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GENERATION OF 3-(1*H*-ISOCHROMEN-1-YL)-1*H*-INDOLE *VIA* SILVER TRIFLATE-CATALYZED TANDEM REACTION OF 2-ALKYNYLBENZALDEHYDE WITH INDOLE

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This paper is dedicated to Prof. Dr. Albert Eschenmoser on the occasion of his 85th birthday.

Abstract – A facile and efficient method is developed for synthesis of 3-(1*H*-isochromen-1-yl)-1*H*-indole *via* silver triflate-catalyzed tandem reaction of 2-alkynylbenzaldehyde with indole. The reaction proceeds smoothly in DMF at room temperature with good substrate generality. The availability of the starting materials combined with mild reaction conditions and the high efficiency of this synthetic route would be attractive and beneficial for the focused library construction.

INTRODUCTION

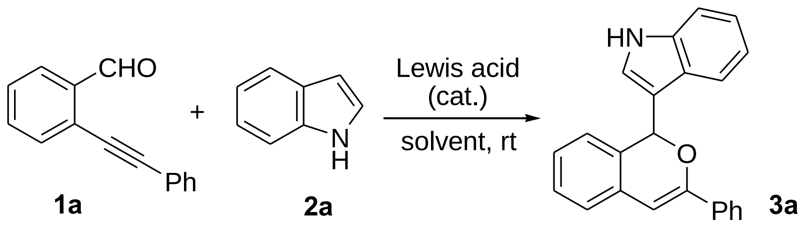
It is well known that natural product-like compounds can be utilized to dissect the circuitry of cells, which is analogous to the use of mutations in genetics.[1] For access such small molecules capable of modulating any pathway or process of interest, diversity-oriented synthesis is an efficient device.[2] Among the methods employed, tandem reactions from easily available starting materials provide an efficient and powerful tool to produce a collection of structurally diverse compounds.[3,4] As we know, the 1*H*-isochromene core is regarded as a privileged scaffold which can be found in many natural products and drug candidates with remarkable biological activities.[5] Thus, continuous efforts have been observed for the development of new methods for its construction.[6] On the other hand, the indole skeleton is an important substructure as well in both natural products and therapeutic agents.[7] As part of an ongoing program in our laboratory for accessing natural product-like compounds used in different biological assays,[8,9] we conceived that the 1*H*-isochromene with an indole substituent might be a good candidate for library development. Therefore, we started to consider the possibility for the synthesis of this kind of compound.

Recently, 2-alkynylbenzaldehyde was discovered as a versatile building block for carbocycles and heterocycles formation.[10,11] Its reliability and the ready availability of the starting materials made it attractive for reaction development. For instance, Yamamoto and Asao described the naphthyl ketones synthesis *via* $AuCl_3$-catalyzed [4+2] benzannulation of 2-alkynylbenzaldehydes with alkynes.[11a,b] Very recently, Li and co-workers reported a $PdCl_2$-catalyzed domino reaction of 2-alkynylbenzaldehyde with indole for generation of fluorescent 5*H*-benzo[*b*]carbazol-6-yl ketones.[10i] We also found that 1*H*-isochromen-1-ylphosphonates could be easily accessible *via* AgOTf-catalyzed reaction of 2-alkynylbenzaldehyde with diethyl phosphite. During the reaction process, it was recognized that the metal-catalyzed cyclization would occur firstly to generate an isobenzopyrylium complex, which then triggered intermolecular attack of the nucleophile thus affording 1*H*-isochromene derivatives. Encouraged by these results, we reasoned that 3-(1*H*-isochromen-1-yl)-1*H*-indoles could be synthesized *via* metal-catalyzed tandem reactions of 2-alkynylbenzaldehydes with indoles under suitable conditions. Herein, we would like to disclose our recent efforts for this transformation.

