8.5 Hz, 1H), 2.36 (s, 3H).^{13}C NMR (126 MHz, $CDCl_3$) δ 184.62, 154.90, 140.75, 137.12, 135.66, 133.63, 131.36, 129.32, 128.49, 128.45, 127.90, 127.88, 127.76, 127.33, 126.68, 126.16, 124.68, 122.86, 119.82, 62.96, 42.07, 39.49, 16.89 ppm. HRMS (ESI) m/z calcd for $[C_{27}H_{25}N+H]^+$ 364.2026, found 364.2057.

4a-((2E,4E)-5-Phenylpenta-2,4-dien-1-yl)-2,3,4,4a-tetrahydro-1H-carbazole (3av). Total isolated yield: 40%, 25.3 mg, 0.08 mmol, *2E/2Z* =7.3:1. **3av**, yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.63 (d, *J* = 7.7 Hz, 1H), 7.38-7.27 (m, 6H), 7.20 (dtd, *J* = 13.0, 7.3, 1.1 Hz, 2H), 6.55 (dd, *J* = 15.6, 10.4 Hz, 1H), 6.38 (d, *J* = 15.7 Hz, 1H), 6.14 (dd, *J* = 15.0, 10.4 Hz, 1H), 5.22 (dt, *J* = 15.0, 7.5 Hz, 1H), 2.96-2.88 (m, 1H), 2.76 (dd, *J* = 14.3, 6.8 Hz, 1H), 2.59 (ddd, *J* = 18.8, 13.3, 6.7 Hz, 2H), 2.44-2.37 (m, 1H), 2.26-2.19 (m, 1H), 1.85 (qt, *J* = 13.6, 3.7 Hz, 1H), 1.77-1.67 (m, 1H), 1.45 (qt, *J* = 13.4, 4.2 Hz, 1H), 1.18 (td, *J* = 13.5, 4.1 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 188.74, 154.79, 144.53, 137.15, 133.55, 131.20, 128.50, 128.46, 128.04, 127.63, 127.27, 126.12, 124.64, 121.87, 120.15, 57.80, 36.75, 36.54, 30.11, 28.78, 21.05 ppm. HRMS (ESI) m/z calcd for $[C_{23}H_{23}N+H]^+$ 314.1903, found 314.1905.

1,3-Dimethyl-1-((2E,4E)-5-phenylpenta-2,4-dien-1-yl)naphthalen-2(1H)-one (5a). Total isolated yield: 97%, 61 mg, 0.19 mmol, *2E/2Z* =5.0:1. **5a**, yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43 (ddt, *J* = 24.4, 14.6, 7.8 Hz, 3H), 7.32-7.26 (m, 6H), 7.21-7.15 (m, 1H), 6.51 (dd, *J* = 15.6, 10.5 Hz, 1H), 6.34 (d, *J* = 15.7 Hz, 1H), 6.03 (dd, *J* = 14.5, 10.6 Hz, 1H), 5.28 (dt, *J* = 15.0, 7.4 Hz, 1H), 2.91 (dd, *J* = 13.5, 8.2 Hz, 1H), 2.64 (dd, *J* = 13.5, 6.9 Hz, 1H), 2.00 (s, 3H), 1.53-1.47 (m, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 203.79, 144.92, 141.57, 137.34, 133.39, 132.87, 132.54, 131.04, 131.00, 130.21, 129.35, 128.80, 128.77, 128.57, 128.48, 128.11, 127.42, 127.21, 126.73, 126.58, 126.48, 126.39, 126.13, 124.13, 51.60, 46.29, 41.53, 26.53, 26.31, 15.87 ppm. HRMS (ESI) m/z calcd for $[C_{23}H_{23}O+H]^+$ 315.1743, found 315.1745.

1,3-Dimethyl-1-((2E,4E)-5-(3-fluorophenyl)penta-2,4-dien-1-yl)naphthalen-2(1H)-one (5b). Total isolated yield: 94%, 62.5 mg, 0.19 mmol, *2E/2Z* =9.4:1. **5b**, yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44-7.37 (m, 2H), 7.31-7.25 (m, 3H), 7.21 (td, *J* = 8.0, 6.1 Hz, 1H), 7.07-6.97 (m, 2H), 6.89-6.84 (m, 1H), 6.49 (dd, *J* = 15.6, 10.5 Hz, 1H), 6.29 (d, *J* = 15.6 Hz, 1H), 6.01 (dd, *J* = 15.1, 10.5 Hz, 1H), 5.31 (dt, *J* = 15.1, 7.6 Hz, 1H), 2.93 (dd, *J* = 13.9, 8.5 Hz, 1H), 2.65 (dd, *J* = 13.2, 7.2 Hz, 1H), 2.00 (d, *J* = 1.3 Hz, 3H), 1.50 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 203.72, 164.02, 162.08, 144.83, 141.64, 139.75 (d, *J* = 7.7 Hz), 132.95, 132.51, 130.56, 130.29-129.64 (m), 128.85, 128.61, 126.78, 126.37, 122.09, 114.03, 113.86, 112.43, 112.26, 51.53, 46.14, 26.71, 15.87 ppm. HRMS (ESI) m/z calcd for $[C_{23}H_{21}FO+H]^+$ 333.1655, found 333.1651.

