A New Approach to 3-Substituted Indoles through Palladium-Catalyzed C–H Activation Followed by Intramolecular Amination Reaction of Enamines

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Abstract: Palladium-catalyzed C–H activation followed by intramolecular amination reaction of enamine compounds was achieved using a $Pd(OAc)_2$ (10 mol%)/$Cu(OAc)_2$ (100 mol%) catalyst system in DMSO. This work introduces an entirely new approach to 3-substituted indoles.

Key words: palladium, catalysis, C–H activation, indoles, aminations

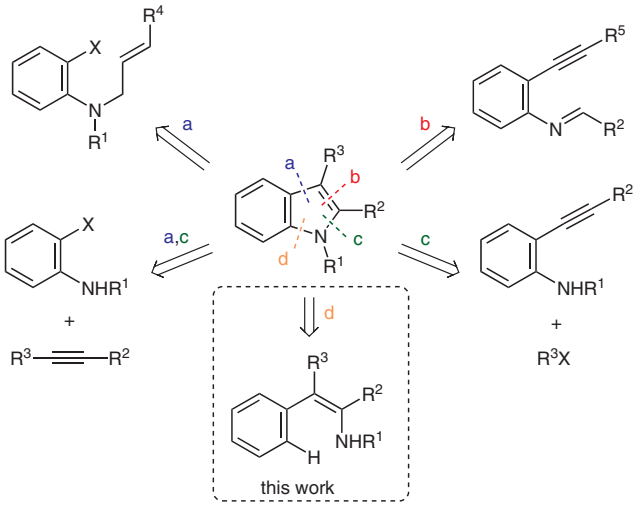
The indole scaffold occurs frequently in numerous biologically active compounds, ranging from natural products[1] to designed medicinal agents.[2] Therefore, the development of more practical and efficient procedures for synthesizing indoles, especially using catalytic approaches with transition metals, remains an area of intensive research.[3]

Among the transition-metal sources, the palladium (Pd) catalyst is one of the most widely studied and used metals for the construction of indoles;[4–13] Scheme 1 shows some of the representative procedures. Arguably, cycloadditions of 2-haloanilines with terminal or internal alkynes (disconnections a and c)[4] and intermolecular reactions of 2-alkynyl anilides with electrophiles (R^3X; disconnection c)[5] are the most frequently used methods for the synthesis of indoles with substituent(s) at 2- and/or 3-position(s). Several efficient approaches through tandem-type coupling reactions have also been reported recently.[9–12]

Herein, we describe an entirely new approach to indoles using a Pd-catalyzed C–H activation–intramolecular amination sequence (C–H amination) using enamine compounds as starting materials (Scheme 1, disconnection d).

The amount of 10 mol% of $Pd(OAc)_2$, along with the reoxidant $Cu(OAc)_2$, effectively catalyzed this process, producing 3-substituted indoles with good functional group compatibility (e.g., alkoxycarbonyl and cyano groups).[13] Indeed, the method developed in this manuscript represents one of the rare examples of Pd-catalyzed C–H amination reactions.[14,15]

We began our study by examining the reaction of enamine **1**[16] to indole **2** to obtain the optimal reaction conditions (Table 1). The effect of reoxidant was initially screened in the presence of 10 mol% of $Pd(OAc)_2$ in DMSO at 80 °C



Scheme 1 Representative Pd-catalyzed approaches to indoles

(entries 1–9). We were pleased to find that the use of 100 mol% of $Cu(OAc)_2$ enabled this process to be performed in fairly good yield (entry 9). Dimethyl sulfoxide is crucial for this transformation.[17] The use of a higher catalyst loading improved the yield (entry 11), whereas increasing reaction temperature to 120 °C resulted in a slightly lower yield (entry 12). Unfortunately, no further improvement in yield was obtained from the screening of additional Pd sources (Table 1, entries 13–19).[18,19]

We next examined the scope of the above-optimized catalyst system using several kinds of enamines **5**, which were prepared by the Wittig reaction of benzophenones **3** followed by one-pot conversion of enol ethers **4** into **5** (Table 2). Both of the reactions proceeded generally in high yields.[20]

In the reactions of enamines **5a–c** possessing two substituents symmetrically at the 4- and 4′-positions on the benzene rings, the desired indoles **6a–c** were obtained generally in good yields at 120 °C (Table 3, entries 2, 4, and 6). Low conversion was observed in the reaction of enamine **5d** (entries 7 and 8). Substrate **5e**, which has two methoxy groups at the 3- and 3′-positions, also underwent this cyclization under the same reaction conditions, albeit in relatively low conversion and yield (entries 9 and 10). In this reaction, indole **6e** was obtained as the sole product; no regioisomer, such as 7-methoxy-3-(3-methoxyphenyl)indole, was observed.

