2-Substituted 3-Aryl- and 3-Heteroarylindoles by the Palladium-Catalyzed Reaction of *o*-Trifluoroacetanilides with Aryl Bromides and Triflates.

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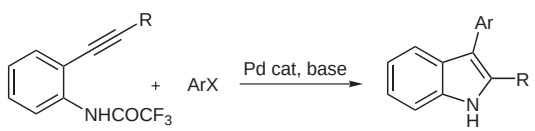
Abstract: The palladium-catalyzed reaction of aryl and heteroaryl bromides and triflates with *o*-alkynyltrifluoroacetanilides affords 2-substituted 3-aryl- and heteroarylindoles usually in excellent yield. The procedure can be applied to the synthesis of 2-substituted indole-3-carboxaldehydes.

Key words: palladium, alkynes, indoles, aryl halides, cyclization

The palladium-catalyzed reaction of *o*-alkynyltrifluoroacetanilides with organopalladium complexes generated in situ has been shown to be a powerful and extremely versatile procedure for the construction of the substituted pyrrole nucleus of the indole system.[1] This chemistry has been employed in the preparation of biologically active compounds.[2] It has also been adapted to a solid-supported synthesis for the preparation of combinatorial libraries of indoles with three variable components.[3] However, while a variety of indole derivatives could be prepared in good to excellent yield by using aryl iodides as the aryl donors, their employment was rather limited. Obviously, extension of the procedure to include aryl bromides and triflates would greatly widen its scope and generality and is highly desirable: reactions that employ the less expensive aryl bromides have significant practical advantages relative to those employing aryl iodides; including aryl triflates among the aryl donors can make it possible to look at phenols, widely diffused among natural products, as precursors of indole derivatives.

Herein we wish to report the successful application of our reaction to the synthesis of 2-substituted 3-aryl-, heteroarylindoles using *o*-trifluoroacetanilides **1** and aryl and heteroaryl bromides or triflates **2** (Scheme 1).



Scheme 1

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Compounds **1** were prepared from *o*-iodoaniline.[4] Our initial attempts focused on achieving optimal reaction conditions for the reaction of phenyl bromide and *o*-(phenylethynyl)trifluoroacetanilide **1a** (R = Ph) in MeCN, selected as the model system. The effect of bases, phosphine ligands, and temperature on the reaction yield was explored and some of our results are shown in Table 1.

At 60 °C and 80 °C a tendency to produce 2-phenylindole **4a** (Figure 1) was observed with a variety of phosphine ligands and bases (Table 1, entries 1–5, 11, 12). Apparently, at these temperatures the oxidative addition of phenyl bromide to Pd(0) is relatively slow and the cyclization of **1a** to **4a** can be a significant side reaction or even the main reaction path. This cyclization appears to be a palladium-catalyzed reaction, as suggested by the observation that no indole product was observed when the reaction was carried out omitting the palladium catalyst. In a few cases (Table 1, entries 1 and 5) the dimer **5a** was also isolated in significant yield.

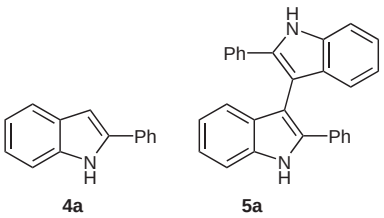


Figure 1

The reaction was shifted towards the aminopalladation-reductive elimination mechanism by increasing the temperature to 100 °C and by using $Pd_2(dba)_3$ and Xantphos [9,9-dimethyl-4,6-bis(diphenylphosphino)xanthene][5] in the presence of K_2CO_3 (Table 1, entry 6) or Cs_2CO_3 (Table 1, entry 7) or even by using $Pd(PPh_3)_4$ in the presence of K_2CO_3 (Table 1, entry 9). Under these conditions the desired indole product was isolated in high yield. However, the best results with regard to reaction time and yield were obtained with Cs_2CO_3 and $Pd(PPh_3)_4$ (Table 1, entry 10). The latter conditions proved satisfactory also for the reaction of **1a** with phenyl triflate (Table 1, entry 15) and have been used when the procedure has been extended to include other aryl and heteroaryl bromides

Table 1 Ligands, Bases, and Temperature Dependence of the Reaction of *o*-(Phenylethynyl)trifluoroacetanilide (**1a**) with Phenyl Bromide and Triflate[a]

Entry	X	Base	[Pd]	T (°C)	Time (h)	Yield%[b]		
						3a	**4a**	**5a**
1	Br	K_2CO_3	$Pd_2(dba)_3/PPh_3$	80	8	22	45	30
2	Br	K_2CO_3	$Pd_2(dba)_3/P(Bu^t)_3$	80	5	-	80	-
3	Br	*t*-BuONa	$Pd_2(dba)_3$/Xantphos	80	10	-	80	-
4	Br	K_2CO_3	$Pd_2(dba)_3$/Xantphos	80	20	46	27	-
5	Br	Cs_2CO_3	$Pd_2(dba)_3/PPh_3$	80	4	-	60	18
6	Br	K_2CO_3	$Pd_2(dba)_3$/Xantphos	100	8	84	6	-
7	Br	Cs_2CO_3	$Pd_2(dba)_3$/Xantphos	100	4	88	5	-
8	Br	K_2CO_3	$Pd_2(dba)_3$/Xantphos	100	20	-	72[c]	-
9	Br	K_2CO_3	$Pd(PPh_3)_4$	100	1	79	-	-
10	Br	Cs_2CO_3	$Pd(PPh_3)_4$	100	0.5	93	-	-
11	Br	Cs_2CO_3	$Pd(PPh_3)_4$	80	0.5	60	18	-
12	Br	Cs_2CO_3	$Pd(PPh_3)_4$	60	20	-	63	-
13	OTf	Cs_2CO_3	$Pd_2(dba)_3$/Xantphos	100	5	73	27	-
14	OTf	Cs_2CO_3	$Pd(PPh_3)_4$	80	8	-	80	-
15	OTf	Cs_2CO_3	$Pd(PPh_3)_4$	100	0.25	97	-	-