RESULTS AND DISCUSSION

2-Alkynylbenzaldehyde **1** was conveniently prepared from the commercially available 2-bromobenzaldehyde with alkyne *via* Sonogashira coupling reaction according to the literature method.[12] The preliminary experiments were carried out for the reaction of 2-alkynylbenzaldehyde **1a** with indole **2a** catalyzed by different Lewis acids in various solvents at room temperature (Table 1). To our delight, the desired product **3a** was afforded in 40% yield when the reaction was performed in MeCN in the presence of AgOTf (5 mol%) as a catalyst (Table 1, entry 1). Only a trace amount of product was detected when the catalyst was replaced by CuOTf, $Cu(OTf)_2$, $La(OTf)_3$, $Sc(OTf)_3$, or $Bi(OTf)_3$ (Table 1, entries 2-6). The product from double addition of indole to aldehyde was obtained when $Dy(OTf)_3$, $Yb(OTf)_3$, or $Zn(OTf)_2$ was employed as the catalyst in the above reaction (Table 1, entries 7-9). The yield was increased to 56% when 10 mol% of AgOTf was used (Table 1, entry 10). Further screening of solvents demonstrated that the reaction worked the most efficiently in DMF, which furnished the corresponding product **3a** in 66% yield (Table 1, entry 18). Inferior yields were generated when other solvents were utilized in the reaction.

Table 1. Initial studies for reaction of 2-alkynylbenzaldehyde **1a** with indole **2a**



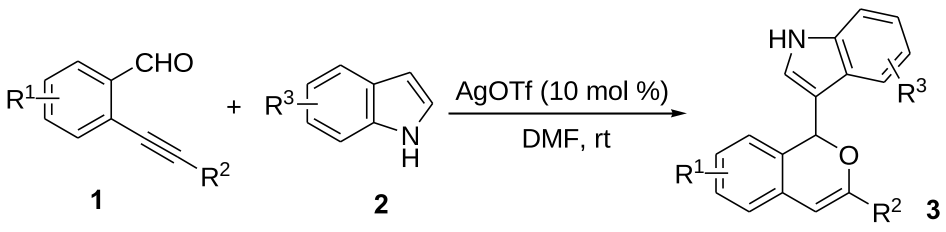
Entry	Lewis acid	solvent	Yield (%)[a]
1	AgOTf (5 mol%)	MeCN	40
2	CuOTf (5 mol%)	MeCN	trace
3	$Cu(OTf)_2$ (5 mol%)	MeCN	trace
4	$La(OTf)_3$ (5 mol%)	MeCN	trace
5	$Sc(OTf)_3$ (5 mol%)	MeCN	trace
6	$Bi(OTf)_3$ (5 mol%)	MeCN	trace
7	$Yb(OTf)_3$ (5 mol%)	MeCN	61[b]
8	$Zn(OTf)_2$ (5 mol%)	MeCN	52[b]
9	$Dy(OTf)_3$ (5 mol%)	MeCN	63[b]
10	AgOTf (10 mol%)	MeCN	56
11	AgOTf (10 mol%)	THF	trace
12	AgOTf (10 mol%)	CH_2Cl_2	trace
13	AgOTf (10 mol%)	acetone	trace
14	AgOTf (10 mol%)	EtOH	trace
15	AgOTf (10 mol%)	MeOH	trace
16	AgOTf (10 mol%)	DMSO	33
17	AgOTf (10 mol%)	NMP	trace
18	AgOTf (10 mol%)	DMF	66
19	AgOTf (10 mol%)	DMAc	50
20	AgOTf (10 mol%)	toluene	trace
21	AgOTf (10 mol%)	$ClCH_2CH_2Cl$	trace

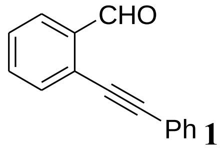
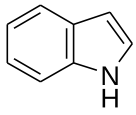
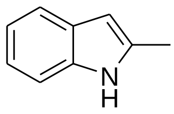
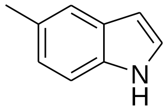
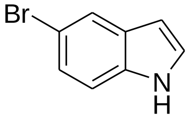
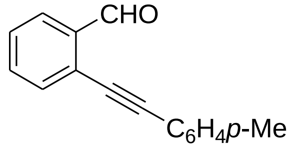
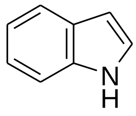
[a] Isolated yield based on 2-alkynylbenzaldehyde **1a**.