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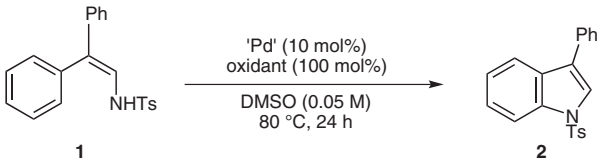
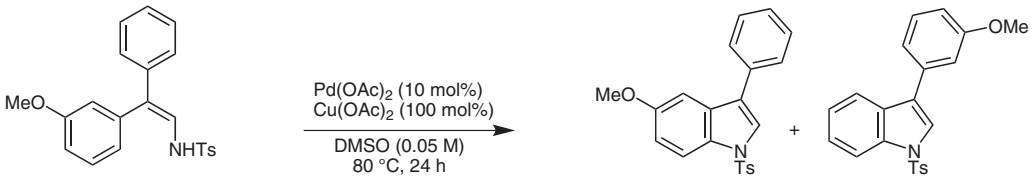
Table 1 Optimization of Reaction Conditions



1 2

Entry	'Pd'	Oxidant	Yield of **2**[a] (%)	Yield of recovered **1**[a] (%)
1	$Pd(OAc)_2$	$PhI(TFA)_2$	0	0
2	$Pd(OAc)_2$	benzoquinone	15	61
3	$Pd(OAc)_2$	CAN	8	0
4	$Pd(OAc)_2$	CuCl	0	39
5	$Pd(OAc)_2$	$CuCl_2$	0	34
6	$Pd(OAc)_2$	$Cu(acac)_2$	31	27
7	$Pd(OAc)_2$	$Cu(OMs)_2$	8	76
8	$Pd(OAc)_2$	$Cu(OTf)_2$	9	74
9	$Pd(OAc)_2$	$Cu(OAc)_2$	53	0
10[b,c]	$Pd(OAc)_2$	$Cu(OAc)_2$	60	0
11[d]	$Pd(OAc)_2$	$Cu(OAc)_2$	84	0
12[e]	$Pd(OAc)_2$	$Cu(OAc)_2$	47	0
13	$Pd(TFA)_2$	$Cu(OAc)_2$	47	0
14	$PdCl_2$	$Cu(OAc)_2$	48	0
15	$[Pd(allyl)Cl]_2$	$Cu(OAc)_2$	43	27
16	$PdCl_2[P(2\text{-}Tol)_3]_2$	$Cu(OAc)_2$	10	53
17	PdI_2	$Cu(OAc)_2$	0	0
18	$Pd_2(dba)_3$[f]	$Cu(OAc)_2$	37	35
19	$Pd(PPh_3)_4$	$Cu(OAc)_2$	15	22

[a] Isolated yield from reaction on 0.14 mmol scale.
[b] Under microwave condition (180 °C, 10 min).
[c] $Cu(OAc)_2$ (200 mol%) was used.
[d] $Pd(OAc)_2$ (30 mol%) was used.
[e] Conditions: 120 °C, 6 h.
[f] Ph_3P (10 mol%) was added.

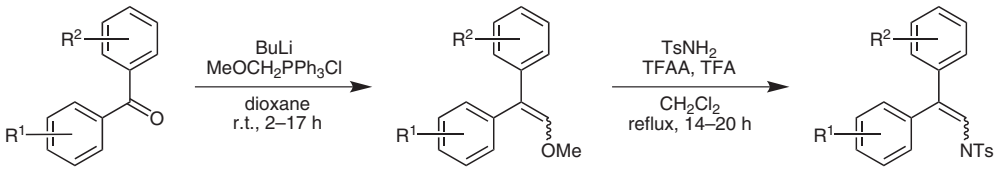


5f (single isomer) **6f-A** **6f-B**
38% (4.8:1)

Scheme 2 Palladium-catalyzed cyclization of dissymmetric substrate **5f**

Although the reaction of the substrate **5f**, which has one methoxy group on the benzene ring (a dissymmetric substrate), produced a relatively low yield, this result provided another insight into the reaction mechanism. Namely, despite the starting **5f** being a single isomer,[21] the cyclized product obtained was a mixture of two indoles, **6f-A** and

Table 2 Synthesis of Enamine **5**

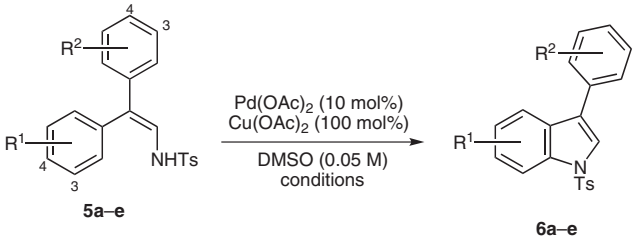


3a–f **4a–f** **5a–f**

Entry	**3**	R^1	R^2	Yield of **4**[a] (%)	Yield of **5**[a] (%)
1	**3a**	4-MeO	4-MeO	**4a** 67	**5a** 79
2	**3b**	4-F	4-F	**4b** 82	**5b** 79
3	**3c**	4-EtO_2C	4-EtO_2C	**4c** 64	**5c** 37[b]
4	**3d**	4-NC	4-NC	**4d** 54	**5d** 86
5	**3e**	3-MeO	3-MeO	**4e** 94	**5e** 67
6	**3f**	3-MeO	H	**4f** 83	**5f** 65