[a] Reactions were conducted under argon, in MeCN, using 1 equiv of **1a**, 1.5 equiv of PhBr or 1 equiv of PhOTf, 0.05 equiv of [Pd], 0.1 equiv of monodentate ligands or 0.05 equiv of Xantphos, 1.5 equiv of base (5 equiv when K_2CO_3 was used).
[b] Yields are given for isolated products.
[c] In toluene.

(Table 2, entries 1–22), triflates (Table 2, entries 23–31) and *o*-alkynyltrifluoroacetanilides (Table 3).

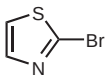
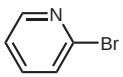
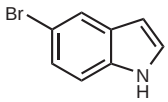
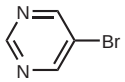
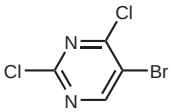
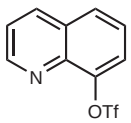
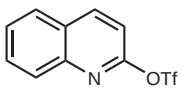
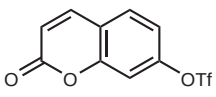
As seen in Table 2, the reaction allows easy access to a wide variety of indole derivatives and tolerates, in the $C_{sp}2$ donor, various functional groups amenable of further functionalization. Aryl bromides and triflates containing aldehyde, ketone, ester, nitro, nitrile functionality all afforded the desired indole product usually in excellent yields. Substituents close to the oxidative addition site do not hamper the reaction (Table 2, entries 4 and 22). As for the alkyne component (Table 3), indole derivatives have been obtained in high yield with alkynes containing both electron-withdrawing and electron-donating substituents.

In conclusion, we have developed an efficient synthesis of various 2-substituted 3-aryl- and 3-heteroarylindoles by the palladium-catalyzed reaction of *o*-alkynyltrifluoroacetanilides with aryl and heteroaryl bromides or triflates. Present results widen significantly the scope of our aminopalladation-reductive elimination domino procedure for the construction of the substituted pyrrole nucleus of the indole system.

Table 2 Synthesis of 2-Substituted 3-Aryl- and 3-Heteroarylindoles from *o*-(Phenylethynyl)trifluoroacetanilide **1a** and Aryl or Heteroaryl Bromides and Triflates **2**[a]

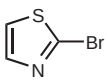
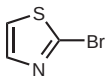
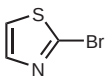
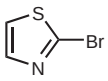
Entry	Aryl or Heteroaryl Bromide and Triflate **2**		Time (h)	Yield %[b] of **3**	
1	**2a**	PhBr	0.5	**3a**	93
2	**2b**	*p*-Me-C_6H_4-Br	1	**3b**	98
3	**2c**	*m*-Me-C_6H_4-Br	1	**3c**	98
4	**2d**	*o*-Me-C_6H_4-Br	1	**3d**	96
5	**2e**	*p*-*t*-BuC_6H_4-Br	0.5	**3e**	91
6	**2f**	3,5-Me_2-C_6H_3-Br	0.5	**3f**	98
7	**2g**	*p*-MeO-C_6H_4-Br	0.25	**3g**	88
8	**2h**	*p*-Ph-C_6H_4-Br	1	**3h**	98
9	**2i**	*m*-MeO-C_6H_4-Br	0.5	**3i**	86
10	**2j**	*m*-F-C_6H_4-Br	0.5	**3j**	98
11	**2k**	*m*-CF_3-C_6H_4-Br	0.5	**3k**	98
12	**2l**	*m*-CN-C_6H_4-Br	0.5	**3l**	99

Table 2 Synthesis of 2-Substituted 3-Aryl- and 3-Heteroarylindoles from *o*-(Phenylethynyl)trifluoroacetanilide **1a** and Aryl or Heteroaryl Bromides and Triflates **2**[a] (continued)

Entry	Aryl or Heteroaryl Bromide and Triflate **2**		Time (h)	Yield %[b] of **3**	
13	**2m**	*p*-CN-C_6H_4-Br	0.5	**3m**	90
14	**2n**	*m*-CHO-C_6H_4-Br	0.5	**3n**	84
15	**2o**	*p*-CHO-C_6H_4-Br	1	**3o**	94
16	**2p**	*p*-MeCO-C_6H_4-Br	0.5	**3p**	98
17	**2q**	*p*-NO_2-C_6H_4-Br	1	**3q**	97
18	**2r**		2	**3r**	70
19	**2s**		2	**3s**	94
20	**2t**		5	**3t**	56
21	**2u**		5	**3u**	85
22	**2v**		5	**3v**	70
23	**2w**	PhOTf	0.5	**3a**	97
24	**2x**	*p*-MeO-C_6H_4-OTf	1	**3g**	98
25	**2y**	3,4,5-$(MeO)_3$-C_6H_2-OTf	1	**3w**	98
26	**2z**	*p*-Ph-C_6H_4-ONf	1	**3h**	89
27	**2za**	*p*-PhCO-C_6H_4-OTf	1	**3x**	99
28	**2zb**	*p*-NO_2-C_6H_4-OTf	1	**3q**	94
29	**2zc**		2	**3y**	35
30	**2zd**		1	**3z**	91
31	**2ze**		1	**3za**	80