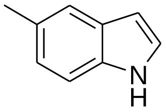
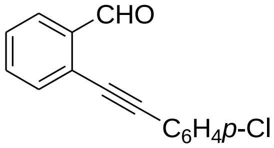
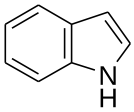
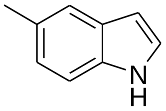
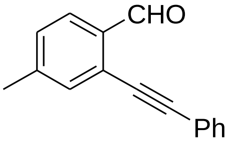
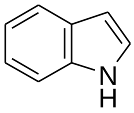
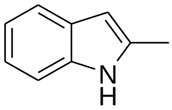
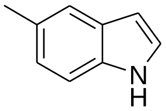
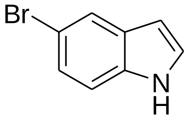
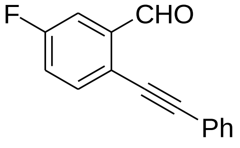
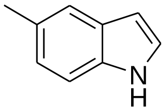
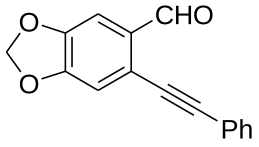
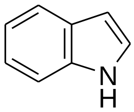
[b] Product from double addition of indole to aldehyde was obtained.

Next, the scope of the tandem reaction of 2-alkynylbenzaldehyde **1** with indole **2** was examined and the results were presented in Table 2. From Table 2, we found that all reactions proceeded smoothly leading to the desired 3-(1*H*-isochromen-1-yl)-1*H*-indole **3** in good to excellent yields. For example, reaction of 2-alkynylbenzaldehyde **1a** with 2-methylindole **2b** gave rise to the 1*H*-isochromene **3b** in 70% yield (Table 2, entry 2). A slightly lower yield was obtained when 5-methyl or 5-bromoindole was used as a replacement (Table 2, entries 3 and 4). Substrate **1b** or **1c** also worked well to generate the corresponding product in good yield (Table 2, entries 5-8). Under the standard conditions, the methyl-, fluoro-, or [1,3]dioxolyl-substituted 2-alkynylbenzaldehyde **1d**-**1f** were tested as well in the reactions of various indoles (Table 2, entries 9-14). As expected, all reactions gave rise to the desired products in good yields. In addition, we did not observe the influence of the electron effect on the aromatic backbone of the substrates.

Table 2. Synthesis of 3-(1*H*-isochromen-1-yl)-1*H*-indole **3** *via* silver triflate-catalyzed tandem reaction of 2-alkynylbenzaldehyde **1** with indole **2**



Entry	Substrate **1**	Indole **2**	Product **3**	Yield (%)[a]
1	 **1a**	 **2a**	**3a**	66
2	**1a**	 **2b**	**3b**	70
3	**1a**	 **2c**	**3c**	62
4	**1a**	 **2d**	**3d**	55
5	 **1b**	 **2a**	**3e**	67

6	**1b**	 **2c**	**3f**	75
7	 **1c**	 **2a**	**3g**	60
8	**1c**	 **2c**	**3h**	95
9	 **1d**	 **2a**	**3i**	78
10	**1d**	 **2b**	**3j**	62
11	**1d**	 **2c**	**3k**	62
12	**1d**	 **2d**	**3l**	91
13	 **1e**	 **2c**	**3m**	63
14	 **1f**	 **2a**	**3n**	80

[a] Isolated yield based on 2-alkynylbenzaldehyde **1**.