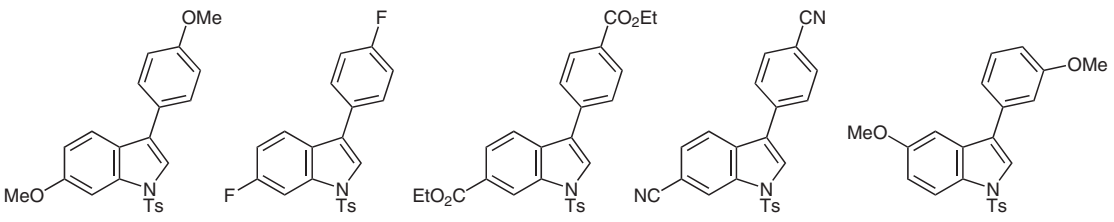
[a] Isolated yield.
[b] Compound **5c** was prepared stepwise from **4c** (hydration of **4c** followed by enamine formation); yield over 2 steps.

Table 3 Palladium-Catalyzed Synthesis of Indoles **6a–e**



5a–e **6a–e**

Entry	Enamine **5** (R^1, R^2)	Conditions	Indole **6**	Yield of **6**[a,b] (%)	Yield of recovered **5** (%)
1	**5a** (4-MeO, 4-MeO)	80 °C, 17 h	**6a**	41 (41)	0
2		120 °C, 5 h		55 (55)	0
3	**5b** (4-F, 4-F)	80 °C, 24 h	**6b**	42 (42)	0
4		120 °C, 6 h		59 (51)	13
5	**5c** (4-EtO_2C, 4-EtO_2C)	80 °C, 22 h	**6c**	60 (60)	0
6		120 °C, 6 h		71 (68)	4
7	**5d** (4-NC, 4-NC)	80 °C, 22 h	**6d**	81 (29)	64
8		150 °C, 6 h		89 (42)	53
9	**5e** (3-MeO, 3-MeO)	80 °C, 22 h	**6e**	50 (45)	10
10		120 °C, 6 h		30 (30)	0



6a **6b** **6c** **6d** **6e**

[a] Conversion yield based on recovered starting material.
[b] Isolated yield in parentheses.

6f-B, suggesting that the *E*/*Z* isomerization of the enamine occurs rapidly during this process (Scheme 2).[22]

In conclusion, we have developed a new approach to indoles through Pd-catalyzed C–H activation followed by intramolecular amination of enamine compounds. Although the yields were moderate under our conditions, this method can be employed complementarily with previously reported techniques to obtain a variety of indoles. Furthermore, our atom-economical and straightforward procedure represents one of the rare examples of Pd-catalyzed C–H amination reactions. Studies to expand the substrate scope, increase yields, and apply this reaction to other nitrogen-based heterocycles are currently under way.

Acknowledgment

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(17) Use of solvents such as DMF, NMP, MeCN, dioxane, toluene, and DCE resulted in decreased yields.

(18) We also examined the effect of a variety of additives such as phosphines, N-heterocyclic carbenes, tetraalkylammonium salts, inorganic bases, lithium and silver salts, and so on, all of which led to unsatisfactory results.

(19) **Typical Procedure for the Pd-Catalyzed C–H Amination of Enamines (Table 1, entry 9)**
A mixture of **1** (50.0 mg, 0.14 mmol), $Pd(OAc)_2$ (3.2 mg, 0.014 mmol), and $Cu(OAc)_2$ (26.0 mg, 0.14 mmol) in DMSO (2.9 mL) was stirred at 80 °C for 24 h. The reaction mixture was extracted with EtOAc (3 × 5 mL) and the combined organic layer was washed with brine (10 mL), and dried over $MgSO_4$. The solvent was evaporated and the residue was purified by silica gel column chromatography (hexane–EtOAc, 9:1) to give indole **2** (26.2 mg, 53%) as a colorless solid.
1-(4-Methylphenylsulfonyl)-3-phenylindole (2)
Mp 151–152 °C (colorless needles from hexane–EtOAc). IR (film): 2924, 1597, 1447, 1371, 1175, 669 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 2.34 (3 H, s), 7.22 (2 H, d, *J* = 8.2 Hz), 7.26–7.30 (1 H, m), 7.34–7.38 (2 H, m), 7.46 (2 H, t, *J* = 7.8 Hz), 7.59–7.61 (2 H, m), 7.69 (1 H, s), 7.77 (1 H, d, *J* = 7.8 Hz), 7.80 (2 H, d, *J* = 8.4 Hz), 8.05 (1 H, d, *J* = 8.4 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.5, 113.7, 120.3, 122.8, 123.4, 123.8, 124.8, 126.7, 127.4, 127.8, 128.8, 129.1, 129.8, 132.9, 135.0, 135.4, 144.9. MS: *m/z* = 347 (50.2) [M^+], 192 (100). HRMS: *m/z* calcd for $C_{21}H_{17}NO_2S$: 347.0980; found: 347.0967. Anal. Calcd for $C_{21}H_{17}NO_2S$: C, 72.60; H, 4.93; N, 4.03. Found C, 72.63; H, 5.08; N, 3.99.

