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Gold(I)-Catalyzed Intermolecular Hydroarylation of Alkenes with Indoles under Thermal and Microwave-Assisted Conditions

Ming-Zhong Wang, Man-Kin Wong,* and Chi-Ming Che*[a]

Abstract: An efficient method for intermolecular hydroarylation of aryl and aliphatic alkenes with indoles using a combination of [(PR_3)AuCl]/AgOTf as catalyst under thermal and microwave-assisted conditions has been developed. The gold(I)-catalyzed reactions of indoles with aryl alkenes were achieved in toluene at 85 °C over a reaction time of 1–3 h with 2 mol % of [(PR_3)AuCl]/AgOTf as catalyst. This method works for a variety of styrenes bearing electron-deficient, electron-rich, and sterically bulky substituents to give the corresponding products in good to high yields (60–95 %). Under microwave irradiation, coupling of unactivated aliphatic alkenes with indoles gave the corresponding adducts in up to 90 % yield. Selective hydroarylation of terminal C=C bond of conjugated dienes with indoles gave good product yields (62–81 %). On the basis of deuterium-labeling experiments, a reaction mechanism involving nucleophilic attack of Au(I)-coordinated alkenes by indoles is proposed.

Keywords: C–C coupling · gold · homogeneous catalysis · hydroarylation · synthetic methods

Introduction

Intermolecular hydroarylation of alkenes is an efficient approach for functionalization of arenes through carbon–carbon bond formation.[1] Transition-metal-catalyzed hydroarylation of alkenes is of particular importance due to its high selectivity, synthetic efficiency, and environmental friendliness. Ruthenium(II) and rhodium(I) complexes are effective catalysts for intermolecular hydroarylation of unactivated alkenes with arenes possessing directing groups such as ketones[2a,b] and imines.[2c] Recently, $Bi(OTf)_3$-catalyzed[3a] and $FeCl_3$-catalyzed[3b] hydroarylation of styrenes was reported for the synthesis of a variety of 1,1-diaryl alkanes in good yields.

Alkylated indoles are important structural motifs commonly found in many bioactive natural products and drug candidates.[4] Conventionally, alkylated indoles are synthesized by carbon–carbon bond-forming reactions such as acid- or base-promoted alkylation.[5] However, these literature methods require the use of stoichiometric or excess amounts of strong acids/bases and air-sensitive/moisture-sensitive organometallic reagents. Also, halide salts are obtained as byproducts. Palladium,[6] platinum,[7] ruthenium,[8a] nickel,[8b] and indium[8c] complexes have been employed as catalysts for the functionalization of indoles through carbon–carbon bond formation. Recently, Widenhoefer and co-workers reported platinum(II)-catalyzed intermolecular hydroarylation of unactivated alkenes with indoles in high product yields. Hydroarylation of styrenes gave mixtures of Markovnikov and anti-Markovnikov adducts.[7c]

Gold-catalyzed organic transformations have become of considerable interest in organic synthesis in recent years.[9,10] Gold(I) catalysts are soft and carbophilic Lewis acids that have been used to activate alkenes towards nucleophilic attack by oxygen,[11] nitrogen,[12] and carbon nucleophiles.[13] Indeed, gold(I)-catalyzed coupling of indoles with alkynes,[14a–c] allenes,[14d] aldehydes,[14e] electron-deficient alkenes,[14f–i] and 1,3-dicarbonyl compounds[14j] have been reported. Gold-catalyzed functionalization of dienes[11b,12b] has also been developed. During the preparation of this manuscript, Liu and co-workers[13c] reported the use of $AuCl_3$/AgOTf or triflic acid (HOTf) as a catalyst for hydroarylation of alkenes. Nevertheless, this reported hydroarylation reaction was limited to *N*-phenylsulfonyl-protected indole. As part of our ongoing effort to develop gold-catalyzed

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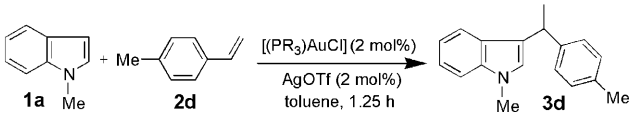
C–O, C–N, and C–C bond-formation reactions,[15] we here report an efficient gold(I)-catalyzed intermolecular hydroarylation of unactivated alkenes with indoles and extension of the substrate scope to include indoles with different electronic properties and various cycloalkenes and conjugated dienes. We demonstrate that microwave irradiation[16] is an effective means to promote indole coupling with unactivated aliphatic alkenes, which could not be achieved under thermal reaction conditions.

Results

Gold(I)-catalyzed coupling of indoles with aryl alkenes: First, we examined the coupling reaction between *N*-methylindole (**1a**) and *p*-methylstyrene (**2d**; see Table 1). In the presence of [(PPh_3)AuCl] (2 mol%) and AgOTf (2 mol%), **1a** (0.3 mmol) reacted with **2d** (0.33 mmol) in toluene at 85°C over 1.25 h to give 3-alkylated indole **3d** (Markovnikov product) in 85% yield based on 95% substrate conversion (Table 1, entry 1). When either [(PPh_3)AuCl] or AgOTf was used, less than 10% substrate conversion was observed. At 65°C, less than 5% substrate conversion was found (Table 1, entry 2). No reaction was observed at room temperature (Table 1, entry 3). With 1.5 equivalents of **2d**, **3d** was obtained in 75% yield and with complete substrate conversion (Table 1, entry 4). A number of gold(I) catalysts having different phosphine ligands were screened (Table 1, entries 5–9), of which those with a P(*t*Bu)$_2$(*o*-biphenyl), P(4-$C_6H_4OMe)_3$, or PCy_3 ligand were most effective. The reaction between **1a** and **2d** to give **3d** in 72% yield could be achieved by using 5 mol% of triflic acid as catalyst, but the reaction time was 12 h instead of the 1.25 h when a gold(I) catalyst was used. With 2/20% of [(PPh_3)AuMe]/H_2SO_4 as catalyst, **1a** reacted with **2d** in toluene at 85°C over 4 h to give **3d** in 77% yield (Table 1, entry 10).[11f–g,12h]

Table 1. Effect of temperature and catalyst screening.[a]



Entry	PR_3	*T* [°C]	Conversion [%][b]	Yield [%][c]
1	PPh_3	85	95	85
2	PPh_3	65	<5	trace
3	PPh_3	RT	0	–
4[d]	PPh_3	85	100	75
5	P(*t*Bu)$_2$(*o*-biphenyl)	85	99	87
6	P(4-$C_6H_4OMe)_3$	85	95	82
7	PCy_3	85	95	80
8	P($C_6F_5)_3$	85	70	52
9	PEt_3	85	50	40
10[e]	[(PPh_3)AuMe]/H_2SO_4	85	86	77

[a] Reactions were conducted with **1a** (0.3 mmol), **2d** (0.33 mmol), and [(PPh_3)AuCl]/AgOTf (2 mol%) in toluene (1 mL) for 1.25 h. [b] Determined by ^{1}H NMR analysis of crude reaction mixture. [c] Yield of isolated product. [d] 0.45 mmol of **2d** was used. [e] 2 mol% of [(PPh_3)AuMe] and 20 mol% of H_2SO_4 for 4 h.

To determine the substrate scope, we extended our study to different indoles **1** and aryl alkenes **2** using 2 mol% of [(PPh_3)AuCl]/AgOTf as catalyst (Table 2). Coupling of *N*-methylindole (**1a**) with styrenes **2a–e** bearing electron-donating substituents (*p*-MeO, *p*-dimethylamino, *p*-*tert*-butyl, and *p*-Me) or an electron-withdrawing *p*-Cl substituent gave the corresponding products in high substrate conversions and product yields (Table 2, entries 1–5).

The coupling reaction worked for bulky 1,1-diphenylethylene (**2f**) and indene (**2g**; Table 2, entries 6–7), and *N*-aryl indoles **1b,c** (Table 2, entries 8–10). The present protocol also allows direct coupling of NH indoles **1d–g** with styrenes **2a** and **2c** to give 3-alkylated indoles **3k–o** without formation of *N*-alkylated indoles (Table 2, entries 11–15).

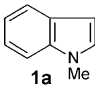
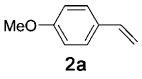
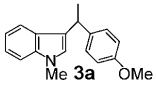
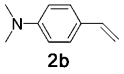
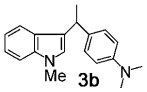
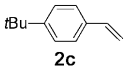
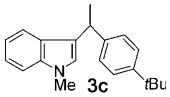
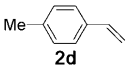
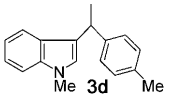
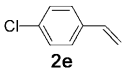
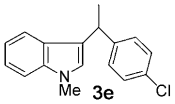
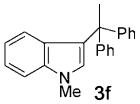
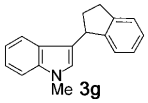
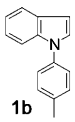
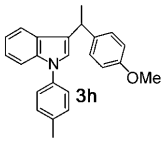
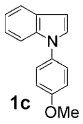
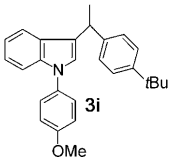
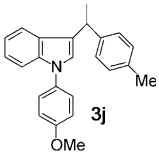
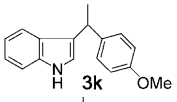
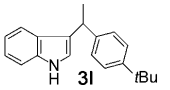
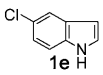
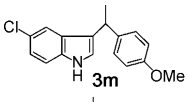
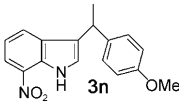
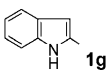
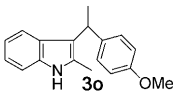
By using 2 mol% of [(PPh_3)AuCl]/AgOTf as catalyst, a gram-scale coupling of **1a** (10 g) with **2a** (11.25 g) can be conducted as a one-pot reaction to give 17.1 g of **3a** in 85% yield over a reaction time of 6 h.