1,3-Dimethyl-1-((2E,4E)-5-(3-chlorophenyl)penta-2,4-dien-1-yl)naphthalen-2(1H)-one (5c). Total isolated yield: 91%, 63.5 mg, 0.18 mmol, *2E/2Z* =5.3:1. **5c**, yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44-7.35 (m, 2H), 7.31-7.26 (m, 4H), 7.20-7.12 (m, 3H), 6.49 (dd, *J* = 15.6, 10.5 Hz, 1H), 6.25 (d, *J* = 15.7 Hz, 1H), 6.00 (dd, *J* = 15.0, 10.5 Hz, 1H), 5.31 (dt, *J* = 15.1, 7.6 Hz, 1H), 2.92 (dd, *J* = 13.7, 8.2 Hz, 1H), 2.65 (dd, *J* = 13.6, 6.9 Hz, 1H), 1.99 (d, *J* = 1.3 Hz, 3H), 1.50 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 203.68, 144.83, 141.62, 139.28, 134.44, 132.94, 132.53, 130.67, 130.19, 130.15, 129.66, 129.44, 128.85, 128.61, 127.05, 126.79, 126.37,

125.87, 124.39, 51.54, 46.17, 26.70, 15.87 ppm. HRMS (ESI) m/z calcd for $[C_{23}H_{21}ClO+H]^+$ 349.1359, found 349.1354.

1-((2E,4E)-5-(3-Chlorophenyl)penta-2,4-dien-1-yl)-1-methylnaphthalen-2(1H)-one (5d). Total isolated yield: 80%, 53.6 mg, 0.16 mmol, *2E/2Z* =4.7:1. **5d**, yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.48-7.42 (m, 3H), 7.35-7.30 (m, 2H), 7.28-7.24 (m, 1H), 7.21-7.12 (m, 3H), 6.49 (dd, *J* = 15.6, 10.5 Hz, 1H), 6.28 (t, *J* = 18.3 Hz, 1H), 6.20-6.12 (m, 1H), 6.00 (dt, *J* = 20.5, 10.4 Hz, 1H), 5.34 (dt, *J* = 15.1, 7.6 Hz, 1H), 2.95 (dd, *J* = 14.0, 8.4 Hz, 1H), 2.66 (dt, *J* = 13.2, 6.6 Hz, 1H), 1.51 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 203.69, 145.54, 145.16, 139.25, 134.44, 133.19, 130.37, 130.05 (d, *J* = 8.3 Hz), 129.63 (dd, *J* = 12.2, 4.1 Hz), 127.08, 126.88, 126.66, 125.88, 125.17, 124.39, 51.92, 45.83, 26.65 ppm. HRMS (ESI) m/z calcd for $[C_{22}H_{19}ClO+H]^+$ 335.1203, found 335.1201.

3-Ethyl-1-methyl-1-((2E,4E)-5-(3-chlorophenyl)-2,4-dien-1-yl)naphthalen-2(1H)-one (5e), Total isolated yield: 82%, 59.5 mg, 0.16 mmol, *2E/2Z* =3.4:1. **5e**, yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42-7.35 (m, 2H), 7.30-7.25 (m, 3H), 7.21-7.10 (m, 4H), 6.48 (dd, *J* = 15.6, 10.5 Hz, 1H), 6.24 (d, *J* = 15.7 Hz, 1H), 5.99 (dd, *J* = 15.0, 10.5 Hz, 1H), 5.34-5.26 (m, 1H), 2.90 (dd, *J* = 13.7, 8.3 Hz, 1H), 2.63 (dd, *J* = 13.7, 6.9 Hz, 1H), 2.41 (q, *J* = 7.8 Hz, 2H), 1.48 (s, 3H), 1.12 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 203.24, 144.66, 139.96, 139.27, 137.97, 134.42, 133.00, 130.65, 130.22, 130.13, 129.65, 129.41, 128.83, 127.03, 126.78, 126.31, 125.85, 124.37, 51.53, 46.20, 29.69, 26.41, 22.43, 12.76 ppm. HRMS (ESI) m/z calcd for $[C_{24}H_{23}ClO+H]^+$ 363.1516, found 363.1521.