(20) **Typical Procedure for the Synthesis of Enol Ether (4a, Table 2, entry 1)**
To a solution of(methoxymethyl)triphenylphosphinium chloride (1.1 g, 3.1 mmol) in anhyd dioxane (5 mL) was

slowly added BuLi (1.53 M solution in hexane, 2.3 mL, 3.1 mmol) at 0 °C and stirred for 30 min at the same temperature. A solution of **3a** (0.50 g, 2.1 mmol) in anhyd dioxane (10 mL) was then slowly added at 0 °C, and the mixture was heated under reflux for 10 h. The reaction mixture was treated with sat. aq NH_4Cl soln (5 mL), and the aqueous phase was extracted with EtOAc (3 × 10 mL). The combined organic layer was washed with brine (5 mL) and dried over $MgSO_4$. The solvent was evaporated, and the residue was purified by silica gel column chromatography (hexane–EtOAc, 9:1) to give **4a** (0.4 g, 67%) as a colorless oil.

1,1-Bis(4-methoxyphenyl)-2-methoxyethene (4a)

IR (film): 2359, 1341, 1508, 1244 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 3.73 (3 H, s), 3.80 (6 H, s), 6.32 (1 H, s), 6.82 (2 H, d, *J* = 8.8 Hz), 6.85 (2 H, d, *J* = 8.8 Hz), 7.13 (2 H, d, *J* = 8.8 Hz), 7.31 (2 H, d, *J* = 8.8 Hz). ^{13}C NMR (100 MHz, $CDCl_3$). δ = 55.1, 55.2, 60.3, 113.2, 113.5, 119.5, 129.2, 130.2, 130.7, 133.0, 133.6, 157.9, 158.2. MS: *m/z* = 270 (100) [M^+].

1,1-Bis(4-fluorophenyl)-2-methoxyethene (4b)

IR (film): 2934, 2361, 1636, 1508, 1229, 1109, 835 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 3.76 (3 H, s), 6.37 (1 H, s), 6.95–7.02 (4 H, m), 7.14 (2 H, dd, *J* = 8.8, 5.6 Hz), 7.32 (2 H, dd, *J* = 8.8, 5.6 Hz). MS: *m/z* = 246 (100) [M^+]. HRMS: *m/z* calcd for $C_{15}H_{12}F_2O$: 246.0856; found: 246.0841.

1,1-Bis(4-ethoxycarbonylphenyl)-2-methoxyethene (4c)

IR (film): 3477, 2981, 1717, 1277 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.39 (6 H, t, *J* = 7.2 Hz), 3.82 (3 H, s), 4.37 (4 H, q, *J* = 7.2 Hz), 6.61 (1 H, s), 7.24 (2 H, d, *J* = 8.0 Hz), 7.42 (2 H, d, *J* = 8.4 Hz), 7.96 (2 H, d, *J* = 8.4 Hz), 8.00 (2 H, d, *J* = 8.0 Hz). MS: *m/z* = 355 (4.58) [M^+ + 1], 177 (100). HRMS: *m/z* calcd for $C_{21}H_{22}O_5$: 354.1467; found: 354.1438.

1,1-Bis(4-cyanophenyl)-2-methoxyethene (4d)

IR (film): 2922, 2849, 2226, 1628, 1601, 1240, 1103 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 3.86 (3 H, s), 6.64 (1 H, s), 7.26 (2 H, d, *J* = 8.2 Hz), 7.44 (2 H, d, *J* = 8.4 Hz), 7.58 (2 H, d, *J* = 8.2 Hz), 7.61 (2 H, d, *J* = 8.4 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 61.3, 110.2, 110.3, 117.7, 118.7, 118.8, 128.3, 130.2, 131.8, 132.2, 141.1, 143.9, 149.7. MS: *m/z* (%) = 260 (100) [M^+]. HRMS: *m/z* calcd for $C_{17}H_{12}N_2O$: 260.0950; found: 260.0965.