CONCLUSION

In summary, we have described an efficient AgOTf-catalyzed tandem reaction of 2-alkynylbenzaldehyde with indole, which generates the diverse 3-(1*H*-isochromen-1-yl)-1*H*-indoles in good yields. This transformation proceeds through cascade intramolecular cyclization and intermolecular nucleophilic addition. The easily availability of the starting materials combined with mild reaction conditions, good substrate generality, and the high efficiency of this synthetic route would be attractive and beneficial for the focused library construction.

EXPERIMENTAL

General experimental procedure for the synthesis of 3-(1*H*-isochromen-1-yl)-1*H*-indole 3 *via* silver triflate-catalyzed tandem reaction of 2-alkynylbenzaldehyde 1 with indole 2: Silver triflate (10 mol%) was added to a solution of 2-alkynylbenzaldehyde **1** (0.25 mmol) and indole **2** (0.3 mmol) in DMF. The mixture was stirred at room temperature. After completion of reaction as indicated by TLC, the mixture was diluted with water (10 mL), extracted with EtOAc (10 × 2 mL). The combined organic layers were then washed with brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by flash column chromatography (*n*-hexane/ethyl acetate) to afford the desired product **3**.

3-(3-Phenyl-1*H*-isochromen-1-yl)-1*H*-indole (**3a**): White solid, mp 153-154 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (s, 1H), 7.86 (d, *J* = 8.0 Hz, 1H), 7.64-7.66 (m, 2H), 7.35 (d, *J* = 8.0 Hz, 1H), 7.30-7.10 (m, 8H), 6.97 (d, *J* = 7.2 Hz, 1H), 6.85 (d, *J* = 2.4 Hz, 1H), 6.68 (s, 1H), 6.49 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.6, 136.6, 134.8, 132.0, 130.3, 128.6, 128.2, 128.1, 126.5, 126.4, 125.4, 125.1, 124.9, 123.6, 122.4, 120.1, 120.0, 115.3, 111.3, 100.8, 74.0; IR (KBr): ν (cm^{-1}) 3415, 3022, 1622, 1491, 1455. HRMS calcd for $C_{23}H_{18}NO$ (M+H): 324.1388, found: 324.1386.

2-Methyl-3-(3-phenyl-1*H*-isochromen-1-yl)-1*H*-indole (**3b**): Yellow solid, mp 63-65 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (s, 1H), 7.72 (d, *J* = 7.6 Hz, 2H), 7.44 (d, *J* = 4.0 Hz, 1H), 7.34-7.23 (m, 5H), 7.18-7.11 (m, 2H), 7.05-6.98 (m, 2H), 6.74 (d, *J* = 7.6 Hz, 1H), 6.57 (s, 1H), 6.50 (s, 1H), 2.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.3, 135.4, 134.5, 132.8, 130.8, 128.7, 128.2, 128.0, 127.8, 126.5, 125.2, 125.0, 123.4, 121.3, 120.1,119.7, 110.2, 109.5, 101.0, 74.5, 12.3; IR (KBr): ν (cm^{-1}) 3400, 3057, 2918, 2849, 1621, 1492, 1460. HRMS calcd for $C_{24}H_{20}NO$ (M+H): 338.1545, found: 338.1539.

5-Methyl-3-(3-phenyl-1*H*-isochromen-1-yl)-1*H*-indole (**3c**): White solid, mp 179-180 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (s, 1H), 7.67-7.63 (m, 3H), 7.29-7.09 (m, 7H), 7.03 (d, *J* = 8.4 Hz, 1H), 6.95 (d, *J* = 7.2 Hz, 1H), 6.82 (d, *J* = 2.4 Hz, 1H), 6.63 (s, 1H), 6.49 (s, 1H), 2.44 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.8, 134.9, 134.8, 132.1, 130.5, 129.3, 128.6, 128.2, 128.1, 126.7, 126.4, 125.5, 125.1, 125.0, 124.1, 123.6, 119.8, 114.7, 110.9, 100.9, 74.2, 21.6; IR (KBr): ν (cm^{-1}) 3412, 3057, 2922, 2858, 1625, 1488, 1453. HRMS calcd for $C_{24}H_{20}NO$ (M+H): 338.1545, found: 338.1541.