For the reaction of **1a** with styrene in toluene at 85°C for 1.25 h (2 mol% of [(PPh_3)AuCl]/AgOTf), only a trace amount of coupling product could be detected by ^{1}H NMR analysis of the crude reaction mixture, and extensive styrene polymerization was detected;[3a,b] the latter accounted for the low product yield.

Microwave-assisted gold(I)-catalyzed coupling of indoles with aliphatic alkenes: No product was found when unactivated aliphatic alkenes such as allylbenzene (**4a**) were treated with indole **1b** under the reaction conditions described above. When the reaction between **1b** and **4a** was conducted in dichloroethane at 120°C for 16 h, a trace amount of product **5a** could be detected on the basis of the ^{1}H NMR spectrum of the crude reaction mixture. However, we found that product formation was accompanied by subsequent decomposition of **5a**. The reaction between **1h** and **4j** gave **5m** in 21% yield based on 38% substrate conversion in dichloroethane at 120°C over 36 h. Our recent work revealed that microwave radiation is an effective means to accelerate gold(I)-catalyzed hydroamination of alkenes.[15c,e] The accelerating effects of microwave irradiation on organic syntheses can not be easily achieved by conventional heating.[16c] In this work, we employed microwave radiation to assist the gold(I)-catalyzed intermolecular hydroarylation of aliphatic alkenes with indoles (Table 3).

Under microwave irradiation (43 W, 7 min), coupling of *N*-*p*-tolylindole (**1b**) and allylbenzene **4a** with 5 mol% of [(PPh_3)AuCl]/AgOTf as catalyst in dichloroethane at 130°C gave alkylated indole **5a** in 81% yield (Table 3, entry 1). Yet, **5a** is not the expected product resulting from hydroarylation of the terminal C=C bond of **4a** with **1b**. Likely, migration of the C=C bond of **4a** occurred and generated *trans*-β-methylstyrene in situ under the reaction conditions (see below). Similar gold-catalyzed migration of C=C bonds has been reported.[11a,15c] Without microwave irradiation,

Table 2. Gold(I)-catalyzed coupling of indoles with aryl alkenes.[a]

Entry	Indole	Alkene	Product	Conversion [%][b]/yield [%][c]
1	 1a	 2a	 3a	100/95
2	**1a**	 2b	 3b	92/86
3	**1a**	 2c	 3c	90/82
4	**1a**	 2d	 3d	95/85
5[d]	**1a**	 2e	 3e	74/65
6[e]	**1a**	 2f	 3f	75/60
7	**1a**	 2g	 3g	82/78
8	 1b	**2a**	 3h	100/90
9	 1c	**2c**	 3i	95/93
10	**1c**	**2d**	 3j	95/90
11	 1d	**2a**	 3k	95/85
12	**1d**	**2c**	 3l	95/82
13	 1e	**2a**	 3m	95/90
14	 1f	**2a**	 3n	95/89
15	 1g	**2a**	 3o	95/86

[a] Reactions were conducted with **1** (0.3 mmol), **2** (0.33 mmol) and 2 mol% of [(PPh_3)AuCl]/AgOTf in toluene (1 mL) at 85 °C for 1.25 h. [b] Determined by ^{1}H NMR analysis of the crude reaction mixture. [c] Yield of isolated product. [d] Reaction time was 3 h. [e] 0.6 mmol of **2** were used.

coupling of **1b** with *trans*-β-methylstyrene gave **5a** in lower yield (67%) over 2 h at 85 °C.

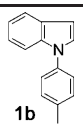
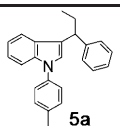
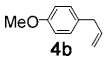
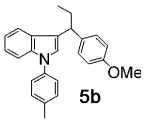
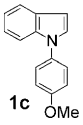
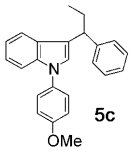
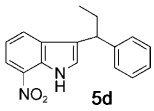
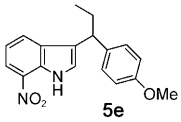
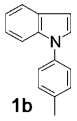
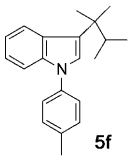
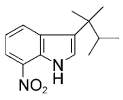
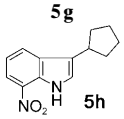
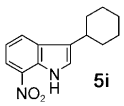
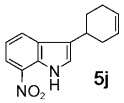
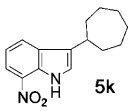
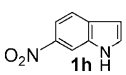
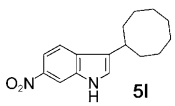
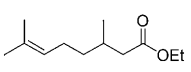
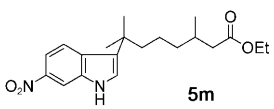
Similarly, alkylated indoles **5b–e** were obtained by coupling of *N*-aryl indoles **1b**,**c** and NH indole **1f** with allylbenzenes **4a**,**b** under microwave irradiation (Table 3, entries 2–5).

When unactivated 3,3-dimethyl-1-butene (**4c**) was treated with 4-tolylindole (**1b**) under microwave irradiation, alkylated indole **5f** was obtained (Table 3, entry 6). Note that **5f** could also be obtained by direct coupling of 2,3-dimethyl-2-butene (**4d**) with **1b** (Table 3, entry 7); no reaction was observed without microwave irradiation. This suggests that **4c** may be converted to **4d** by gold-catalyzed methyl-group migration,[17] and the **4d** generated in situ coupled with **1b** to give **5f**. Furthermore, NH indole **1f** coupled with **4c**,**d** to afford **5g** (Table 3, entries 8 and 9).

Under microwave irradiation, gold-catalyzed coupling of a series of unactivated aliphatic cycloalkenes **4e–i** with indoles **1f**,**h** were accomplished (Table 3, entries 10–14). No reaction was observed between **1f** and 1-hexene or *trans*-5-decene.

Microwave-assisted gold-catalyzed coupling of indoles with unactivated aliphatic alkenes bearing remote functional groups such as ester, ether, and amide were also examined. Direct coupling of 6-nitroindole (**1h**) with alkenes **4j**,**k** gave products **5m**,**n** with the ester and ether groups remaining intact (Table 3, entries 15 and 16). For the reaction between **1h** and amide-containing alkene **4l**, less than 5% conversion of **1h** was found by ^{1}H NMR analysis of the crude reaction mixture (Table 3,

Table 3. Microwave-assisted gold(I)-catalyzed coupling of substituted indoles with aliphatic alkenes.[a]

Entry	Indole	Alkene	Product	Conversion [%][b]/ yield [%][c]
1	 **1b**	 **4a**	 **5a**	89/81
2	**1b**	 **4b**	 **5b**	92/86
3	 **1c**	**4a**	 **5c**	90/82
4	 **1f**	**4a**	 **5d**	90/80
5	**1f**	**4b**	 **5e**	95/90
6	 **1b**	 **4c**	 **5f**	95/75
7	**1b**	 **4d**	**5f**	100/85
8	**1f**	**4c**	 **5g**	50/45
9	**1f**	**4d**	**5g**	95/84
10	**1f**	 **4e**	 **5h**	51/42
11	**1f**	 **4f**	 **5i**	65/60
12	**1f**	 **4g**	 **5j**	95/83
13	**1f**	 **4h**	 **5k**	80/65
14	 **1h**	 **4i**	 **5l**	75/62
15	**1h**	 **4j**	 **5m**	92/85

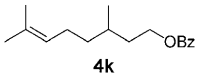
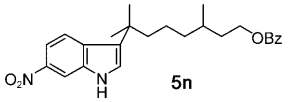
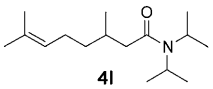
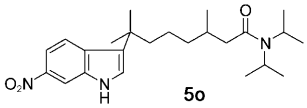
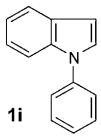
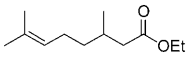
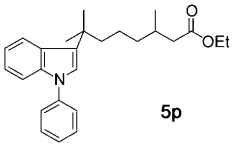
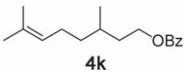
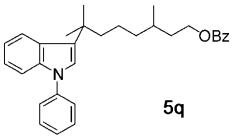
entry 17). Coupling of *N*-phenylindole (**1i**) with ester- and ether-containing alkenes **4j**,**k** was also achieved (Table 3, entries 18 and 19).

Microwave-assisted gold-catalyzed coupling of **1h** and **4j** gave **5m** in 85% yield based on 92% substrate conversion at 140°C over 5 min (Table 3, entry 15). By using 5 mol% of triflic acid as catalyst, **5m** could also be obtained in 32% yield based on 45% conversion at 50°C, but the reaction time was 16 h.

In view of the exceptional accelerating effect of microwave irradiation, we decided to study microwave-assisted coupling of aryl alkenes with indoles. Notably, under microwave irradiation, gold-catalyzed coupling of indole **1a** with aryl alkenes **2a**, **2e**, and **2g** afforded the corresponding adducts **3a** (93% yield), **3e** (68% yield), and **3g** (62% yield) at 120°C in just 1 min. These findings could provide a useful basis for further development of high-throughput gold(I) organic catalysis.