1,1-Bis(3-methoxyphenyl)-2-methoxyethene (4e)

IR (film): 2999, 2936, 2833, 1597, 1576, 1485, 1285, 1252, 1229, 1105, 1049 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 3.75 (3 H, s), 3.761 (3 H, s), 3.764 (3 H, s), 6.46 (1 H, s), 6.76–6.81 (4 H, m), 6.93–6.97 (2 H, m), 7.17 (1 H, d, *J* = 8.0 Hz), 7.21 (1 H, d, *J* = 8.0 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): d = 55.17, 55.21, 111.7, 112.0, 113.9, 115.5, 120.2, 120.7, 122.3, 128.7, 129.0, 138.7, 141.6, 146.5, 146.5, 159.1, 159.4. MS: *m/z* = 270 (100) [M^+], 135 (17.5). HRMS: *m/z* calcd for $C_{17}H_{18}O_3$: 270.1256; found: 270.1248.

1-Phenyl-1-(3-methoxyphenyl)-2-methoxyethene (4f)

Obtained as a mixture of *E*- and *Z*-isomers (1.2:1). IR (film): 2932, 2835, 1634, 1597, 1236, 1107, 696 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 3.75–3.76 (6 H, m), 6.44 (0.55 H, s), 6.47 (0.45 H, s), 6.76–6.81 (2 H, m), 6.93–6.96 (1 H, m), 7.19–7.38 (6 H, m). MS: *m/z* (%) = 240 (100) [M^+], 197 (26.2). HRMS: *m/z* calcd for $C_{16}H_{16}O_2$: 240.1150; found: 240.1134.

Typical Procedure for the Synthesis of Enamines (5a, Table 2, Entry 1)

A solution of **4a** (48.9 mg, 0.18 mmol) in CH_2Cl_2 (2 mL) was added to a solution of 4-toluenesulfonamide (34.1 mg, 0.20 mmol) in CH_2Cl_2 (2 mL). Then, TFAA (42.0 mg, 0.20 mmol) and TFA (22.8 mg, 0.20 mmol) were added to the reaction mixture at r.t., and the mixture was heated under reflux for 13.5 h. The mixture was poured into cold H_2O and extracted with CH_2Cl_2 (3 × 5 mL), and dried over $MgSO_4$. The solvent was evaporated, and the residue was purified by silica gel column chromatography (hexane–EtOAc, 9:1) to give **5a** (58.5 mg, 79%) as a colorless amorphous solid.

***N*-[2,2-Bis(4-methoxyphenyl)vinyl] 4-Methylphenylsulfonamide (5a)**

IR (film): 3273, 1607, 1512, 1352, 1246, 1165 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 2.44 (3 H, s), 3.77 (3 H, s), 3.82 (3 H, s), 6.22 (1 H, d, *J* = 11.4 Hz), 6.65 (1 H, d, *J* = 11.4 Hz), 6.76–6.86 (6 H, m), 7.02 (2 H, d, *J* = 8.8 Hz), 7.33 (2 H, d, *J* = 8.4 Hz), 7.71 (2 H, d, *J* = 8.4 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.6, 55.28, 55.30, 113.7, 114.6, 118.5, 125.8, 126.7, 127.6, 128.5, 129.8, 130.6, 132.2, 136.6, 143.7, 158.7, 159.1. MS: *m/z* (%) = 409 (33.4) [M^+], 254 (100). HRMS: *m/z* calcd for $C_{23}H_{23}NO_4S$: 409.1348; found: 409.1341.

***N*-[2,2-Bis(4-fluorophenyl)vinyl] 4-Methylphenylsulfonamide (5b)**

Mp 144–145 °C (colorless plates from hexane–EtOAc). IR (film): 3267, 2361, 1638, 1601, 1510, 1167 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): d = 2.46 (3 H, s), 6.25 (1 H, d, *J* = 11.4 Hz), 6.71 (1 H, d, *J* = 11.4 Hz), 6.87–6.95 (4 H, m), 7.01–7.06 (4 H, m), 7.35 (2 H, d, *J* = 8.4 Hz), 7.72 (2 H, d, *J* = 8.4 Hz). MS *m/z* (%) = 385 (41.0), 230 (100). HRMS: *m/z* calcd for $C_{21}H_{17}F_2NO_2S$: 385.0948; found: 385.0930. Anal. Calcd for $C_{21}H_{17}F_2NO_2S$: C, 65.44; H, 4.45; N, 3.63. Found: C, 65.38; H, 4.50; N, 3.62.