5-Bromo-3-(3-phenyl-1*H*-isochromen-1-yl)-1*H*-indole (**3d**): Green solid, mp 67-68 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (s, 1H), 7.96 (s, 1H), 7.63 (d, *J* = 7.2 Hz, 2H), 7.29-7.22 (m, 5H), 7.17 (d, *J* = 7.6 Hz, 1H), 7.13-7.10 (m, 2H), 6.91 (d, *J* = 7.2 Hz, 1H), 6.75 (d, *J* = 2.0 Hz, 1H), 6.57 (s, 1H), 6.48 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.5, 135.2, 134.6, 131.9, 130.0, 128.8, 128.3, 128.2, 128.1, 126.6, 126.1, 125.4, 125.3, 125.0, 123.8, 122.7, 115.0, 113.4, 112.9, 101.0, 73.8; IR (KBr): *v* (cm^{-1}) 3420, 3062, 1626, 1601, 1492, 1454. HRMS calcd for $C_{23}H_{17}BrNO$ (M+H): 402.0494, found: 402.0499.

3-(3-*p*-Tolyl-1*H*-isochromen-1-yl)-1*H*-indole (**3e**): Yellow solid, mp 144-145 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (s, 1H), 7.85 (d, *J* = 8.0 Hz, 1H), 7.54 (d, *J* = 8.0 Hz, 2H), 7.33 (d, *J* = 8.0 Hz, 1H), 7.28-7.07 (m, 7H), 6.96 (d, *J* = 7.6 Hz, 1H), 6.84 (d, *J* = 2.0 Hz, 1H), 6.66 (s, 1H), 6.44 (s, 1H), 2.29 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.8, 138.6, 136.6, 132.2, 132.0, 130.3, 128.9, 128.1, 126.5, 126.2, 125.4, 125.1, 124.8, 123.5, 122.4, 120.2, 120.0, 115.4, 111.3, 100.1, 74.0, 21.3; IR (KBr): *v* (cm^{-1}) 3416, 3064, 3014, 2922, 1621, 1509, 1456. HRMS calcd for $C_{24}H_{20}NO$ (M+H): 338.1545, found: 338.1557.

5-Methyl-3-(3-*p*-tolyl-1*H*-isochromen-1-yl)-1*H*-indole (**3f**): Brown solid, mp 148-149 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (s, 1H), 7.61 (s, 1H), 7.55 (d, *J* = 8.0 Hz, 2H), 7.25-6.91 (m, 8H), 6.78 (d, *J* = 2.4 Hz, 1H), 6.59 (s, 1H), 6.44 (s, 1H), 2.43 (s, 3H), 2.29 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.0, 138.7, 134.9,132.3, 132.0, 130.5, 129.3, 129.0, 128.1, 126.8, 126.2, 125.5, 125.1, 125.0, 124.0, 123.5, 119.8, 114.7, 111.0, 100.2, 74.2, 21.6, 21.3; IR (KBr): *v* (cm^{-1}) 3422, 3030, 2919, 2857, 1623, 1511, 1487. HRMS calcd for $C_{25}H_{22}NO$ (M+H): 352.1701, found: 352.1709.

3-(3-(4-Chlorophenyl)-1*H*-isochromen-1-yl)-1*H*-indole (**3g**): White solid, mp 150-151 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (s, 1H), 7.83 (d, *J* = 7.2 Hz, 1H), 7.56 (d, *J* = 7.8 Hz, 2H), 7.34-7.11 (m, 8H), 6.96 (d, *J* = 7.6 Hz, 1H), 6.81 (d, *J* = 2.4 Hz, 1H), 6.67 (s, 1H), 6.45 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.5, 136.6, 134.3, 133.3, 131.7, 130.3, 128.4, 128.2, 126.6, 126.4, 125.2, 124.9, 123.8, 122.5, 120.1, 120.0, 115.3, 111.4, 101.2, 74.1; IR (KBr): *v* (cm^{-1}) 3391, 3066, 1623, 1490, 1455. HRMS calcd for $C_{23}H_{17}ClNO$ (M+H): 358.0999, found: 358.0410.