Gold(I)-catalyzed coupling of indoles with conjugated dienes: We performed hydroarylation of conjugated diene **6a** ($E/Z = 1.4/1$) with *N*-methylindole (**1a**) using 5 mol% of [(PPh_3)AuCl]/AgOTf at 70°C to give adduct **7a** in 81% yield (Table 4, entry 1). The C=C bond of **7a** obtained is of *E* configuration. Of particular interest is that the configuration of diene **6a** recovered is predominantly *Z* ($E/Z = 1/10$; see below for a more detailed discussion). This coupling reaction also worked well for indoles having different electronic properties (Table 4, entries 2–10), and the C=C bonds of all products are *E*-configured. For the reaction of electron-deficient conjugated diene

Table 3. (Continued)

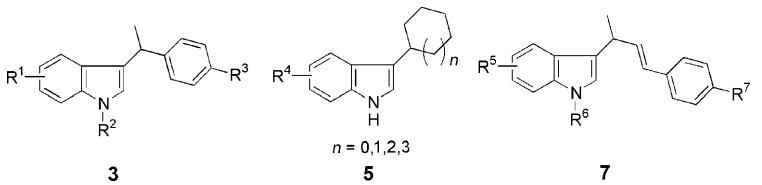
Entry	Indole	Alkene	Product	Conversion [%][b]/ yield [%][c]
16	**1h**	 **4k**	 **5n**	89/80
17	**1h**	 **4l**	 **5o**	<5%/nd
18	 **1i**	 **4j**	 **5p**	85/75
19	**1i**	 **4k**	 **5q**	26/20

[a] Reactions were conducted with **1** (0.3 mmol), **4** (0.6 mmol), and 5 mol% of [(PPh_3)AuCl]/AgOTf in $ClCH_2CH_2Cl$ (1 mL) with microwave irradiation (43 W, 5–30 min, 130–140 °C). [b] Determined by ^1H NMR analysis of the crude reaction mixture. [c] Yield of isolated product.

6d with *N*-methylindole (**1a**), only a trace amount of product was identified by ^1H NMR analysis of the crude reaction mixture (Table 4, entry 11). Interestingly, when *Z*-configured conjugated diene **8a** was treated with **1a**, adduct **7a** of *E* configuration was again obtained (Table 4, entry 12). When 5 mol% of triflic acid was used as a catalyst instead of gold(I) catalysts in the coupling reaction of **1a** with **6a**, no product was detected.

Discussion

We have developed an efficient method using [(PR_3)AuCl]/AgOTf (2 mol%) as catalyst for direct coupling of indoles with aryl and aliphatic alkenes to give C3-alkylated indoles (Markovnikov adducts) in thermal and microwave-assisted reactions. Unactivated aliphatic alkenes such as cyclohexene do not readily react with indoles under thermal conditions but smoothly react with indoles in the presence of 5 mol% of [(PPh_3)AuCl]/AgOTf as catalyst in dichloroethane at 130 °C under microwave irradiation. This present protocol provides a convenient way to synthesize the three classes of C3-substituted indole derivatives **3**, **5**, and **7** depicted in Scheme 1.



3 **5** **7**

Scheme 1. Three classes of C3-alkylated indoles synthesized in this work.

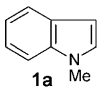
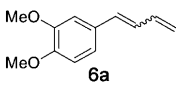
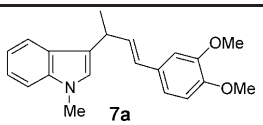
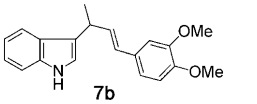
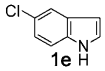
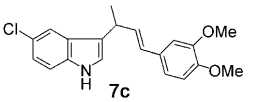
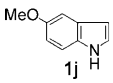
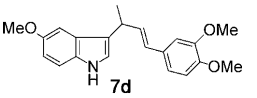
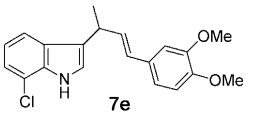
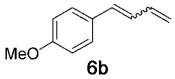
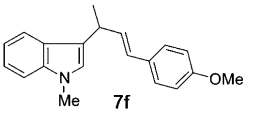
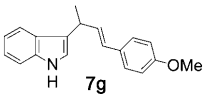
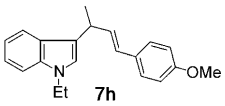
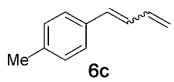
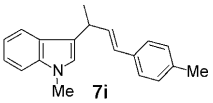
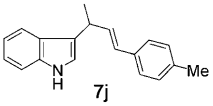
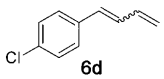
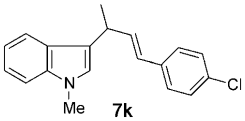
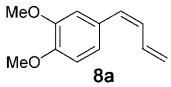
It has been reported that alkylated indoles **3** can be synthesized by three methods: substitution of benzotriazole-containing anilines by indoles,[18a] Friedel–Crafts reaction of indoles with α-amido sulfones in the presence of acidic promoters,[18b] and Brønsted acid-catalyzed dehydrative nucleophilic substitution of benzyl alcohols by indoles.[18c] However, these methods require the use of air-sensitive/moisture-sensitive organometallic reagents and/or acids. The gold-based protocol reported here allows preparation of indoles **3**, **5**, and **7** in good yields under mild reaction conditions.

A series of heterocyclic scaffolds featuring 3-cycloalkyl-substituted indoles **5** as the major structural elements have been found to exhibit potent inhibitory effects on hepatitis C virus (HCV) NS5B polymerase.[18d] The preparation of these cycloalkyl-substituted indoles required a two-step synthetic approach including condensation of indoles with cyclic ketones under basic conditions followed by palladium-catalyzed hydrogenation.[18d] In this work, indoles **5** could be synthesized in good yields by gold-catalyzed direct coupling of indoles with unactivated aliphatic cycloalkenes in one step under microwave irradiation.

Alkylated indoles **7** have been prepared by iodine-catalyzed[18e] and metal-catalyzed[18f–g] alkylation of indoles with allylic alcohol derivatives. The gold-catalyzed direct coupling of indoles with conjugated dienes described here offers a simple, efficient, and one-step method to prepare this class of compounds.

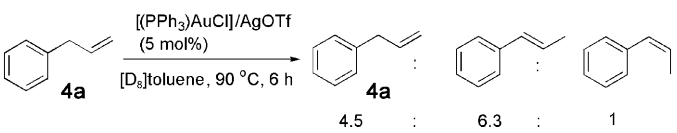
Gold-catalyzed migration of C=C bonds: As depicted in Table 3, under microwave irradiation, gold-catalyzed coupling of *p*-tolyl indole **1b** with allylbenzene (**4a**) gave alkylated indole **5a**, yet the latter is not the direct coupling product coming from hydroarylation of the terminal C=C bond of **4a** with **1b**. We propose that migration of the C=C bond of **4a** occurs to generate *trans*-β-methylstyrene in situ under the current reaction conditions. An independent experiment in which **4a** was heated at 90 °C for 6 h in [D_8]toluene in the presence of 5 mol% of [(PPh_3)AuCl]/AgOTf was performed. On the basis of ^1H NMR analysis of the crude reaction mixture, a

Table 4. Gold(I)-catalyzed coupling of indoles with conjugated dienes.[a]

Entry	Indole	Diene	Product	Conversion [%][b]/ yield [%][c]
1	 **1a**	 **6a**	 **7a**	89/81
2	 **1d**	**6a**	 **7b**	82/76
3	 **1e**	**6a**	 **7c**	80/72
4	 **1j**	**6a**	 **7d**	85/75
5	 **1l**	**6a**	 **7e**	82/70
6	**1a**	 **6b**	 **7f**	85/80
7	**1d**	**6b**	 **7g**	86/75
8	 **1k**	**6b**	 **7h**	87/74
9	**1a**	 **6c**	 **7i**	83/65
10	**1d**	**6c**	 **7j**	81/62
11	**1a**	 **6d**	 **7k**	trace
12	**1a**	 **8a**	**7a**	85/73

[a] Reactions were conducted with **1** (0.3 mmol), **6** (0.45 mmol) (E/Z = 1.2/1–1.4/1), and 5 mol% of [(PPh_3)AuCl]/AgOTf in toluene (1 mL) at 70 °C for 16 h. [b] Determined by ^{1}H NMR analysis of the crude reaction mixture. [c] Yield of isolated product.

mixture of **4a**, *trans*-β-methylstyrene, and *cis*-β-methylstyrene (4.5:6.3:1) was found (Scheme 2). Thus, conversion of

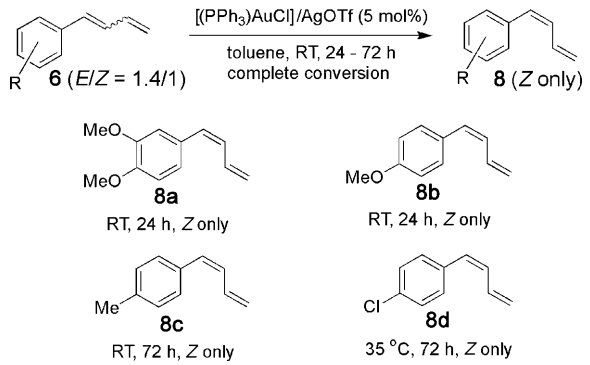


Scheme 2. Gold-catalyzed migration of C=C bonds.

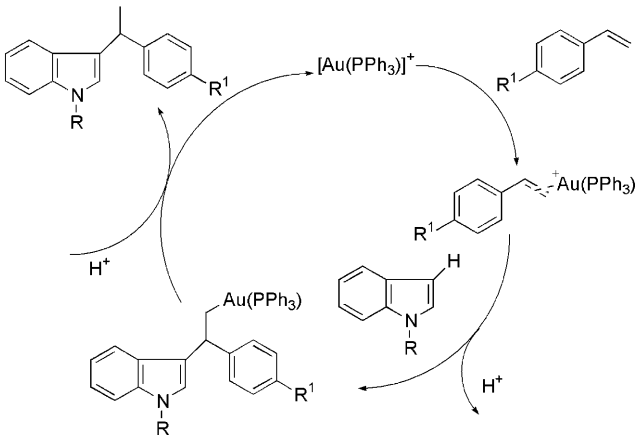
4a to *trans*-β-methylstyrene and *cis*-β-methylstyrene by heating in the presence of the gold catalyst may account for the formation of **5a**. We have attempted to detect the conversion of **4a** to *trans*-β-methylstyrene in the absence of indole **1b** under microwave irradiation. However, intractable mixtures of products were obtained in several attempts, which may result from alkene polymerization.[19] Zirconium,[20a] palladium,[20b] and ruthenium[20c] complexes were reported to be effective catalysts for the isomerization of allylbenzene (**4a**) to *trans*-β-methylstyrene and *cis*-β-methylstyrene.