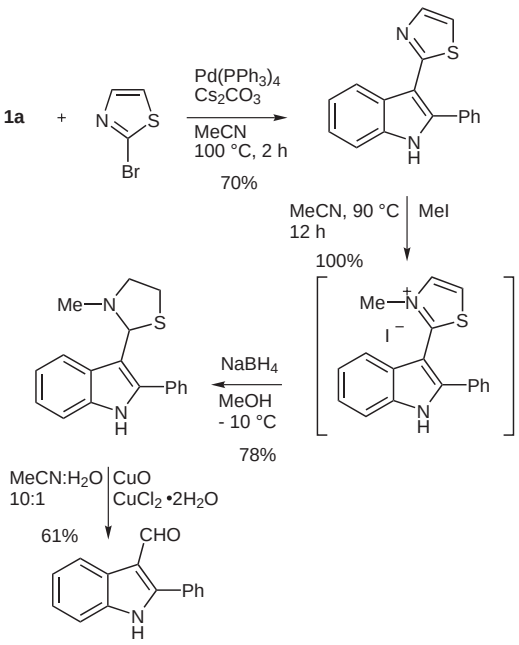
[a] Reactions were conducted at 100 °C under argon, in MeCN, using 1 equiv of **1a**, 1.5 equiv of ArBr or 1 equiv of ArOTf, 0.05 equiv of $Pd(PPh_3)_4$, 1.5 equiv of Cs_2CO_3.
[b] Yields are given for isolated products.

Table 3 The Reaction of *o*-Alkynyltrifluoroacetanilides with Aryl and Heteroaryl Bromides[a]

entry	*o*-Alkynyl Trifluoroacetanilide **1** R		Aryl and Heteroaryl Bromide **2**		Time (h)	Yield%[b] of **3**	
1	**1b**	*p*-MeO-C_6H_4-	**2zf**	*p*-*t*-Bu-C_6H_4-Br	1	**3zb**	87
2	**1b**	*p*-MeO-C_6H_4-	**2zg**		2	**3zc**	80
3	**1c**	*p*-MeCO-C_6H_4-	**2zf**	*p*-*t*-Bu-C_6H_4-Br	1	**3zd**	98
4	**1c**	*p*-MeCO-C_6H_4-	**2zg**		2	**3ze**	74
5	**1d**	*p*-NO_2-C_6H_4-	**2zg**		2	**3zf**	40
6	**1e**	C_5H_{11}	**2zh**	*m*-CN-C_6H_4-Br	0.5	**3zg**	88
7	**1e**	C_5H_{11}	**2zf**		3	**3zh**	75

[a] Reactions were conducted at 100 °C under argon, in MeCN, using 1 equiv of **1**, 1.5 equiv of **2**, 0.05 equiv of $Pd(PPh_3)_4$, 1.5 equiv of Cs_2CO_3.
[b] Yields are given for isolated products.

The positive results obtained in the preparation of 2-substituted 3-thiazolylindoles (Table 2, entry 18; Table 3, entries 2, 4, 5, 7) prompted us to explore briefly the combination of our indole synthesis with the conversion of the thiazolyl group into the formyl group[6] to develop a route to 2-substituted indole-3-carboxaldehydes from *o*-alkynyltrifluoroacetanilides. As an example, 2-phenylindole-3-carboxaldehyde was prepared in 33% overall yield according to the sequence shown in Scheme 2.



Scheme 2

Melting points are uncorrected. Aryl and heteroayl bromides, MeCN, palladium precatalysts, and phosphine ligands are commercially available and were used as purchased, without further purification. Aryl triflates were prepared according to known methods.[7] *o*-Alkynyltrifluoroacetanilides **1a**–**e** were prepared as described in the literature.[4] Reaction products were purified on axially compressed columns, packed with SiO_2 25–40 μm, connected to a solvent delivery system and to a refractive index detector, and eluting with hexane–EtOAc. ^{1}H NMR were recorded at 200 MHz and ^{13}C NMR were recorded at 50.3 MHz).

Preparation of 2-Substituted 3-Aryl- and 3-Heteroarylindoles (3); Typical Procedure

To a 50 mL carousel reaction tube (Radely Discovery Technology) containing a magnetic stir bar was added MeCN (2.0 mL), **1a** (0.100 g, 0.346 mmol), phenyl bromide (0.055 mL, 0.519 mmol), Cs_2CO_3 (0.169 g, 0.519 mmol), and $Pd(Ph_3P)_4$ (0.020 g, 0.0173 mmol). The mixture was stirred for 0.5 h at 100 °C under argon. After this time, the reaction mixture was cooled to r.t., diluted with EtOAc (100 mL), and washed with H_2O (3 × 15 mL). The organic extract was dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by chromatography (silica gel, hexane–EtOAc, 85:15) to give 0.087 g of **3a** (93% yield); mp 120–121 °C.

IR (KBr): 3387, 1454 cm^{-1}.

^{1}H NMR ($CHCl_3$): δ = 7.11–7.58 (m, 13 H), 7.62–7.78 (m, 1 H), 8.25 (s, 1 H).

^{13}C NMR ($CHCl_3$): δ = 111.0, 115.1, 119.8, 120.5, 122.8, 126.3, 127.8, 128.3, 128.6, 128.7, 128.9, 130.3, 132,8, 134.2, 135.2, 136.0.

Anal. Calcd for $C_{20}H_{15}N$: C, 89.19; H, 5.61; N, 5,20. Found: C, 89.10; H, 5.59; N, 5.15.

3b

Mp 123–124 °C.