4-((2E,4E)-5-(3-chlorophenyl)penta-2,4-dien-1-yl)-3,4,5-trimethoxycyclohexa-2,5-dienone (5g), Total isolated yield: 44%, 31.8 mg, 0.09 mmol, *2E/2Z* = 5.5:1, **5g**, yellow solid, m. p. 149 – 151 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.41 – 7.13 (m, 4H), 6.62 (dd, *J* = 15.6, 10.5 Hz, 1H), 6.35 (d, *J* = 15.7 Hz, 1H), 6.16 (ddd, *J* = 15.0, 10.5, 0.4 Hz, 1H), 5.65 – 5.60 (m, 2H), 5.41 (dt, *J* = 15.2, 7.7 Hz, 1H), 3.79 (s, 6H), 3.13 (s, 3H), 2.85 (d, *J* = 7.7 Hz, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 186.95 (s), 168.96 (s), 139.00 (s), 134.53 (s), 134.15 (s), 130.33 (s), 129.81 (d, *J* = 12.0 Hz), 127.36 (s), 126.95 (s), 126.16 (s), 124.42 (s), 104.51 (s), 79.02 (s), 56.24 (s), 52.63 (s), 40.25 (s).

2,3-Dimethyl-3-(5-phenylpentyl)-3H-indole (6)
Isolated yield: 84%, 48.9 mg, 0.17 mmol, **6**, yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.74-7.55 (m, 1H), 7.33 (td, *J* = 7.6, 1.7 Hz, 1H), 7.29-7.16 (m, 4H), 7.09 (dd, *J* = 27.0, 7.6 Hz, 2H), 2.52-2.48 (m, 1H), 2.26 (s, 2H), 1.92-1.84 (m, 1H), 1.79-1.72 (m, 1H), 1.53-1.45 (m, 2H), 1.30 (s, 2H), 1.23-1.14 (m, 2H), 0.79 (td, *J* = 12.6, 7.0 Hz, 1H), 0.66 (qd, *J* = 12.8, 7.4 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 187.15, 154.39, 143.82, 142.42, 128.30, 128.17, 127.51, 125.57, 124.97, 121.43, 119.74, 57.83, 37.09, 35.66, 30.88, 29.22, 23.81, 22.69, 15.65 ppm. HRMS (ESI) m/z calcd for $[C_{21}H_{25}N+H]^+$ 292.2065, found 292.2068.

2-Benzyl-4-((2,3-dimethyl-3H-indol-3-yl)methyl)-7-phenyl-3a,4,7,7a-tetrahydro-1H-isoindole-1,3(2H)-dione (7a) Total isolated yield of **7a** and **7b**: 63%, 89.7 mg, 0.19 mmol, **7a:7b** = 1.1:1. **7a**, yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.58 (d, *J* = 7.7 Hz, 1H), 7.44 (d, *J* = 7.1 Hz, 1H), 7.36-7.19 (m, 12H), 6.96 (dd, *J* = 7.6, 1.7 Hz, 2H), 6.00 (dt, *J* = 9.3, 3.3 Hz, 1H), 5.73 (dt, *J* = 9.3, 3.2 Hz, 1H), 4.46 (dd, *J* = 38.3, 14.1 Hz, 2H), 3.24 (dd, *J* = 14.8, 6.7 Hz, 2H), 2.92 (t, *J* = 8.1 Hz, 1H), 2.44 (dd, *J* = 14.8, 5.8 Hz, 1H), 2.35 (s, 3H), 2.30 (dd, *J* = 8.3, 5.4 Hz, 1H), 1.42 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 186.78, 177.15, 175.20, 154.30, 143.01, 138.64, 135.90, 134.16, 130.71, 128.54, 128.37, 128.08 (d, *J* = 3.8 Hz), 127.69, 126.90, 125.26, 122.31, 120.06, 58.01, 46.58, 44.03, 41.93, 41.43, 38.04, 33.43, 29.64, 23.60, 16.08 ppm. HRMS (ESI) m/z calcd for $[C_{32}H_{30}N_2O_2+H]^+$ 475.2386, found 475.2383.