Gold-catalyzed *E*/*Z* isomerization of the C=C bonds of conjugated dienes: Predominately *Z* diene (E/Z = 1/10) was recovered in the coupling reaction of conjugated diene **6a** (E/Z = 1.4/1) with **1a**. We propose that gold-catalyzed isomerization of mixtures of *E*/*Z* conjugated dienes to *Z* conjugated diene occurred (Scheme 3).

Treatment of *E*/*Z* diene **6a** (0.3 mmol, E/Z = 1.4/1) with 5 mol% of [(PPh_3)AuCl]/AgOTf in toluene at room temperature for 24 h gave *Z* diene **8a** (100% *Z* configuration), as confirmed by ^{1}H NMR analysis of the crude reaction mixture. In contrast, when *E*/*Z* diene **6a** was stirred at room temperature or 70 °C for 24 h without [(PPh_3)AuCl]/AgOTf, no change in configuration was observed. We also found that 5 mol% of triflic acid did not change the configuration of *E*/*Z*-diene **6a**. As depicted in Scheme 3, this gold-catalyzed isomerization reaction works well for dienes bearing electron-donating and electron-withdrawing substituents. According to the literature,[21] *Z* aryl dienes can be synthesized by Wittig reactions with bulky phosphonium salts. Exclusive *Z* products could be prepared in low yields at low temperature (−100 °C) by using a strong



Scheme 3. Gold-catalyzed isomerization of *E*/*Z* dienes to *Z* dienes.



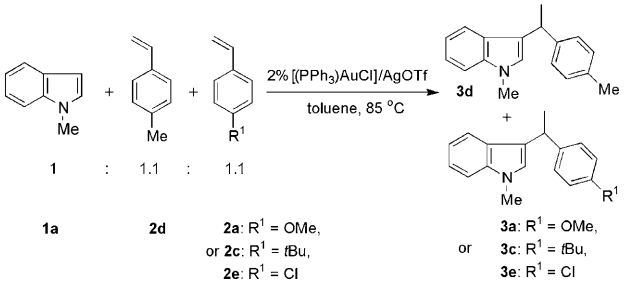
Scheme 4. Proposed reaction pathway.

base such as butyllithium. The gold-catalyzed reaction described here provides convenient and efficient access to *Z* aryl dienes in good yields under mild reaction conditions.

Proposed reaction mechanism: A proposed reaction pathway for the hydroarylation of styrenes with indoles is depicted in Scheme 4. The C=C bond of an alkene coordinated to cationic $[AuPPh_3]^+$ is attacked by nucleophilic indole to give a gold complex intermediate that undergoes subsequent protonolysis at the Au–C bond to give the desired coupling product. This proposed reaction pathway has support from the following experiments.

A competition study was performed to examine the relative reaction rates of indole **1a** with substituted styrenes **2a**, **2c**, **2d**, and **2e**. The relative reaction rates were calculated by means of the integration ratio of the ^{1}H NMR signals of the corresponding products in the crude reaction mixture. The results are depicted in Table 5. Styrene **2a** containing an electron-rich *p*-methoxy substituent showed higher reactivity than styrene **2e** bearing an electron-withdrawing *p*-Cl group. This result is consistent with the positively charged transition state in gold(I)-catalyzed alkene functionalization proposed in the literature.[11–13]

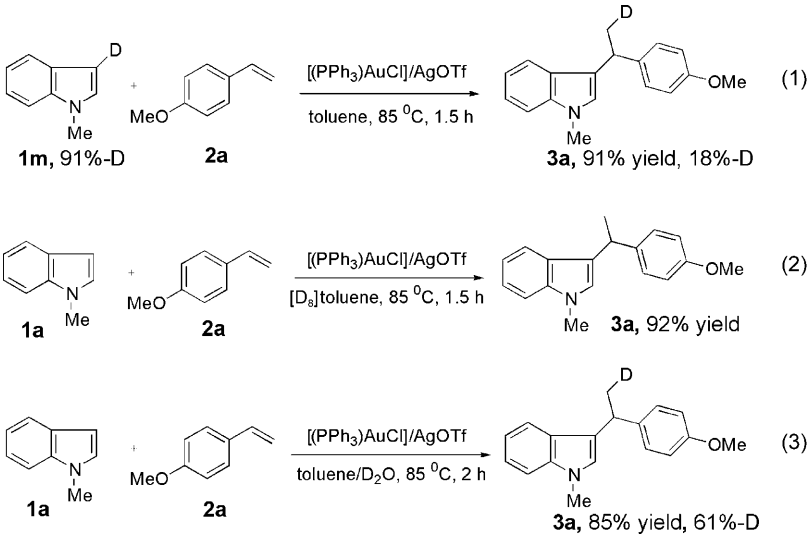
Table 5. Competition experiment of gold(I)-catalyzed hydroarylation of styrenes with **1a**.[a]



3/3d	Product ratio[b]
3a/3d	15
3c/3d	1.03
3d/3d	1
3e/3d	0.42

[a] Reactions were conducted with *N*-methylindole (**1a**, 0.3 mmol), 4-methylstyrene (**2d**, 0.33 mmol), *p*-substituted styrene **2a**, **2c**, or **2e** (0.33 mmol), and 2 mol% of [(PPh$_3$)AuCl]/AgOTf in toluene (1 mL) at 85 °C for 15 min. [b] Product ratio was determined by means of the integration ratios of their corresponding peak areas in the ^{1}H NMR spectrum.

The coupling reaction of deuterium-labeled *N*-methyl indole **1m**[22] with 4-methoxystyrene (**2a**) was attempted (Scheme 5). Product **3a** with 18% deuterium incorporation was obtained in 91% yield [Eq. (1)]. When [D$_8$]toluene was used as solvent, no deuterium-labeled product was observed [Eq. (2)]. When coupling of *N*-methylindole (**1a**) with **2a** was performed in toluene/D$_2$O, **3a** with 61% deuterium incorporation was obtained in 85% yield [Eq. (3)]. All these findings revealed that D (H) incorporated into the ter-



Scheme 5. Deuterium-labeling experiments.

minal methyl group of **3a** mainly comes from D_2O (H_2O).[23–24]

Conclusion

We have developed an efficient intermolecular coupling reaction between indoles and aryl and aliphatic alkenes using a combination of [(PPh_3)AuCl]/AgOTf as catalyst under thermal and microwave-assisted reaction conditions.

Experimental Section

General methods: The microwave-assisted reactions were conducted on a CEM Focused instrument. NMR spectra were recorded on Bruker AMX-300/400 spectrometer for 300/400 MHz ^{1}H NMR and 75/100 MHz ^{13}C NMR in $CDCl_3$. Mass spectra and HR mass spectra were obtained on Finnigan GC-MS 4021 and Finnigan MAT-8430 instruments, respectively, by using the electron-impact ionization technique (70 eV).

General procedure for gold(I)-catalyzed hydroarylation of alkenes with indoles: Indole **1** (0.3 mmol) and styrene **2** (0.33 mmol) were added to a mixture of chloro(triphenylphosphine)gold(I) (3 mg, 0.006 mmol) and silver triflate (1.8 mg, 0.006 mmol) in toluene (1.0 mL). After heating at 85 °C for 1.25–3 h, the reaction mixture was purified by flash column chromatography (hexane/ethyl acetate 50/1 to 30/1) to afford alkylated indole **3**.

3a: Yield: 95%; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.33 (d, J = 7.9 Hz, 1H), 7.12–7.25 (m, 4H), 6.99 (t, J = 7.0 Hz, 1H), 6.77–6.80 (m, 3H), 4.29 (q, J = 7.1 Hz, 1H), 3.74 (s, 3H), 3.71 (s, 3H), 1.65 ppm (d, J = 7.1 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75.3 MHz): δ = 157.8, 139.2, 137.4, 128.2, 127.2, 125.9, 121.2, 120.3, 119.4, 118.3, 113.7, 109.1, 55.2, 36.0, 32.6, 22.6 ppm; EIMS: m/z: 265 [M^+]; HRMS (EI): m/z calcd for $C_{18}H_{19}NO$: 265.1467; found: 265.1465.

3b: Yield: 86%; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.42 (d, J = 7.9 Hz, 1H), 7.23 (d, J = 9.4 Hz, 1H), 7.13–7.18 (m, 3H), 7.01 (t, J = 7.9 Hz, 1H), 6.78 (s, 1H), 6.66 (d, J = 8.7 Hz, 2H), 4.27 (q, J = 7.1 Hz, 1H), 3.72 (s, 1H), 2.89 (s, 6H), 1.64 ppm (d, J = 7.1 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75.3 MHz): δ = 149.0, 135.2, 127.9, 125.8, 121.4, 120.8, 119.9, 118.5, 112.9, 109.0, 40.9, 35.8, 32.6, 22.6 ppm; EIMS: m/z: 278 [M^+]; HRMS (EI): m/z calcd for $C_{19}H_{22}N_2$: 278.1783; found: 278.1782.