IR (KBr): 3401, 1446, 1327 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 2.38 (s, 3 H), 7.05–7.46 (m, 12 H), 7.68 (d, *J* = 7.9 Hz, 1 H), 8.19 (s, 1 H).

^{13}C NMR ($CDCl_3$): δ = 21.4, 111.1, 115.1, 119.9, 120.5, 122.8, 127.7, 128.3, 128.8, 129.0, 129.4, 130.1, 132.2, 133.0, 134.0, 135.9, 136.0.

Anal. Calcd for $C_{21}H_{17}N$: C, 89.01; H, 6.05; N, 4.94. found: C, 88.96; H, 6.04; N, 4.93.

3c

Oil.

IR (neat): 3408, 1455, 1328 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 2.32 (s, 3 H), 7.02–7.45 (m, 12 H), 7.66 (d, *J* = 6.8 Hz, 1 H), 8.15 (s, 1 H).

^{13}C NMR ($CDCl_3$): δ = 21.6, 111.0, 115.3, 119.9, 120.5, 122.8, 127.2, 127.4, 127.7, 128.2, 128.5, 128.8, 129.0, 130.9, 132.9, 134.1, 135.1, 136.0, 138.1.

Anal. Calcd for $C_{21}H_{17}N$: C, 89.01; H, 6.05; N, 4.94: found: C, 88.87, H, 6,01; N, 4.89.

3d

Mp 170–171 °C.

IR (KBr): 3400, 1455, 1328 cm^{-1}.

^{1}H NMR (DMSO-d_6): δ = 1.95 (s, 3 H), 6.90–7.58 (m, 13 H), 11.57 (s, 1 H).

^{13}C NMR (DMSO-d_6): δ = 20.3, 111.9, 113.5, 119.3, 120.0, 122.4, 126.6, 129.2, 127.6, 127.7, 129.1, 129.3, 130.8, 131.7, 133.3, 134.2, 135.5, 136.6, 137.5.

Anal. Calcd for $C_{21}H_{17}N$: C, 89.01; H, 6.05; N, 4.94. Found: C, 88.95; H, 6.03; N, 4.93.

3e

Mp 140–141 °C.

IR (KBr): 3400, 2960, 1455 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.34 (s, 9 H), 7.08–7.42 (m, 11 H), 7.69 (d, *J* = 7.5 Hz, 1 H), 8.10 (s, 1 H).

^{13}C NMR ($CDCl_3$): δ = 31.5, 34.6, 110.9, 114.9, 119.9, 120.3, 122.6, 125.4, 127.6, 128.3, 128.6, 128.9, 129.7, 132.0, 132.9, 134.0, 136.0, 149.0.

Anal. Calcd for $C_{24}H_{23}N$: C, 88.57; H, 7.12; N, 4.30. Found: C, 88.51; H, 7.10; N, 4.29.

3f

Oil.

IR (neat): 3407, 2917, 1601, 1328 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 2.28 (s, 6 H), 6.92 (br s, 1 H), 7.05 (br s, 2 H), 7.11–7.42 (m, 8 H), 7.67 (d, *J* = 7.5 Hz, 1 H), 8.05 (s, 1 H).

^{13}C NMR ($CDCl_3$): δ = 21.4, 110.3, 115.2, 119.9, 120.3, 122.6, 127.6, 127.9, 128.0, 128.1, 128.6, 129.0, 132.8, 133.9, 134.9, 135.9, 137.9.

Anal. Calcd for $C_{22}H_{19}N$: C, 88.85; H, 6.44; N, 4.71. Found: C, 88.78; H, 6.41; N, 4.68.

3g

Mp 184–185 °C.

IR (KBr): 3418, 1602, 1510 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 3.78 (s, 3 H), 6.91–7.55 (m, 13 H), 11.49 (s, 1 H).

^{13}C NMR ($CDCl_3$): δ = 55.4, 111.8, 113.5, 114.6, 119.0, 120.0, 122.3, 127.8, 128.4, 128.6, 128.7, 128.9, 131.3, 133.0, 134.0, 136.5, 158.2.

Anal. Calcd for $C_{21}H_{17}NO$: C, 84.25; H, 5.72; N, 4.68. Found: C, 84.20; H, 5.71; N, 4.66.

3h

Mp 155–156 °C.

IR (KBr): 3417, 3056, 769, 743, 692 cm^{-1}.

^{1}H NMR (DMSO-d_6): δ = 7.08–7.77 (m, 18 H), 8.12 (s, 1 H).

^{13}C NMR (DMSO-d_6): δ = 111.0, 114.6, 119.8, 120.6, 122.8, 127.0, 127.18, 127.23, 127.8, 128.3, 128.74, 128.77, 128.84, 130.5, 132.7, 134.2, 134.3, 136.0, 138.8, 141.0.

Anal. Calcd for $C_{26}H_{19}N$: C, 90.40; H, 5.54; N, 4.05. Found: C, 90.37, H, 5.53; N, 4.01.

3i

Mp 122–123 °C.

IR (KBr): 3373, 2998, 2832, 1600 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 3.79 (s, 3 H), 6.88–6.97 (m, 1 H), 7.07–7.72 (m, 2 H), 7.18–7.72 (m, 9 H), 7.80 (dd, J_1 = 7.8 Hz, J_2 = 1.1 Hz, 1 H), 8.29 (br s, 1 H).

^{13}C NMR ($CDCl_3$): δ = 55.2, 111.0, 112.2, 114.9, 115.5, 119.8, 120.5, 122.7, 122.8, 127.8, 128.3, 128.69, 128.71, 129.6, 132.7, 134.3, 135.9, 136.6, 159.7.