***N*-[2,2-Bis(4-ethoxycarbonylphenyl)vinyl] 4-Methylphenylsulfonamide (5c)**

Compound **4c** (0.91 g, 2.6 mmol) was dissolved in a solution of 10% H_2SO_4 in AcOH (20 mL) and stirred for 18 h at r.t. The reaction mixture was extracted with EtOAc (3 × 10 mL) and the combined organic layer was washed with brine (5 mL) and dried over $MgSO_4$. The solvent was evaporated to give 2,2-bis(4-ethoxycarbonylphenyl)acetaldehyde, which was used to the next reaction without further purification. A solution of the above aldehyde (0.87 g, 2.6 mmol) and TFAA (0.54 g, 2.6 mmol) in CH_2Cl_2 (20 mL) was added to a solution of 4-toluenesulfonamide (0.20 g, 1.2 mmol) in CH_2Cl_2 (10 mL) and heated under reflux for 20.5 h. The reaction mixture was extracted with CH_2Cl_2 (3 × 10 mL) and the combined organic layer was washed with brine (10 mL) and dried over $MgSO_4$. The solvent was evaporated and the residue was purified by silica gel column chromatography (hexane–EtOAc, 9:1) to give **5c** (0.47 g, 37%) as a colorless amorphous solid. IR (film): 3238, 2361, 1717, 1601, 1275, 1167, 1103 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.36–1.43 (6 H, m), 2.47 (3 H, s), 4.33–4.44 (4 H, m), 6.34 (1 H, d, *J* = 12.2 Hz), 6.94 (1 H, d, *J* = 12.2 Hz), 7.03 (2 H, d, *J* = 8.4 Hz), 7.12 (2 H, d, *J* = 8.0 Hz), 7.36 (2 H, d, *J* = 8.4 Hz), 7.73 (2 H, d, *J* = 8.4 Hz), 7.91 (2 H, d, *J* = 8.0 Hz), 8.04 (2 H, d, *J* = 8.4 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.2, 21.5, 60.8, 61.1, 122.8, 123.1, 126.1, 126.5, 127.0, 128.7, 129.5, 129.6, 129.8, 129.9, 130.4, 136.6, 140.6, 143.4, 144.0, 165.6, 165.9. MS: *m/z* (%) = 493 (100) [M^+], 292 (48.5). HRMS: m/z calcd for $C_{27}H_{27}NO_6S$: 493.1559; found: 493.1549.

***N*-[2,2-Bis(4-cyanophenyl)vinyl] 4-Methylphenylsulfonamide (5d)**

Mp 232–233 °C (colorless plates from hexane–$CHCl_3$). IR (film): 3261, 2226, 1634, 1599, 1339, 1165 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 2.47 (3 H, s), 6.82 (1 H, d, *J* = 11.8 Hz), 6.96 (1 H, d, *J* = 11.8 Hz), 7.12 (2 H, d, *J* = 8.0 Hz), 7.13 (2 H, d, *J* = 8.4 Hz), 7.37 (2 H, d, *J* = 8.4 Hz), 7.53 (2 H, d, *J* = 8.0 Hz), 7.65 (2 H, d, *J* = 8.0 Hz), 7.72 (2 H, d, *J* = 8.0 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.7, 110.5, 112.3,

117.9, 118.5, 121.2, 124.3, 126.6, 126.8, 130.1, 130.6, 132.3, 133.3, 136.3, 140.3, 143.1, 144.6. MS: *m/z* (%) = 399 (45.0) [M$^+$], 244 (100). HRMS: *m/z* calcd for $C_{23}H_{17}N_3O_2S$: 399.1042; found: 399.1025.

***N*-[2,2-Bis(3-methoxyphenyl)vinyl] 4-Methylphenylsulfonamide (5e)**

IR (film): 3265, 2937, 2835, 1597, 1578, 1350, 1286, 1161, 1090 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.44 (3 H, s), 3.71 (3 H, s), 3.74 (3 H, s), 6.30 (1 H, d, *J* = 12.0 Hz), 6.46 (1 H, s), 6.49 (1 H, d, *J* = 8.1 Hz), 6.63–6.64 (1 H, m), 6.72 (1 H, dt, *J* = 8.1, 0.8 Hz), 6.75 (1 H, dd, *J* = 8.1, 2.8 Hz), 6.79 (1 H, d, *J* = 12.0 Hz), 6.86 (1 H, dd, *J* = 8.1, 2.8 Hz), 7.16 (1 H, t, *J* = 8.1 Hz), 7.25 (1 H, t, *J* = 8.1 Hz), 7.32 (2 H, d, *J* = 8.2 Hz), 7.71 (2 H, d, *J* = 8.2 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.7, 55.21, 55.24, 112.1, 112.5, 113.8, 114.8, 119.0, 120.4, 121.6, 125.7, 126.7, 129.2, 129.8, 130.4, 136.6, 137.4, 140.6, 143.9, 159.5, 160.2. MS: *m/z* (%) = 409 (49.0) [M$^+$], 254 (100). HRMS: *m/z* calcd for $C_{23}H_{23}NO_4S$: 409.1348; found: 409.1331. Anal. Calcd for $C_{23}H_{23}NO_4S$: C, 67.46; H, 5.66; N, 3.42. Found: C, 67.51; H, 5.69; N, 3.44.