3c: Yield: 82%; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.51 (d, J = 7.9 Hz, 1H), 7.20–7.35 (m, 6H), 7.05 (t, J = 7.1 Hz, 1H), 6.81 (s, 1H), 4.42 (q, J = 7.1 Hz, 1H), 3.75 (s, 3H), 1.72 (d, J = 7.0 Hz, 3H), 1.51 ppm (s, 9H); ^{13}C NMR ($CDCl_3$, 75.3 MHz): δ = 143.7, 138.2, 135.8, 127.5, 126.9, 125.8, 125.1, 121.4, 119.7, 118.5, 118.1, 109.0, 36.2, 32.6, 31.4, 29.7, 22.4 ppm; EIMS: m/z: 291 [M^+]; HRMS (EI): m/z calcd for $C_{21}H_{25}N$: 291.1987; found: 291.1990.

3d: Yield: 85%; ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.56 (d, J = 7.9 Hz, 1H), 7.06–7.38 (m, 6H), 6.96 (t, J = 7.0 Hz, 1H), 6.82 (s, 1H), 4.34 (q, J = 7.0 Hz, 1H), 3.74 (s, 3H), 2.30 (s, 3H), 1.74 ppm (d, J = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 142.5, 138.1, 135.7, 127.3, 126.3, 125.6, 125.0, 121.2, 119.2, 118.3, 117.8, 109.1, 32.5, 31.6, 27.8, 21.5 ppm; EIMS: m/z: 249 [M^+]; HRMS (EI): m/z calcd for $C_{18}H_{19}N$: 249.1517; found: 249.1515.

3e: Yield: 65%; ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.35 (d, J = 8.9 Hz, 1H), 7.18–7.28 (m, 6H), 6.99 (t, J = 6.9 Hz, 1H), 6.83 (s, 1H), 4.34 (q, J = 7.0 Hz, 1H), 3.75 (s, 3H), 1.66 ppm (d, J = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75.3 MHz): δ = 141.7, 134.6, 128.7, 128.4, 127.5, 125.9, 122.3, 121.6, 119.6, 118.7, 116.5, 109.1, 36.3, 32.6, 22.4 ppm; EIMS: m/z: 269 [M^+]; HRMS (EI): m/z calcd for $C_{17}H_{16}NCl$: 269.0971; found: 269.0970.

3f: Yield: 60%; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.14–7.32 (m, 13H), 6.91 (t, J = 7.0 Hz, 1H), 6.27 (s, 1H), 3.68 (s, 3H), 2.26 ppm (s, 3H); ^{13}C NMR ($CDCl_3$, 75.3 MHz): δ = 146.6, 130.0, 128.4, 128.3, 128.2, 128.1, 127.8, 127.7, 125.8, 122.1, 121.2, 118.5, 114.3, 109.2, 47.5, 32.6, 29.5 ppm; EIMS: m/z: 311 [M^+]; HRMS (EI): m/z calcd for $C_{23}H_{21}N$: 311.1674; found: 311.1676.

3g: Yield: 78%; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.40 (d, J = 8.0 Hz, 1H), 7.24 (d, J = 7.6 Hz, 2H), 7.05–7.21 (m, 4H), 6.97 (t, J = 7.0 Hz, 1H), 6.66 (s, 1H), 4.59 (t, J = 8.0 Hz, 1H), 3.70 (s, 3H), 2.92–2.98 (m, 2H), 2.50–2.54 (m, 1H), 2.12 ppm (m, 1H); ^{13}C NMR ($CDCl_3$, 75.3 MHz): δ = 147.5, 135.3, 130.7, 126.3, 126.2, 124.8, 124.4, 121.5, 119.5, 118.6, 115.7, 109.2, 42.3, 35.0, 32.6, 31.7 ppm; EIMS: m/z: 247 [M^+]; HRMS (EI): m/z calcd for $C_{18}H_{17}N$: 247.1361; found: 247.1358.

3h: Yield: 90%; ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.51 (d, J = 7.9 Hz, 1H), 7.36–7.39 (m, 3H), 7.25–7.29 (m, 4H), 7.23 (t, J = 4.0 Hz, 1H), 7.15 (s, 1H), 7.03 (t, J = 4.0 Hz, 1H), 6.81 (d, J = 8.7 Hz, 2H), 4.41 (q, J = 7.1 Hz, 1H), 3.77 (s, 3H), 2.42 (s, 3H), 1.71 ppm (d, J = 7.1 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75.3 MHz): δ = 158.7, 138.7, 137.4, 136.5, 135.8, 130.1, 128.3, 125.0, 124.3, 124.1, 122.4, 122.2, 120.1, 119.9, 113.7, 110.4, 55.2, 36.1, 22.6, 21.0 ppm; EIMS: m/z: 341 [M^+]; HRMS (EI): m/z calcd for $C_{24}H_{23}NO$: 341.1780; found: 341.1776.

3i: Yield: 93%; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.48 (d, J = 7.9 Hz, 1H), 7.37–7.40 (m, 3H), 7.25–7.31 (m, 4H), 7.22 (t, J = 7.1 Hz, 1H), 7.18 (s, 1H), 6.95–7.05 (m, 3H), 4.43 (q, J = 7.0 Hz, 1H), 3.81 (s, 3H), 2.42 (s, 3H), 1.74 (d, J = 7.1 Hz, 3H), 1.35 ppm (s, 9H); ^{13}C NMR ($CDCl_3$, 75.3 MHz): δ = 158.9, 148.7, 143.7, 137.2, 135.1, 133.2, 129.1, 126.9, 125.8, 125.2, 125.1, 122.1, 119.9, 119.4, 114.8, 110.5, 55.6, 36.5, 31.6, 22.6 ppm; EIMS: m/z: 383 [M^+]; HRMS (EI): m/z calcd for $C_{27}H_{29}NO$: 383.2249; found: 383.2245.

3j: Yield: 90%; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.38–7.43 (m, 4H), 7.24–7.25 (m, 2H), 7.00–7.21 (m, 7H), 4.39 (q, J = 7.2 Hz, 1H), 3.87 (s, 3H), 2.30 (s, 3H), 1.72 ppm (t, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75.3 MHz): δ157.9, 144.3, 136.7, 135.6, 129.2, 127.5, 126.0, 125.4, 123.2, 122.3, 120.1, 119.6, 118.3, 117.5, 114.8, 110.4, 55.8, 36.7, 22.6, 21.2 ppm; EIMS: m/z: 341 [M^+]; HRMS (EI): m/z calcd for $C_{24}H_{23}NO$: 341.1780; found: 341.1782.

3k: Yield: 85%; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.95 (brs, NH, 1H), 7.34 (dd, J_1 = 7.9 Hz, J_2 = 0.5 Hz, 2H), 7.20 (d, J = 6.2 Hz, 2H), 7.18 (t, J = 1.5 Hz, 1H), 6.96–6.99 (m, 2H), 6.79 (d, J = 6.9 Hz, 2H), 4.32 (q, J = 7.1 Hz, 1H), 3.77 (s, 3H), 1.67 ppm (d, J = 7.1 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75.3 MHz): δ157.7, 138.9, 136.6, 128.3, 126.8, 121.9, 121.8, 120.9, 120.0, 118.9, 113.9, 110.9, 55.2, 36.0, 22.5 ppm; EIMS: m/z: 251 [M^+]; HRMS (EI): m/z calcd for $C_{17}H_{17}NO$: 251.1310; found: 251.1315.

3l: Yield: 82%; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.96 (brs, NH, 1H), 7.44 (d, J = 7.8 Hz, 1H), 7.22–7.31 (m, 3H), 7.17–7.21 (m, 2H), 7.16 (t, J = 4.0 Hz, 1H), 7.00–7.04 (m, 2H), 4.38 (q, J = 7.1 Hz, 1H), 1.72 (d, J = 7.16 Hz, 3H), 1.31 ppm (s, 9H); ^{13}C NMR ($CDCl_3$, 75.3 MHz): δ = 148.5, 143.5, 136.6, 127.2, 126.9, 125.1, 124.1, 121.9, 120.9, 120.7, 119.7, 110.9, 36.3, 34.3, 31.4, 22.4 ppm; EIMS: m/z: 277 [M^+]; HRMS (EI): m/z calcd for $C_{20}H_{23}N$: 277.1830; found: 277.1832.

3m: Yield: 90%; ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.98 (brs, NH, 1H), 7.30 (s, 1H), 7.16–7.22 (m, 3H), 7.14–7.16 (m, 1H), 7.07 (s, 1H), 6.79 (d, J = 6.6 Hz, 2H), 4.32 (q, J = 7.1 Hz, 1H), 3.77 (s, 3H), 1.62 ppm (d, J = 7.1 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 158.3, 139.0, 135.5, 128.8, 128.7, 125.4, 122.8, 122.1, 121.7, 119.7, 114.3, 112.5, 55.8, 36.4, 23.0 ppm; EIMS: m/z: 285 [M^+]; HRMS (EI): m/z calcd for $C_{17}H_{16}ClNO$: 285.0920; found: 285.0923.

3n: Yield: 89%; ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 9.78 (brs, NH, 1H), 8.05 (d, J = 8.1 Hz, 1H), 7.61 (d, J = 7.8 Hz, 1H), 7.13–7.19 (m, 3H), 7.03 (t, J = 8.0 Hz, 1H), 6.79 (d, J = 6.7 Hz, 2H), 4.31 (q, J = 7.1 Hz, 1H), 3.76 (s, 3H), 1.67 ppm (d, J = 7.1 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 158.5, 138.7, 131.3, 130.6, 128.7, 128.5, 123.9, 123.6, 119.7, 119.1, 114.4, 55.7, 36.4, 23.1 ppm; EIMS: m/z: 296 [M^+]; HRMS (EI): m/z calcd for $C_{17}H_{16}N_2O_3$: 296.1161; found: 296.1157.