Anal. Calcd for $C_{21}H_{17}NO$: C, 84.25; H, 5.72; N, 4.68. Found: C, 84.18; H 5.71; N 4.68.

3j
Mp 148–149 °C.

IR (KBr): 3409, 1605, 1570 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 6.96–7.11 (m, 1 H), 7.11–7.35 (m, 11 H), 7.75 (d, *J* = 7.6 Hz, 1 H), 8.25 (s, 1 H).

^{13}C NMR ($CDCl_3$): δ = 111.0, 113.1 (d, *J* = 21.1 Hz), 113.8 (d, *J* = 2.3 Hz), 116.7 (d, *J* = 21.3 Hz), 119.4, 120.7, 122.9, 125.8 (d, *J* = 2.8 Hz), 128.0, 128.2, 128.4, 128.8, 129.9 (d, *J* = 8.6 Hz), 132.3, 134.6, 135.8, 137.4 (d, *J* = 8.3 Hz), 163.0 (d, *J* = 245.0 Hz).

^{19}F NMR {^1H} ($CDCl_3$): δ = –113.81.

Anal. Calcd for $C_{20}H_{14}FN$: C, 83.60; H, 4.91; N, 4.87. Found: C, 83.54; H, 4.90; N, 4.85.

3k
Mp 70–71 °C.

IR (KBr): 3383, 1456, 1324 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 7.25-7.90 (m, 13 H), 8.27 (s, 1 H).

^{13}C NMR ($CDCl_3$): δ = 111.2, 113.5, 119.2, 120.9, 122.9 (q, *J* = 3.9 Hz), 123.0, 124.3 (q, *J* = 272.5 Hz), 126.7 (q, *J* = 3.9 Hz), 128.2, 128.3, 128.9, 129.0, 130.9 (q, *J* = 31.9 Hz), 132.1, 133.4 (q, *J* = 1.2 Hz), 134.9, 135.9, 136.1.

^{19}F NMR {^1H} ($CDCl_3$): δ = –62.9.

Anal. Calcd for $C_{21}H_{14}F_3N$: C, 74.77; H, 4.18; N, 4.15. Found: C, 74.73; H, 4.17; N, 4.13.

3l
Mp 179–180 °C.

IR (KBr): 3400, 2223, 746, 698 cm^{-1}.

^1H NMR (DMSO-d_6): δ = 7.09 (t, *J* = 7.3 Hz, 1 H), 7.21 (t, *J* = 7.5 Hz, 1 H), 7.27–7.78 (m, 11 H), 11.76 (s, 1 H).

^{13}C NMR (DMSO-d_6): δ = 111.1, 111.7, 111.8, 118.2, 118.9, 120.2, 122.3, 127.4, 128.0, 128.4, 128.7, 129.7, 129.9, 131.9, 132.8, 134.6, 135.2, 136.1, 136.8.

Anal. Calcd for $C_{21}H_{14}N_2$: C, 85.69; H 4.79; N, 9.52. Found: C, 85.60; H, 4.78; N, 9.50.

3m
Mp 212–213 °C.

IR (KBr): 3325, 2227 cm^{-1}.

^1H NMR (DMSO-d_6): δ = 7.09 (t, *J* = 6.4 Hz, 1 H), 7.21 (t, *J* = 7.4 Hz, 1 H), 7.28–7.67 (m, 9 H), 7.80 (d, *J* = 8.2 Hz, 2 H), 11.81 (s, 1 H).

^{13}C NMR (DMSO-d_6): δ = 108.1, 111.5, 111.8, 118.3, 119.1, 120.3, 122.4, 127.1, 128.1, 128.6, 128.8, 130.3, 131.9, 132.5, 135.7, 136.2, 140.7.

Anal. Calcd for $C_{21}H_{14}N_2$ C, 85.69; H, 4.79; N, 9.52. Found: C, 85.61; H, 4.77; N, 9.51.

3n
Mp 203–204 °C.

IR (KBr): 3348, 1676 cm^{-1}.

^1H NMR (DMSO-d_6): δ = 7.08 (t, *J* = 7.4 Hz, 1 H), 7.20 (t, *J* = 7.1 Hz, 1 H), 7.13–7.68 (m, 9 H), 7.78–7.86 (m, 1 H), 7.93 (s, 1 H), 10.01 (s, 1 H), 11.71 (s, 1 H).

^{13}C NMR (DMSO-d_6): δ = 111.7, 111.9, 118.3, 120.0, 122.2, 127.1, 127.7, 127.8, 128.3, 128.7, 129.5, 130.5, 132.1, 134.8, 135.8, 136.2, 136.4, 136.7, 193.2.

Anal. Calcd for $C_{21}H_{15}NO$: C, 84.82; H, 5.08; N, 4.71. Found: C, 84.75; H, 5.07; N, 4.69.

3o
Mp 207–208 °C.

IR (KBr): 3257, 2832, 2744, 1681 cm^{-1}.

^1H NMR (DMSO-d_6): δ = 7.08 (dt, J_1 = 6.7 Hz, J_2 = 0.9 Hz, 1 H), 7.20 (dt, J_1 = 7.2 Hz, J_2 = 1.1 Hz, 1 H), 7.27–7.64 (m, 9 H), 7.88 (d, *J* = 8.2 Hz, 2 H), 9.97 (s, 1 H), 11.78 (s, 1 H).

^{13}C NMR (DMSO-d_6): δ = 112.3, 112.6, 118.9, 120.7, 122.8, 127.8, 128.5, 129.1, 129.2, 130.4, 130.5, 132.5, 134.2, 136.1, 136.8, 142.6, 192.9.