***N*-[2-(3-Methoxyphenyl)-2-phenylvinyl] 4-Methylphenylsulfonamide (5f)**

Obtained as a mixture of *E*- and *Z*-isomers (1.1:1). Recrystallization gave the single isomer. Mp 150–151 °C (colorless needles from hexane–EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.44 (3 H, s), 3.72 (3 H, s), 6.33 (1 H, d, *J* = 11.6 Hz), 6.47 (1 H, s), 6.50 (1 H, d, *J* = 7.7 Hz), 6.78 (1 H, d, *J* = 11.6 Hz), 6.86 (1 H, dd, *J* = 7.7, 2.6 Hz), 7.12 (2 H, d, *J* = 8.2 Hz), 7.20–7.28 (4 H, m), 7.33 (2 H, d, *J* = 8.2 Hz), 7.71 (2 H, d, *J* = 8.2 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.5, 55.2, 113.8, 115.0, 120.3, 121.7, 125.9, 126.5, 126.8, 127.1, 128.4, 129.9, 130.5, 136.9, 137.7, 139.2, 144.0, 160.4. MS: *m/z* (%) = 379 (55.3) [M$^+$], 224 (100). HRMS:
m/z calcd for $C_{22}H_{21}NO_3S$: 379.1242; found: 379.1230. Anal. Calcd for $C_{22}H_{21}NO_3S$: C, 69.63; H, 5.58; N, 3.69. Found: C, 69.37; H, 5.65; N, 3.71.

6-Methoxy-3-(4-methoxyphenyl)-1-(4-methylphenylsulfonyl) indole (6a)

IR (film): 2934, 2837, 1597, 1508, 1369, 1252, 1173, 1115, 1032 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.35 (3 H, s), 2.86 (3 H, s), 2.90 (3 H, s), 6.89 (1 H, dd, *J* = 8.8, 2.6 Hz), 6.96 (1 H, d, *J* = 8.8 Hz), 6.98 (1 H, d, *J* = 8.8 Hz), 7.22 (1 H, d, *J* = 7.6 Hz), 7.49–7.51 (3 H, m), 7.585 (1 H, s), 7.593 (1 H, d, *J* = 7.6 Hz), 7.78–7.80 (3 H, m). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.6, 55.3, 55.8, 98.1, 112.5, 114.2, 120.8, 123.2, 123.6, 125.5, 126.7, 128.8, 129.8, 135.1, 136.5, 144.8, 157.9, 159.0. MS: *m/z* (%) = 407 (31.0) [M$^+$], 252 (100). HRMS: *m/z* calcd for $C_{23}H_{21}NO_4S$: 407.1191; found: 407.1184.

6-Fluoro-3-(4-fluorophenyl)-1-(4-methylphenylsulfonyl) indole (6b)

IR (film): 3111, 2926, 1504, 1375, 1188, 1175, 1107, 679 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.36 (3 H, s), 7.00–7.06 (1 H, m), 7.12–7.16 (2 H, m), 7.26 (2 H, d, *J* = 8.0 Hz), 7.49–7.53 (2 H, m), 7.59–7.63 (1 H, m), 7.61 (1 H, s), 7.76–7.81 (3 H, m). MS: *m/z* = 383 (40.0) [M$^+$], 319 (9.0), 228 (100). HRMS: *m/z* calcd for $C_{21}H_{15}F_2NO_2S$: 383.0781; found: 383.0782.

6-Ethoxycarbonyl-3-(4-ethoxycarbonylphenyl)-1-(4-methylphenylsulfonyl) indole (6c)

IR (film): 2982, 1715, 1375, 1279, 1177, 1163 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.41–1.47 (6 H, m), 2.36 (3 H, s), 4.39–4.47 (4 H, m), 7.27 (2 H, d, *J* = 8.6 Hz), 7.66 (2 H, d, *J* = 8.0 Hz), 7.80 (2 H, d, *J* = 8.6 Hz), 7.85 (1 H, d, *J* = 8.6 Hz), 7.90 (1 H, s), 7.99 (1 H, d, *J* = 8.6 Hz), 8.14 (2 H, d, *J* = 8.0 Hz), 8.74 (1 H, s). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.4, 14.5, 21.7, 61.1, 61.2, 115.5, 119.9, 122.6, 124.7, 126.3, 127.0, 127.3, 127.5, 129.6, 130.1, 130.2, 132.1, 134.7, 134.8, 137.0, 145.5, 166.1, 166.4. MS: *m/z* (%) = 491 (81.9) [M$^+$], 336 (100). HRMS: *m/z* calcd for $C_{27}H_{25}NO_6S$: 491.1403; found: 491.1409.