3o: Yield: 86%; ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.71 (brs, NH, 1H), 7.36 (d, J = 7.8 Hz, 1H), 7.23–7.25 (m, 3H), 7.06 (t, J = 7.1 Hz, 1H), 6.96 (t, J = 7.1 Hz, 1H), 6.80 (d, J = 6.58 Hz, 2H), 4.37 (q, J = 7.1 Hz, 1H), 3.76 (s, 3H), 2.32 (s, 3H), 1.74 ppm (d, J = 7.1 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75.3 MHz): δ = 158.6, 138.3, 135.1, 130.3, 128.2, 120.7, 119.3, 118.9, 118.1,

116.3, 113.4, 110.1, 55.2, 34.6, 20.7, 12.2 ppm; EIMS: *m/z*: 265 [M^+]; HRMS (EI): *m/z* calcd for $C_{18}H_{19}NO$: 265.1467; found: 265.1463.

General procedure for gold(I)-catalyzed hydroarylation of alkenes with indoles under microwave-assisted conditions: Indole **1** (0.3 mmol) and alkene **4** (0.6 mmol) were added to a mixture of chloro(triphenylphosphine)gold(I) (7.4 mg, 0.015 mmol) and silver triflate (3.8 mg, 0.015 mmol) in dichloroethane (1.0 mL) in a microwave reaction vessel. The reaction vessel was sealed and subjected to microwave irradiation at a power of 43 W at 130–140 °C for 5–30 min.

5a: Reaction was conducted at 130 °C for 7 min. Yield: 81 %; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.47–7.50 (m, 2H), 7.25–7.47 (m, 8H), 7.04–7.16 (m, 4H), 4.10 (t, J = 7.2 Hz, 1H), 2.42 (s, 3H), 2.24–2.29 (m, 1H), 2.05–2.08 (m, 1H), 0.98 ppm (t, J = 7.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75.3 MHz): δ = 141.2, 139.7, 137.8, 134.9, 132.6, 130.1, 128.3, 128.1, 127.2, 125.9, 124.9, 124.1, 123.5, 122.2, 119.8, 119.6, 110.4, 44.8, 29.1, 21.0, 12.9 ppm; EIMS: *m/z*: 325 [M^+]; HRMS (EI): *m/z* calcd for $C_{24}H_{23}N$: 325.1830; found: 325.1833.

5b: Reaction was conducted at 130 °C for 10 min. Yield: 86 %; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.49 (t, J = 7.8 Hz, 1H), 7.35–7.37 (m, 3H), 7.25–7.30 (m, 4H), 7.13–7.14 (m, 2H), 7.03 (t, J = 7.1 Hz, 1H), 6.81 (m, 3H), 4.18 (t, J = 7.1 Hz, 1H), 3.75 (s, 3H), 2.42 (s, 3H), 2.24–2.29 (m, 1H), 2.02–2.08 (m, 1H), 0.98 ppm (t, J = 7.1 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75.3 MHz): δ = 158.7, 137.2, 135.8, 130.1, 128.9, 128.7, 128.0, 124.8, 124.0, 122.2, 121.0, 120.2, 119.6, 118.1, 113.6, 110.4, 55.2, 43.9, 29.2, 20.9, 12.8 ppm; EIMS: *m/z*: 355 [M^+]; HRMS (EI): *m/z* calcd for $C_{25}H_{25}NO$: 355.1936; found: 355.1932.

5c: Reaction was conducted at 130 °C for 7 min. Yield: 82 %; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.71 (d, J = 7.2 Hz, 1H), 7.40–7.51 (m, 2H), 7.23–7.49 (m, 6H), 7.15–7.21 (m, 2H), 7.05 (t, J = 7.2 Hz, 1H), 6.83 (d, J = 7.0 Hz, 2H), 4.10 (t, J = 7.0 Hz, 1H), 3.79 (s, 3H), 2.25–2.27 (m, 1H), 2.04–2.05 (m, 1H), 1.02 ppm (t, J = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75.3 MHz): δ = 158.9, 137.4, 135.6, 130.2, 128.8, 128.6, 128.3, 124.5, 124.1, 122.6, 121.5, 120.4, 119.7, 119.2, 118.3, 114.2, 110.3, 55.1, 43.6, 29.5, 12.5 ppm; EIMS: *m/z*: 355 [M^+]; HRMS (EI): *m/z* calcd for $C_{25}H_{25}NO$: 355.1936; found: 355.1932.

5d: Reaction was conducted at 135 °C for 7 min. Yield: 80 %; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 9.75 (brs, NH, 1H), 8.11 (d, J = 8.1 Hz, 1H), 7.70 (d, J = 8.1 Hz, 1H), 7.16–7.31 (m, 6H), 7.03 (t, J = 7.9 Hz, 1H), 4.06 (t, J = 7.6 Hz, 1H), 2.18–2.25 (m, 1H), 2.03–2.10 (m, 1H), 0.97 ppm (t, J = 7.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75.3 MHz): δ = 144.4, 138.7, 131.2, 128.4, 127.8, 127.7, 126.3, 125.6, 123.2, 121.9, 119.2, 118.6, 44.5, 28.9, 12.6 ppm; EIMS: *m/z*: 280 [M^+]; HRMS (EI): *m/z* calcd for $C_{17}H_{16}N_2O_2$: 280.1212; found: 280.1210.

5e: Reaction was conducted at 130 °C for 7 min. Yield: 90 %; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 9.73 (brs, NH, 1H), 8.06 (d, J = 8.1 Hz, 1H), 7.67 (d, J = 8.1 Hz, 1H), 7.23 (s, 1H), 7.13 (d, J = 8.5 Hz, 1H), 7.06 (t, J = 7.8 Hz, 1H), 6.78 (d, J = 8.5 Hz, 2H), 4.01 (t, J = 7.9 Hz, 1H), 3.75 (s, 3H), 2.13–2.19 (m, 1H), 1.96–2.03 (m, 1H), 0.89 ppm (t, J = 7.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75.3 MHz): δ = 158.7, 138.5, 136.5, 130.0, 128.7, 127.8, 123.1, 122.2, 119.2, 118.5, 118.1, 113.8, 55.2, 43.6, 29.0, 12.6 ppm; EIMS: *m/z*: 310 [M^+]; HRMS (EI): *m/z* calcd for $C_{18}H_{18}N_2O_3$: 310.1317; found: 310.1321.

5f: Reaction was conducted at 140 °C for 10 min. Yield: 75 %; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.83 (d, J = 7.2 Hz, 1H), 7.53 (t, J = 8.1 Hz, 1H), 7.36 (d, J = 8.2 Hz, 2H), 7.28–7.30 (m, 3H), 7.03–7.25 (m, 2H), 6.90 (s, 3H), 2.42–2.46 (m, 4H), 1.45 (s, 6H), 0.85 ppm (d, J = 7.0 Hz, 6H); ^{13}C NMR ($CDCl_3$, 75.3 MHz): δ = 139.6, 135.7, 131.7, 129.9, 124.8, 124.2, 122.7, 122.5, 121.8, 121.5, 118.9, 110.5, 37.9, 35.5, 24.5, 20.9, 18.0 ppm; EIMS: *m/z*: 291 [M^+]; HRMS (EI): *m/z* calcd for $C_{21}H_{25}N$: 291.1987; found: 291.1985

5g: Reaction was conducted at 140 °C for 10 min. Yield: 45 %; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 9.78 (brs, NH, 1H), 8.12–8.16 (m, 2H), 7.10–7.17 (m, 2H), 2.30–2.32 (m, 3H), 1.36 (s, 6H), 0.83 ppm (d, J = 6.8 Hz, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 132.7, 131.5, 129.6, 129.1, 123.0, 122.8, 118.8, 118.1, 45.3, 37.8, 24.6, 17.9 ppm; EIMS: *m/z*: 246 [M^+]; HRMS (EI): *m/z* calcd for $C_{14}H_{18}N_2O_2$: 246.1368; found: 246.1370.

5h: Reaction was conducted at 140 °C for 30 min. Yield: 42 %; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 9.72 (brs, NH, 1H), 8.17 (d, J = 8.1 Hz, 1H), 7.98 (d, J = 7.7 Hz, 1H), 7.15–7.21 (m, 2H), 3.21 (m, 1H), 2.17–2.19 (m, 2H), 1.70–1.83 ppm (m, 6H); ^{13}C NMR ($CDCl_3$, 75.3 MHz): δ = 127.7, 121.9, 119.2, 118.4, 118.2, 36.5, 33.3, 25.2 ppm.

5i: Reaction was conducted at 140 °C for 30 min. Yield: 60 %; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 9.70 (brs, NH, 1H), 8.16 (d, J = 7.5 Hz, 1H), 7.97 (d, J = 7.6 Hz, 1H), 7.11–7.19 (m, 2H), 2.85 (m, 1H), 2.08–2.09 (m, 4H), 1.77–1.89 ppm (m, 6H); ^{13}C NMR ($CDCl_3$, 75.3 MHz): δ = 132.5, 128.7, 127.3, 121.9, 121.8, 119.1, 118.9, 118.3, 39.9, 34.1, 26.7, 26.3 ppm; EIMS: *m/z*: 244 [M^+]; HRMS (EI): *m/z* calcd for $C_{14}H_{16}N_2O_2$: 244.1212; found: 244.1209.