Anal. Calcd for $C_{21}H_{15}NO$: C, 84.82; H, 5.08; N, 4.71. Found: C, 84.77; H, 5.09; N, 4.70.

3p
Mp 203–204 °C.

IR (KBr): 3264, 2923, 1658, 1599 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 2.61 (s, 3 H), 7.00–7.68 (m, 11 H), 7.99 (d, *J* = 8.3 Hz, 2 H), 11.77 (s, 1 H).

^{13}C NMR ($CDCl_3$): δ = 26.6, 111.7, 112.1, 118.5, 120.2, 122.3, 127.4, 128.0, 128.5, 128.6, 128.7, 129.6, 132.2, 134.3, 135.3, 136.3, 140.6, 197.4.

Anal. Calcd for $C_{22}H_{17}NO$: C, 84.86; H, 5.50; N, 4.50. Found: C, 84.61; H, 5.50; N, 4.48.

3q
Mp 228–229 °C.

IR (KBr): 3374, 1591, 1500, 1336 cm^{-1}.

^1H NMR (DMSO-d_6): δ = 7.11 (dt, J_1 = 7.5 Hz, J_2 = 1.1 Hz, 1 H), 7.23 (dt, J_1 = 7.5 Hz, J_2 = 1.2 Hz, 1 H), 7.35–7.68 (m, 9 H), 8.22 (d, *J* = 8.8 Hz, 2 H), 11.88 (s, 1 H).

^{13}C NMR (DMSO-d_6): δ = 111.1, 111.9, 118.3, 120.5, 122.5, 123.9, 127.0, 128.3, 128.7, 128.8, 130.2, 131.7, 136.1, 136.3, 143.0, 145.0.

Anal. Calcd for $C_{20}H_{14}N_2O_2$: C, 76.42; H, 4.49; N, 8.91. Found: C, 76.35; H, 4.48; N, 8.90.

3r
Mp 163–164 °C.

IR (KBr): 3400, 3052, 1499, 1545 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 7.16 (d, *J* = 3.3 Hz, 1 H), 7.20–7.47 (m, 6 H), 7.47–7.58 (m, 2 H), 7.80 (d, *J* = 3.3 Hz, 1 H), 8.22–8.30 (m, 1 H), 8.69 (s, 1 H).

^{13}C NMR ($CDCl_3$): δ = 108.7, 110.9, 117.4, 121.1, 121.5, 123.3, 127.4, 128.8, 129.1, 129.5, 131.9, 135.6, 138.1, 142.5, 162.7.

Anal. Calcd for $C_{17}H_{12}N_2S$: C, 73.88; H, 4.38; N, 10.14. Found: C, 73.81; H, 4.37;N, 10.12.

3s
Mp 198–199 °C.

IR (KBr): 3366, 1594 cm^{-1}.

^1H NMR (DMSO-d_6): δ = 7.02–7.27 (m, 4 H), 7.27–7.58 (m, 6 H), 7.58–7.70 (m, 1 H), 7.91 (d, *J* = 7.8 Hz, 1 H), 8.58–8.71 (m, 1 H), 11.66 (s, 1 H).

^{13}C NMR (DMSO-d_6): δ = 111.4, 112.9, 120.0, 120.2, 120.6, 122.1, 123.9, 127.7, 128.1, 128.6, 128.7, 132.6, 136.0, 136.1, 136.4, 149.4, 155.0.

Anal. Calcd for $C_{19}H_{14}N_2$: C, 84.42; H, 5.22; N, 10.36. Found: C, 84.35; H, 5.21; N, 10.33.

3t
Oil.

IR (neat): 3257, 1735 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 6.55–6.65 (m, 1 H), 7.11–7.57 (m, 11 H), 7.69–7.88 (m, 2 H), 8.16 (s, 1 H), 8.25 (s, 1 H).

^{13}C NMR ($CDCl_3$): δ = 102.9, 110.9, 111.2, 116.3, 120.1, 120.3, 122.2, 122.6, 124.4, 125.1, 126.5, 127.4, 128.1, 128.6, 129.6, 133.2, 133.6, 134.8, 136.0.

Anal. Calcd for $C_{22}H_{16}N_2$: C, 85.69; H, 5.23; N, 9.08. Found: C, 85.61; H, 5.20; N, 9.04.

3u
Mp 224–225 °C.

IR (KBr): 3170, 1554, 1451 cm^{-1}.

^1H NMR (DMSO-d_6): δ = 7.05–7.31 (m, 2 H), 7.31–7.68 (m, 7 H), 8.76 (s, 2 H), 9.10 (s, 1 H), 11.91 (s, 1 H).

^{13}C NMR (DMSO-d_6): δ = 105.9, 112.1, 118.1, 120.5, 122.6, 127.2, 127.3, 128.2, 128.6, 128.9, 129.7, 131.6, 136.1, 136.3, 155.8, 156.9.

Anal. Calcd for $C_{18}H_{13}N_3$: C, 79.68; H, 4.83; N, 15.49. Found: C, 79.62; H, 4.81; N, 15.48.

3v
Mp 218–219 °C.

IR (KBr): 3222, 1538 cm^{-1}.

^1H NMR (DMSO-d_6): δ = 6.93–7.60 (m, 9 H), 8.96 (s, 1 H), 12.12 (s, 1 H).

^{13}C NMR (DMSO-d_6): δ = 108.6, 111.9, 119.4, 119.9, 120.6, 122.8, 127.3, 127.6, 128.7, 129.1, 132.0, 136.1, 138.8, 158.5, 162.5, 165.0.