2-Benzyl-4-((2,3-dimethyl-3H-indol-3-yl)methyl)-7-phenyl-3a,4,7,7a-tetrahydro-1H-isoindole-1,3(2H)-dione (7b). 7b, yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53 (d, *J* = 7.7 Hz, 1H), 7.37-7.18 (m, 12H), 6.97 (dd, *J* = 7.7, 1.4 Hz, 2H), 5.78 (dt, *J* = 9.3, 3.3 Hz, 1H), 5.36 (dt, *J* = 9.3, 3.2 Hz, 1H), 4.50 (dd, *J* = 45.5, 14.1 Hz, 2H), 3.26-3.22 (m, 1H), 3.12 (t, *J* = 7.9 Hz, 1H), 2.90-2.82 (m, 2H), 2.63 (dd, *J* = 14.8, 8.5 Hz, 1H), 2.40 (s, 3H), 1.43 (s, 3H).^{13}C NMR (126 MHz, $CDCl_3$) δ 186.74, 177.16, 175.18, 154.35, 142.71, 138.61, 135.81, 134.30, 132.03 (d, *J* = 9.9 Hz), 129.42, 128.69-128.29 (m), 127.99 (d, *J* = 9.4 Hz), 127.70, 126.85, 125.13, 122.16, 120.09, 58.08, 46.52, 45.19, 42.02, 41.23, 38.67, 33.33, 29.62, 23.24, 16.00 ppm. HRMS (ESI) m/z calcd for $[C_{32}H_{30}N_2O_2+H]^+$ 475.2386, found 475.2386.

Conflicts of interest

There are no conflicts to declare.

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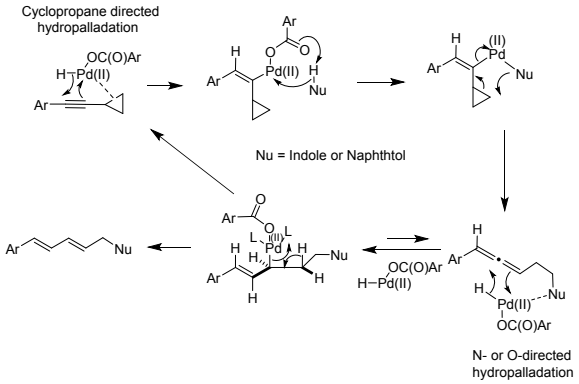
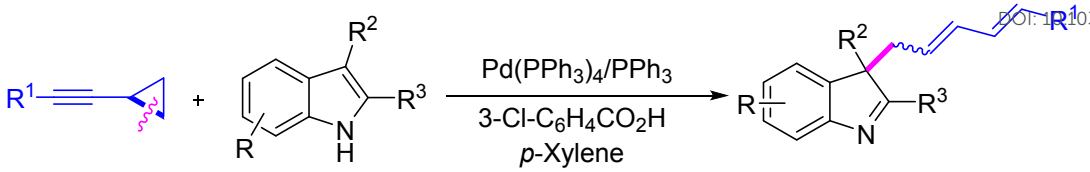
19 We can't rule out another mechanism proposed by one reviewer, hydridopalladium complex **A** undergoing initial cyclopropane-directed hydropalladation to the cyclopropyl phenylacetylene to give a cyclopropyl vinylpalladium(II) intermediate which then subsequently coordination to the donor nucleophile. The tethered nucleophilic indole or naphthol then attacks the cyclopropane ring to cause a loss of Pd(0)Ln and give the homoallenyl derivative containing incorporated nucleophile by a formal internal S_N2 ring-opening process. The homoallenyl species subsequently undergoing a hydropalladation followed β-hydride elimination to afford the diene and achieve the catalytic cycle. Further work is currently being pursued to look into this possibility.



20 It is also mechanistically conceivable that the RCH=C(Pd[II]Ln)cyclopropyl intermediate could be losing Pd(0)Ln to give a highly stabilized cyclopropylvinyl cation, with this then undergoing nucleophilic ring cleavage via an extended S_N2 type mechanism. However, on the basis of recent discussions of Hale et al on cyclopropyl vinyl cation ring-openings by nucleophiles usually being highly unfavourable, with nucleophiles always preferring to attack the vinyl cation carbon instead, a) H. A. Watson, S. Manaviazar, H. G. Steeds, and K. J. Hale, *Tetrahedron*, **2020**, 76, 131061; b) S. A. Sherrod and R.G. Bergman, *J. Am. Chem. Soc.*, **1971**, 93, 1925; c) S.A. Sherrod, R.G. Bergman, *J. Am. Chem. Soc.*, **1969**, 91, 2115; d) M. Hanack and T. Bassler, *J. Am. Chem. Soc.*, 1969, 91, 2117; e) M. Hanack, *Acc. Chem. Res.*, **1976**, 9, 364.



Cleavage of C-C bond
Linear and *E*-selectivity
100% Atom economy
Dearomative of indoles

A palladium catalyzed dearomative allylic alkylation of of indoles with cyclopropyl acetylenes for the synthesis of indolenines with 1,3-diene motifs was developed in high regio-, and stereoselectivities.