5j: Reaction was conducted at 140 °C for 10 min. Yield: 83 %; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 9.78 (brs, NH, 1H), 8.17 (d, J = 8.1 Hz, 1H), 7.97 (d, J = 8.1 Hz, 1H), 7.14–7.21 (m, 2H), 5.80 (m, 2H), 3.18–3.20 (m, 1H), 2.24–2.28 (m, 1H), 2.10–2.23 (m, 3H), 1.75–1.86 ppm (m, 2H); ^{13}C NMR ($CDCl_3$, 75.3 MHz): δ = 133.2, 132.1, 131.9, 127.2, 127.1, 126.3, 124.8, 122.2, 119.1, 118.4, 32.5, 30.8, 29.4, 25.4 ppm; EIMS: *m/z*: 242 [M^+]; HRMS (EI): *m/z* calcd for $C_{14}H_{14}N_2O_2$: 242.1055; found: 242.1057.

5k: Reaction was conducted at 140 °C for 30 min. Yield: 65 %; ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 9.81 (brs, NH, 1H), 8.12–8.17 (m, 2H), 7.12–7.25 (m, 2H), 3.08 (m, 0.12H), 2.06–2.17 (m, 3H), 1.62–1.76 (m, 4H), 1.53–1.62 ppm (m, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 129.4, 127.4, 122.8, 119.1, 118.7, 118.0, 38.3, 35.8, 34.9, 28.2, 27.8, 26.9, 26.4, 22.5 ppm; EIMS: *m/z*: 258 [M^+]; HRMS (EI): *m/z* calcd for $C_{15}H_{18}N_2O_2$: 258.1368; found: 258.1369.

5l: Reaction was conducted at 140 °C for 30 min. Yield: 62 %; ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.48 (brs, NH, 1H), 8.32–8.33 (m, 1H), 7.95–7.98 (m, 1H), 7.82 (d, J = 8.9 Hz, 0.73H); 7.65 (d, J = 8.5 Hz, 0.27H), 3.12–3.16 (m, 0.27H), 2.15–2.64 (m, 2H), 1.91–1.98 (m, 0.73H), 1.83–1.87 (m, 3H), 1.52–1.83 ppm (m, 9H); ^{13}C NMR ($CDCl_3$, 75.3 MHz): δ = 127.9, 126.0, 125.7, 121.3, 119.1, 114.5, 114.1, 108.0, 40.7, 38.3, 36.1, 34.9, 32.8, 30.1, 27.2, 26.2, 25.6, 23.2, 22.3 ppm; EIMS: *m/z*: 272 [M^+]; HRMS (EI): *m/z* calcd for $C_{16}H_{20}N_2O_2$: 272.1525; found: 272.1525.

5m: Reaction was conducted at 140 °C for 5 min. Yield: 85 %; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 8.59 (brs, NH, 1H), 8.33 (s, 1H), 7.97 (d, J = 5.6 Hz, 1H), 7.79 (d, J = 6.7 Hz, 1H), 7.22 (s, 1H), 4.09 (q, J = 5.3 Hz, 2H), 2.16 (dd, J_1 = 6.5 Hz, J_2 = 4.4 Hz, 1H), 2.02 (dd, J_1 = 6.1 Hz, J_2 = 6.1 Hz, 1H), 1.75–1.96 (m, 3H), 1.40 (s, 6H), 1.21 (t, J = 5.3 Hz, 3H), 1.07–1.11 (m, 1H), 0.81 ppm (d, J = 4.9 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75.3 MHz): δ = 173.3, 142.6, 135.6, 130.5, 126.4, 120.7, 120.5, 118.1, 114.1, 108.1, 60.0, 42.5, 41.7, 37.1, 34.7, 36.0, 29.6, 28.6, 22.1, 19.5, 14.1 ppm; EIMS: *m/z*: 360 [M^+]; HRMS (EI): *m/z* calcd for $C_{20}H_{28}N_2O_4$: 360.2049; found: 360.2047.

5n: Reaction was conducted at 140 °C for 5 min. Yield: 80 %; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 8.41 (brs, NH, 1H), 8.30 (d, J = 2.1 Hz, 1H), 7.95 (d, J = 2.1 Hz, 1H), 7.79 (d, J = 8.9 Hz, 1H), 7.25–7.32 (m, 5H), 7.18 (d, J = 2.8 Hz, 1H), 4.45 (s, 2H), 3.38–3.45 (m, 2H), 1.74–1.77 (m, 2H), 1.34–1.60 (m, 7H), 1.03–1.09 (m, 4H), 0.74 ppm (d, J = 6.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75.3 MHz): δ = 142.4, 135.4, 130.6, 129.5, 128.3, 127.6, 127.5, 128.4, 120.8, 118.1, 114.2, 108.1, 72.9, 68.7, 42.9, 37.7, 36.6, 34.8, 29.6, 28.7, 22.2, 19.6 ppm; EIMS: *m/z*: 408 [M^+]; HRMS (EI): *m/z* calcd for $C_{25}H_{32}N_2O_3$: 408.2413; found: 408.2414.

5p: Reaction was conducted at 140 °C for 5 min. Yield: 75 %; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.86 (d, J = 6.8 Hz, 1H), 7.58–7.61 (m, 2H), 7.53–7.55 (m, 3H), 7.23–7.37 (m, 1H), 7.16–7.23 (m, 2H), 7.09 (s, 1H), 4.13 (t, J = 7.2 Hz, 2H), 2.22 (dd, J_1 = 5.7 Hz, J_2 = 2.0 Hz, 1H), 2.08 (dd, J_1 = 8.2 Hz, J_2 = 3.0 Hz, 1H), 1.87–2.05 (m, 3H), 1.48 (s, 6H), 1.18–1.31 (m, 5H), 0.88 ppm (d, J = 6.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75.3 MHz): δ = 173.4, 139.9, 136.9, 129.5, 127.5, 126.0, 124.4, 124.3, 121.8, 121.5, 119.3, 110.6, 60.0, 42.6, 41.9, 37.4, 34.9, 30.2, 28.7, 22.2, 19.7, 14.3 ppm; EIMS: *m/z*: 391 [M^+]; HRMS (EI): *m/z* calcd for $C_{26}H_{33}NO_2$: 391.2511; found: 391.2510.

5q: Reaction was conducted at 140 °C for 5 min. Yield: 20 %; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.85 (d, J = 6.8 Hz, 1H), 7.50–7.58 (m, 4H), 7.27–7.50 (m, 7H), 7.06–7.21 (m, 3H), 4.55 (s, 3H), 3.41–3.47 (m, 2H), 1.82–1.87 (m, 2H), 1.66 (s, 6H), 1.01–1.32 (m, 7H), 0.81 ppm (d, J = 6.6 Hz,

3H); ^{13}C NMR ($CDCl_3$, 75.3 MHz): δ=139.8, 136.5, 129.5, 128.3, 127.6, 125.9, 124.4, 124.3, 121.8, 121.6, 119.3, 118.7, 110.6, 72.8, 68.8, 42.8, 37.8, 36.8, 34.9, 29.7, 28.7, 22.2, 19.7 ppm; EIMS: *m/z*: 439 [M^+]; HRMS (EI): *m/z* calcd for $C_{31}H_{37}NO$: 439.2875; found: 439.2876.

General procedure for gold(I)-catalyzed coupling of indoles with dienes: Indole **1** (0.3 mmol) and diene **6** (0.45 mmol) were added to a mixture of chloro(triphenylphosphine)gold(I) (7.5 mg, 0.015 mmol) and silver triflate (4.5 mg, 0.015 mmol) in toluene (1.0 mL). After heating at 70 °C for 16 h, the reaction mixture was purified by flash column chromatography (hexane/ethyl acetate 50/1 to 15/1) to afford allylated indole **7**.

7a: Yield: 81%; ^{1}H NMR ($CDCl_3$, 500 MHz): δ=7.66 (d, J=7.9 Hz, 1H), 7.27 (d, J=8.2 Hz, 1H), 7.21 (t, J=7.2 Hz, 1H), 7.08 (t, J=7.1 Hz, 1H), 6.86–6.90 (m, 2H), 6.76 (d, J=8.25 Hz, 1H), 6.45 (d, J=15.9 Hz, 1H), 6.30 (dd, J_1=7.9 Hz, J_2=15.8 Hz, 1H), 3.90–3.94 (m, 1H), 3.85 (s, 3H), 3.84 (s, 3H), 3.73 (s, 3H), 1.55 ppm (d, J=7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ=148.9, 148.3, 137.2, 133.8, 130.9, 127.5, 127.2, 125.3, 121.5, 119.7, 119.1, 118.7, 111.1, 109.2, 108.7, 55.9, 55.8, 34.1, 32.6, 20.9 ppm; EIMS: *m/z*: 321 [M^+]; HRMS (EI): *m/z* calcd for $C_{21}H_{23}NO_2$: 321.1729; found: 321.1728.

7b: Yield: 76%; ^{1}H NMR ($CDCl_3$, 300 MHz): δ=8.03 (brs, NH, 1H), 7.68 (d, J=7.9 Hz, 1H), 7.35 (d, J=8.2 Hz, 1H), 7.19 (t, J=7.2 Hz, 1H), 7.06 (t, J=7.2 Hz, 1H), 7.02 (d, J=2.2 Hz, 1H), 6.88–6.92 (m, 2H), 6.81 (d, J=8.0 Hz, 1H), 6.43 (d, J=15.6 Hz, 1H), 6.35 (dd, J_1=6.7 Hz, J_2=15.6 Hz, 1H), 3.91–3.96 (m, 1H), 3.91 (s, 3H), 3.87 (s, 3H), 1.59 ppm (d, J=7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75.3 MHz): δ=148.8, 148.2, 136.6, 133.7, 130.9, 127.8, 126.9, 121.9, 120.6, 120.4, 119.6, 119.4, 119.1, 111.2, 111.1, 108.7, 55.9, 55.8, 34.2, 20.8 ppm; EIMS: *m/z*: 307 [M^+]; HRMS (EI): *m/z* calcd for $C_{20}H_{21}NO_2$: 307.1572; found: 307.1574.