Anal. Calcd for $C_{18}H_{11}Cl_2N_3$: C, 63.55; H, 3.26; N, 12.35. Found: C, 63.49; H, 3.25; N, 12.33.

3w
Mp 140–141 °C.

IR (KBr): 3357, 2962, 2934, 1375 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 3.77 (s, 6 H), 3.97 (s, 3 H), 6.70 (s, 2 H), 7.15–7.52 (m, 8 H), 7.20–7.87 (m, 1 H), 7.43 (s, 1 H).

^{13}C NMR ($CDCl_3$): δ = 56.0, 61.0, 107.1, 111.0, 119.6, 120.5, 122.7, 127.8, 128.3, 128.6, 130.6, 132.6, 134.1, 135.8, 153.2.

Anal. Calcd for $C_{23}H_{21}NO_3$: C, 76.86; H, 5.89; N, 3.90. Found: C, 76.81; H, 5.87; N, 3.89.

3x
Mp 131–132 °C.

IR (KBr): 3329, 1641, 1598 cm^{-1}.

^1H NMR (DMSO-d_6): δ = 7.04–7.27 (m, 2 H), 7.30–7.83 (m, 16 H), 11.76 (s, 1 H).

^{13}C NMR (DMSO-d_6): δ = 111.7, 112.1, 118.5, 120.2, 122.3, 127.5, 128.0, 128.6, 128.6, 128.7, 129.5, 129.6, 130.3, 132.1, 132.4, 134.1, 135.4, 136.3, 137.4, 140.4, 195.2.

Anal. Calcd for $C_{27}H_{19}NO$: C, 86.84; H, 5.13; N, 3.75. Found: C, 86.78; H, 5.12; N, 3.74.

3y
Mp 271–272 °C.

IR (KBr): 3169, 1600, 1504 cm^{-1}.

^1H NMR (DMSO-d_6): δ = 7.08–7.32 (m, 3 H), 7.35–7.63 (m, 7 H), 7.73 (t, J = 7.5 Hz, 1 H), 7.87 (d, J = 8.1 Hz, 1 H), 8.06 (dd, J_1 = 8.7, J_2 = 8.4 Hz, 2 H), 8.25 (d, J = 7.8 Hz, 1 H), 11.80 (s, 1 H).

^{13}C NMR (DMSO-d_6): δ = 111.5, 113.0, 120.4, 120.9, 122.5, 122.7, 125.7, 125.9, 127.7, 127.9, 128.5, 128.6, 128.8, 129.1, 129.5, 132.6, 135.3, 136.3, 137.9, 148.0, 155.5.

Anal Calcd for $C_{23}H_{16}N_2$: C, 86.22; H, 5.03; N, 8.74. Found: C, 86.15; H, 5.01; N, 8.73.

3z
Mp 232–233 °C.

IR (KBr): 3255, 1736 cm^{-1}.

^1H NMR (DMSO-d_6): δ 6.83–7.01 (m, 2 H), 7.07–7.19 (m, 4 H), 7.19–7.35 (m, 2 H), 7.42–7.55 (m, 2 H), 7.55–7.69 (m, 2 H), 7.93–8.04 (m, 1 H), 8.41 (dd, J_1 = 8.3 Hz, J_2 = 1.7 Hz, 1 H), 8.67 (dd, J_1 = 4.1 Hz, J_2 = 1.8 Hz, 1 H), 11.60 (s, 1 H).

^{13}C NMR (DMSO-d_6): δ = 111.2, 111.9, 119.1, 119.5, 121.3, 121.6, 126.5, 126.9, 127.1, 127.5, 128.3, 128.5, 130.0, 132.0, 132.9, 134.8, 135.0, 136.0, 136.4, 146.9, 149.8.

Anal. Calcd for $C_{23}H_{16}N_2$: C, 86.22; H, 5.03; N, 8.74. Found: C, 86.16; H, 5.02; N, 8.72.

3za
Mp 226–227 °C.

IR (KBr): 3305, 1702, 1610 cm^{-1}.

^1H NMR (DMSO-d_6): δ = 6.44 (d, J = 9.5 Hz, 1 H), 7.02–7.56 (m, 10 H), 7.56–7.73 (m, 2 H), 8.05 (d, J = 9.5 Hz, 1 H), 11.80 (s, 1 H).

^{13}C NMR (DMSO-d_6): δ = 111.6, 111.8, 115.1, 116.4, 116.7, 118.5, 120.3, 122.4, 126.0, 127.3, 128.1, 128.6, 128.7, 128.8, 132.0, 135.7, 136.2, 139.7, 144.2, 153.9, 160.2.

Anal Calcd for $C_{23}H_{15}NO_2$: C, 81.88; H, 4.48; N, 4.15. Found: C, 81.81; H, 4.47; N, 4.13.

3zb
Mp 145–146 °C.

IR (KBr): 3402, 2959, 1456, 1249 cm^{-1}.

^1H NMR (DMSO-d_6): δ = 1.41 (s, 9 H), 3.87 (s, 3 H), 6.87–6.95 (m, 2 H), 7.12–7.35 (m, 3 H), 7.38–7.52 (m, 6 H), 7.75 (d, J = 7.5 Hz, 1 H), 8.19 (s, 1 H).

^{13}C NMR (DMSO-d_6): δ = 31.0, 34.0, 54.8, 110.2, 113.6, 119.2, 119.7, 121.8, 124.9, 128.0, 128.5, 129.0, 129.1, 129.7, 131.6, 133.5, 135.3, 148.3, 158.7.