3-(3-(4-Chlorophenyl)-1*H*-isochromen-1-yl)-5-methyl-1*H*-indole (**3h**): Yellow solid, mp 197-198 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (br, 1H), 7.62-7.57 (m, 2H), 7.28-7.11 (m, 6H), 7.05 (d, *J* = 8.4 Hz, 1H), 6.96 (d, *J* = 7.6 Hz, 1H), 6.83 (d, *J* = 2.4 Hz, 1H), 6.63 (s, 1H), 6.47 (s, 1H), 2.45 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.6, 134.9, 134.3, 133.3, 131.8, 130.4, 129.4, 128.4, 128.1, 126.7, 126.6, 125.2, 125.0, 124.1, 123.7, 119.7, 114.6, 111.0, 101.2, 74.2, 21.6; IR (KBr): *v* (cm^{-1}) 3415, 3072, 2919, 1626, 1490, 1405. HRMS calcd for $C_{24}H_{19}ClNO$ (M+H): 372.1155, found: 372.1163.

3-(6-Methyl-3-phenyl-1*H*-isochromen-1-yl)-1*H*-indole (**3i**): Yellow solid, mp 152-153 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (s, 1H), 7.83 (d, *J* = 7.6 Hz, 1H), 7.62 (d, *J* = 6.8 Hz, 2H), 7.26-7.11 (m, 5H), 6.98 (s, 1H), 6.91 (d, *J* = 7.6 Hz, 1H), 6.82 (d, *J* = 7.6 Hz, 1H), 6.77 (d, *J* = 2.4 Hz, 1H), 6.62 (s, 1H), 6.43 (s, 1H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.6, 137.7, 136.6, 134.9, 132.0, 128.6, 127.7, 127.2, 126.5, 125.4, 125.1, 125.0, 124.4, 122.4, 120.2, 120.0, 115.4, 111.4, 100.9, 74.0, 21.4; IR (KBr): *v* (cm^{-1}) 3415, 3059, 2916, 1621, 1492, 1455. HRMS calcd for $C_{24}H_{20}NO$ (M+H): 338.1545, found: 338.1551.

2-Methyl-3-(6-methyl-3-phenyl-1*H*-isochromen-1-yl)-1*H*-indole (**3j**) Yellow solid, mp 69-70 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (s, 1H), 7.71-7.69 (m, 2H), 7.44 (d, *J* = 7.6 Hz, 1H), 7.29-7.25 (m, 4H), 7.10 (t, *J* = 8.0 Hz, 1H), 7.00-7.01 (m, 2H), 6.82 (d, *J* = 7.6 Hz, 1H), 6.60 (d, *J* = 8.0 Hz, 1H), 6.52 (s, 1H), 6.46 (s, 1H), 2.33 (s, 3H), 2.32 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.3, 137.7, 135.4, 134.7, 134.6, 132.8, 128.7, 128.3, 128.2, 127.9, 127.2, 125.3, 125.0, 124.2, 121.3,120.2, 119.7, 110.4, 109.6, 101.1, 74.6, 21.3, 12.3; IR (KBr): *v* (cm^{-1}) 3403, 3058, 2920, 2851, 1622, 1460, 1046. HRMS calcd for $C_{25}H_{22}NO$ (M+H): 352.1701, found: 352.1712.