7c: Yield: 72%; ^{1}H NMR ($CDCl_3$, 300 MHz): δ=8.09 (brs, NH, 1H), 7.71 (s, 1H), 7.24 (s, 1H), 7.11 (d, J=8.6 Hz, 1H), 7.04 (s, 1H), 6.91 (d, J=8.9 Hz, 2H), 6.81 (d, J=8.0 Hz, 1H), 6.45 (d, J=15.8 Hz, 1H), 6.29 (dd, J_1=6.7 Hz, J_2=15.8 Hz, 1H), 3.82–4.01 (m, 1H), 1.53 ppm (d, J=7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75.3 MHz): δ=148.9, 148.4, 134.9, 133.1, 130.8, 128.1, 127.9, 124.9, 122.3, 121.9, 120.4, 119.1, 119.4, 112.1, 111.2, 108.8, 55.9, 55.8, 34.0, 20.8 ppm; EIMS: *m/z*: 341 [M^+]; HRMS (EI): *m/z* calcd for $C_{20}H_{20}ClNO_2$: 341.1183; found: 341.1182.

7d: Yield: 75%; ^{1}H NMR ($CDCl_3$, 400 MHz): δ=7.90 (brs, NH, 1H), 7.25 (d, J=4.8 Hz, 1H), 7.11 (s, 1H), 7.0 (s, 1H), 6.83–6.90 (m, 3H), 6.77 (d, J=8.2 Hz, 1H), 6.42 (d, J=15.8 Hz, 1H), 6.35 (dd, J_1=6.7 Hz, J_2=15.8 Hz, 1H), 3.83–3.88 (m, 7H), 3.81 (s, 3H), 1.56 ppm (d, J=7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75.3 MHz): δ=153.7, 148.9, 148.2, 133.5, 131.7, 130.9, 127.8, 127.2, 121.3, 120.2, 119.0, 111.9, 111.7, 111.1, 108.6, 104.9, 101.7, 55.9, 55.8, 34.2, 20.8 ppm; EIMS: *m/z*: 337 [M^+]; HRMS (EI): *m/z* calcd for $C_{21}H_{23}NO_3$: 337.1678; found: 337.1680.

7e: Yield: 70%; ^{1}H NMR ($CDCl_3$, 300 MHz): δ=8.20 (brs, NH, 1H), 7.55 (d, J=7.9 Hz, 1H), 7.71 (d, J=7.5 Hz, 1H), 7.09 (d, J=2.0 Hz, 1H), 7.04 (t, J=7.8 Hz, 1H), 6.90–6.96 (m, 2H), 6.77 (d, J=8.1 Hz, 1H), 6.39 (d, J=15.8 Hz, 1H), 6.27 (dd, J_1=6.7 Hz, J_2=15.8 Hz, 1H), 3.86–3.94 (m, 7H), 1.56 ppm (d, J=7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ=148.9, 148.3, 138.9, 133.1, 128.1, 121.3, 121.1, 120.0, 119.1, 118.3, 111.1, 101.6, 55.9, 55.8, 34.3, 20.7 ppm; EIMS: *m/z*: 341 [M^+]; HRMS (EI): *m/z* calcd for $C_{20}H_{20}ClNO_2$: 341.1183; found: 341.1182.

7f: Yield: 80%; ^{1}H NMR ($CDCl_3$, 300 MHz): δ=7.68 (d, J=7.3 Hz, 1H), 7.21–7.30 (m, 4H), 7.07 (t, J=6.9 Hz, 1H), 6.81–6.92 (m, 3H), 6.43 (d, J=15.8 Hz, 1H), 6.31 (dd, J_1=6.7 Hz, J_2=15.8 Hz, 1H), 3.91–3.97 (m, 1H), 3.88 (s, 3H), 3.75 (s, 3H), 1.53 ppm (d, J=7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75.3 MHz): δ=158.6, 136.5, 133.5, 130.8, 127.4, 127.2, 125.2, 121.5, 119.7, 118.6, 113.9, 109.2, 55.3, 34.2, 32.6, 20.9 ppm; EIMS: *m/z*: 291 [M^+]; HRMS (EI): *m/z* calcd for $C_{20}H_{21}NO$: 291.1623; found: 291.1622.

7g: Yield: 75%; ^{1}H NMR ($CDCl_3$, 400 MHz): δ=7.91 (brs, 1H, NH), 7.66 (d, J=7.9 Hz, 1H), 7.33 (d, J=8.1 Hz, 1H), 7.29 (d, J=8.6 Hz, 2H), 7.17 (t, J=6.1 Hz, 1H), 7.07 (t, J=7.0 Hz, 1H), 6.99 (s, 1H), 6.82 (d, J=8.8 Hz, 2H), 6.42 (d, J=15.8 Hz, 1H), 6.30 (dd, J_1=6.7 Hz, J_2=15.8 Hz, 1H), 3.87–3.91 (m, 1H), 3.77 (s, 3H), 1.55 ppm (d, J=7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75.3 MHz): δ=158.7, 136.6, 133.4, 130.7, 127.6, 127.2, 126.9, 121.9, 120.8, 120.4, 119.7, 119.3, 113.9, 111.1, 55.3, 34.2, 20.8 ppm; EIMS: *m/z*: 277 [M^+]; HRMS (EI): *m/z* calcd for $C_{19}H_{19}NO$: 277.1467; found: 277.1466.

7h: Yield: 74%; ^{1}H NMR ($CDCl_3$, 300 MHz): δ=7.69 (d, J=7.3 Hz, 1H), 7.28–7.33 (m, 3H), 7.26 (t, J=6.7 Hz, 1H), 7.06 (t, J=7.1 Hz, 1H), 6.93 (s, 1H), 6.81 (d, J=8.6 Hz, 2H), 6.44 (d, J=15.8 Hz, 1H), 6.34 (dd, J_1=6.7 Hz, J_2=15.8 Hz, 1H), 4.15 (q, J=7.3 Hz, 2H), 3.79–3.93 (m, 4H), 1.55 (d, J=7.0 Hz, 3H), 1.38 ppm (d, J=7.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75.3 MHz): δ=158.6, 136.4, 133.6, 130.5, 127.3, 127.2, 123.4, 121.3, 119.8, 118.5, 118.1, 113.8, 113.6, 109.2, 55.3, 40.8, 34.2, 20.9, 15.4 ppm; EIMS: *m/z*: 305 [M^+]; HRMS (EI): *m/z* calcd for $C_{21}H_{23}NO$: 305.1780; found: 305.1779.

7i: Yield: 65%; ^{1}H NMR ($CDCl_3$, 400 MHz): δ=7.71 (d, J=7.2 Hz, 1H), 7.22–7.29 (m, 5H), 7.08 (d, J=8.0 Hz, 2H), 6.87 (s, 1H), 6.46 (d, J=15.8 Hz, 1H), 6.35 (dd, J_1=6.7 Hz, J_2=15.8 Hz, 1H), 3.91–3.95 (m, 1H), 3.76 (s, 3H), 2.32 (s, 3H), 1.55 ppm (d, J=7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ=137.8, 137.5, 135.2, 134.5, 129.1, 128.9, 127.8, 126.0, 125.2, 121.5, 119.7, 118.6, 109.1, 34.2, 32.6, 21.1, 20.9 ppm; EIMS: *m/z*: 275 [M^+]; HRMS (EI): *m/z* calcd for $C_{20}H_{21}N$: 275.1674; found: 275.1673.

7j: Yield: 62%; ^{1}H NMR ($CDCl_3$, 300 MHz): δ=7.89 (brs, NH, 1H), 7.67 (d, J=7.9 Hz, 1H), 7.33 (d, J=8.1 Hz, 1H), 7.24 (d, J=8.1 Hz, 1H), 7.17 (t, J=7.1 Hz, 1H), 7.06–7.08 (m, 3H), 6.98 (s, 1H), 6.45 (d, J=15.8 Hz, 1H), 6.38 (dd, J_1=6.7 Hz, J_2=15.8 Hz, 1H), 3.87–3.95 (m, 1H), 2.30 (s, 3H), 1.53 ppm (d, J=7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75.3 MHz): δ=136.6, 135.0, 134.4, 129.1, 129.0, 128.6, 128.0, 126.9, 126.1, 122.2, 121.9, 120.7, 120.4, 119.7, 119.2, 118.2, 110.1, 34.2, 21.0, 20.8 ppm; EIMS: *m/z*: 261 [M^+]; HRMS (EI): *m/z* calcd for $C_{19}H_{19}N$: 261.1517; found: 261.1516.

General procedure for competitive gold(I)-catalyzed hydroarylation of styrenes with 1a: Compound **1a** (0.3 mmol), 4-methyl styrene **2d** (0.33 mmol), and *p*-substituted styrene **2a**, **2c**, or **2e** (0.33 mmol) were added to a mixture of chloro(triphenylphosphine)gold(I) (3 mg, 0.006 mmol) and silver triflate (1.8 mg, 0.006 mmol) in toluene (1.0 mL). After heating at 85 °C for 15 min, the solvent was removed under reduced pressure and the crude mixture was analyzed by ^{1}H NMR spectroscopy. The ratios of indoles **3a**, **3c**, or **3e** to **3d** were determined by means of the integration ratios of their corresponding peak areas in the ^{1}H NMR spectra. Conversion based on styrene was determined by GC analysis.

Conversion of **2a**/**2d** (31/3.2%), **2c**/**2d** (3.2/3.1%), **2e**/**2d** (1.5/3.2%), Chemical shift of C*H*CH_3: **3a** (4.29), **3c** (4.42), **3d** (4.34), and **3e** (4.34 ppm). Chemical shift of CHC*H*$_3$: **3a** (1.65), **3c** (1.72), **3d** (1.74), and **3e** (1.66 ppm).

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