6-Cyano-3-(4-cyanophenyl)-1-(4-methylphenylsulfonyl)-indole (6d)

Mp 238–239 °C (colorless prisms from hexane–EtOAc). IR (film): 2922, 2228, 1611, 1431, 1379, 1175 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.40 (3 H, s), 7.32 (2 H, d, *J* = 8.4 Hz), 7.56 (1 H, dd, *J* = 8.4, 1.2 Hz), 7.67 (2 H, d, *J* = 8.0 Hz), 7.77 (2 H, d, *J* = 8.0 Hz), 7.82 (1 H, d, *J* = 8.4 Hz), 7.84 (2 H, d, *J* = 8.4 Hz), 7.95 (1 H, s), 8.38 (1 H, s). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.8, 108.4, 109.7, 111.6, 118.2, 118.4, 119.0, 120.9, 121.7, 126.8, 127.0, 127.1, 128.3, 130.4, 131.3, 132.8, 134.3, 136.6, 146.2. MS: *m/z* (%) = 397 (100) [M$^+$]. HRMS: *m/z* calcd for $C_{23}H_{15}N_3O_2S$: 397.0885; found: 397.0873.

5-Methoxy-3-(3-methoxyphenyl)-1-(4-methylphenylsulfonyl) indole (6e)

IR (film): 2934, 2835, 1597, 1472, 1371, 1219, 1173, 1132, 667 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.33 (3 H, s), 3.81 (3 H, s), 3.86 (3 H, s), 6.91 (1 H, dd, *J* = 8.1, 2.4 Hz), 6.97 (1 H, dd, *J* = 9.2, 2.4 Hz), 7.10 (1 H, s), 7.16 (1 H, d, *J* = 8.1 Hz), 7.19–7.22 (3 H, m), 7.37 (1 H, t, *J* = 8.1 Hz), 7.64 (1 H, s), 7.76 (2 H, d, *J* = 8.1 Hz), 7.93 (1 H, d, *J* = 9.2 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.6, 55.3, 55.7, 102.9, 113.0, 113.3, 113.8, 114.7, 120.1, 123.83, 123.85, 126.7, 129.8, 129.9, 130.1, 130.2, 134.4, 135.0, 144.8, 156.6, 159.9. MS: *m/z* (%) = 407 (59.9) [M$^+$], 252 (100). HRMS: *m/z* calcd for $C_{23}H_{21}NO_4S$: 407.1191; found: 407.1178. Anal. Calcd for $C_{23}H_{21}NO_4S$: C, 67.79; H, 5.19; N, 3.44. Found C, 67.86; H, 5.33; N, 3.44.

5-Methoxy-1-(4-methylphenylsulfonyl)-3-phenylindole (6f-A) and 3-(3-Methoxyphenyl)-1-(4-methylphenylsulfonyl) indole (6f-B)

IR (film): 2926, 2361, 1597, 1470, 1371, 1173, 1134, 669 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.33 (3 H, s), 3.80 (2.49 H, s), 3.86 (0.51 H, s), 6.91 (0.17 H, ddd, *J* = 8.2, 2.5, 1.3 Hz), 6.97 (0.83 H, dd, *J* = 9.2, 2.4 Hz), 7.13 (0.17 H, dd, *J* = 2.5, 1.3 Hz), 7.18–7.25 (3 H, m), 7.28 (0.17 H, d, *J* = 7.6 Hz), 7.34–7.38 (1.17 H, m), 7.45 (1.66 H, dd, *J* = 8.0, 7.2 Hz), 7.56 (1.66 H, dd, *J* = 8.2, 1.4 Hz), 7.63 (0.83 H, s), 7.69 (0.17 H, s), 7.76 (1.66 H, d, *J* = 8.4 Hz), 7.78–7.80 (0.51 H, m), 7.94 (0.83 H, d, *J* = 8.8 Hz), 8.04 (0.17 H, d, *J* = 8.4 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.5, 55.7, 103.0, 113.8, 114.8, 123.8, 124.1, 126.8, 127.5, 127.8, 128.9, 129.87, 129.92, 130.3, 133.2, 135.2, 144.9, 156.8. MS: *m/z* (%) = 377 (60.4) [M$^+$], 222 (100). HRMS: *m/z* calcd for $C_{22}H_{19}NO_3S$: 377.1086; found: 377.1068.

(21) Geometry of enamine **5f** was determined by NOESY.

(22) Regioisomeric products **6f-A** and **6f-B** could not be separated from one another; their ratio was determined by ^{1}H NMR spectroscopy.

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