5-Methyl-3-(6-methyl-3-phenyl-1*H*-isochromen-1-yl)-1*H*-indole (**3k**) Yellow solid, mp 172-173 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (s, 1H), 7. 65-7.62 (m, 3H), 7.26-7.18 (m, 4H), 7.02-6.99 (m, 2H), 6.91 (d, *J* = 8.0 Hz, 1H), 6.84-6.80 (m, 2H), 6.59 (s, 1H), 6.44 (s, 1H), 2.43 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.8, 137.6, 134.9, 132.0, 129.2, 128.6, 128.2, 127.8, 127.1, 126.8, 125.5, 125.0, 124.3, 124.0, 119.8, 114.8, 111.0, 100.9, 74.1, 21.6, 21.3; IR (KBr): *v* (cm^{-1}) 3419, 2922, 2851, 1624, 1493, 1450. HRMS calcd for $C_{25}H_{22}NO$ (M+H): 352.1701, found: 352.1709.

5-Bromo-3-(6-methyl-3-phenyl-1*H*-isochromen-1-yl)-1*H*-indole (**3l**) Green solid, mp 64-65 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (br, 1H), 7.95 (s, 1H), 7.62 (d, *J* = 7.2 Hz, 2H), 7.28-7.21 (m, 4H), 7.08 (d, *J* = 8.4 Hz, 1H), 6.98 (s, 1H), 6.92 (d, *J* = 7.6 Hz, 1H), 6.78 (d, *J* = 7.6 Hz, 1H), 6.75 (s, 1H), 6.53 (s, 1H), 6.43 (s, 1H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.5, 137.9, 135.3, 134.7, 131.8, 128.7, 128.3, 128.1, 127.3, 126.1, 125.4, 125.3, 124.9, 124.8, 124.5, 122.7, 115.1, 113.3, 112.9, 101.1, 73.8, 21.4; IR (KBr): *v* (cm^{-1}) 3421, 2919, 1626, 1492, 1449. HRMS calcd for $C_{24}H_{19}BrNO$ (M+H): 416.0650, found: 416.0656.

3-(7-Fluoro-3-phenyl-1*H*-isochromen-1-yl)-5-methyl-1*H*-indole (**3m**) Yellow solid, mp 198-199 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (s, 1H), 7.66-7.64 (m, 2H), 7.58 (s, 1H), 7.29-7.23 (m, 4H), 7.14-7.11 (m, 1H), 7.05 (d, *J* = 8.4 Hz, 1H), 6.99-6.94 (m, 1H), 6.89 (d, *J* = 1.6 Hz, 1H), 6.66 (d, *J* = 7.2 Hz, 1H), 6.56 (s, 1H), 6.48 (s, 1H), 2.44 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.3, 134.9, 134.6, 132.7, 129.5, 128.7, 128.4, 128.3, 128.2, 126.5, 125.3, 125.0, 124.9, 124.2, 119.7, 114.8 (d, $^2J_{CF}$ = 22.0 Hz), 113.9, 112.5 (d, $^2J_{CF}$ = 23.0 Hz), 111.0, 100.1, 74.0, 21.6; IR (KBr): *v* (cm^{-1}) 3412, 3065, 2929, 2855, 1609, 1494. HRMS calcd for $C_{24}H_{19}FNO$ (M+H): 356.1451, found: 356.1455.

3-(7-Phenyl-5*H*-[1,3]dioxolo[4,5-*g*]isochromen-5-yl)-1*H*-indole (**3n**) Blue solid, mp 194-195 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (s, 1H), 7.83 (d, *J* = 8.0 Hz, 1H), 7.61 (d, *J* = 7.2 Hz, 2H), 7.32 (d, *J* = 8.0 Hz, 1H), 7.26-7.12 (m, 4H), 6.89 (s, 1H), 6.68 (s, 1H), 6.55 (s, 1H) , 6.46 (s, 1H) , 6.38 (s, 1H) , 5.89 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.3, 147.4, 146.1, 136.7, 134.7, 128.4, 128.2, 126.5, 126.4, 125.2, 124.8, 124.1, 122.4, 120.2, 120.1, 115.3, 111.3, 106.3, 104.5, 101.0, 100.9, 74.1; IR (KBr): *v* (cm^{-1}) 3384, 3069, 2900, 1640, 1499, 1482. HRMS calcd for $C_{24}H_{18}NO_3$ (M+H): 368.1287, found:

368.1298.

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