Anal. Calcd for $C_{25}H_{25}NO$: C, 84.47; H, 7.09; N, 3.94. Found: C, 84.41; H, 7.07; N, 3.93.

3zc
Mp 180–181 °C.

IR (KBr): 3155, 1608, 1453 cm^{-1}.

^1H NMR (DMSO-d_6): δ = 3.29 (s, 3 H), 7.05–7.30 (m, 2 H), 7.11 (d, J = 8.8 Hz, 2 H), 7.38–7.52 (m, 1 H), 7.49 (d, J = 3.4 Hz, 1 H), 7.59 (d, J = 8.8 Hz, 2 H), 7.84 (d, J = 3.4 Hz, 1 H), 8.23 (d, J = 7.8 Hz, 1 H), 11.81 (s, 1 H).

^{13}C NMR (DMSO-d_6): δ = 55.3, 107.0, 111.4, 114.2, 117.5, 120.4, 120.6, 122.4, 123.8, 126.5, 131.1, 135.6, 138.6, 142.1, 160.0, 162.3.

Anal. Calcd for $C_{18}H_{14}N_2OS$: C, 70.56; H, 4.61; N, 9.14. Found: C, 70.51; H, 4.59; N, 9.12.

3zd
Mp 202–203 °C.

IR (KBr): 3330, 2957, 1360 cm^{-1}.

^1H NMR (DMSO-d_6): δ = 1.34 (s, 9 H), 2.59 (s, 3 H), 7.00–7.53 (m, 9 H), 7.63 (d, J = 8.5 Hz, 2 H), 7.94 (d, J = 8.5 Hz, 2 H), 11.72 (s, 1 H).

^{13}C NMR (DMSO-d_6): δ = 26.7, 31.2, 34.3, 111.6, 114.9, 119.1, 119.9, 122.6, 125.5, 127.9, 128.1, 128.4, 129.4, 131.9, 132.5, 135.2, 136.5, 137.1, 148.7, 197.3.

Anal. Calcd for $C_{26}H_{25}NO$: C, 84.98; H, 6.86; N, 3.81. Found: C, 84.91; H, 6.85; N, 3.80.

3ze
Mp 207–208 °C.

IR (KBr): 3089, 1678 cm^{-1}.

^{1}H NMR (DMSO-d_6): δ = 2.66 (s, 3 H), 7.15–7.35 (m, 2 H), 7.52 (d, *J* = 7.3 Hz, 1 H), 7.63 (d, *J* = 3.3 Hz, 1 H), 7.82 (d, *J* = 8.3 Hz, 2 H), 7.89 (d, *J* = 3.3 Hz, 1 H), 8.05–8.20 (m, 3 H), 12.07 (s, 1 H).

^{13}C NMR (DMSO-d_6): δ = 26.8, 107.9, 111.8, 118.5, 120.3, 120.9, 123.1, 126.7, 128.4, 129.7, 136.0, 136.2, 136.6, 136.8, 142.5, 161.5, 197.5.

Anal. Calcd for $C_{19}H_{14}N_2OS$: C, 71.67; H, 4.43; N, 8.80. Found: C, 71.61; H, 4.42; N, 8.77.

3zf
Mp 240–241 °C.

IR (KBr): 3351, 1509, 1597 cm^{-1}.

^{1}H NMR (DMSO-d_6): δ = 11.1 (s, 1 H), 8.34–8.30 (m, 2 H), 7.77 (d, *J* = 3.1 Hz, 1 H), 7.64–7.60 (m, 2 H), 7.59–7.55 (m, 2 H), 7.34–7.30 (m, 2 H), 7.22–7.17 (m, 1 H).

^{13}C NMR (DMSO-d_6): δ = 163.9, 148.2, 147.6, 146.1, 142.2, 135.2, 126.5, 124.3, 121.4, 121.3, 121.0, 120.4, 110.4, 102.5.

Anal. Calcd for $C_{17}H_{11}N_3O_2S$: C, 63.54; H, 3.45; N, 13.08. Found: C, 63.49; H, 3.43; N, 13.01.

3zg
Mp 124–125 °C.

IR (KBr): 3157, 2948, 2854, 2237, 1460, 1320 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 0.82–0.96 (m, 3 H), 1.24–1.47 (m, 4 H), 1.63–1.79 (m, 2 H), 2.84 (t, *J* = 8.3 Hz, 2 H), 7.09–7.33 (m, 2 H), 7.33–7.53 (m, 1 H), 7.53–7.72 (m, 3 H), 7.72–7.80 (m, 2 H), 8.24 (s, 1 H). ^{13}C NMR ($CDCl_3$): δ = 14.0, 22.4, 26.3, 29.5, 31.5, 110.8, 112.3, 112.6, 118.2, 119.3, 120.4, 122.0, 127.3, 129.4, 132.8, 134.0, 135.2, 136.0, 137.1.

Anal. Calcd for $C_{20}H_{20}N_2$: C, 83.30; H, 6.99; N, 9.71. Found: C, 83.25, H, 6.98; N, 9.69.

3zh
Mp 86–87 °C.

IR (KBr): 3147, 2950, 2849, 1377 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 0.88–0.93 (m, 3 H), 1.28–1.41 (m, 4 H), 1.64–1.77 (m, 2 H), 3.12 (t, *J* = 7.6 Hz, 2 H), 7.20–7.37 (m, 4 H), 7.95 (d, *J* = 3.4 Hz, 1 H), 8.23 (d, *J* = 7.8 Hz, 1 H), 8.86 (s, 1 H).

^{13}C NMR ($CDCl_3$): δ = 14.0, 22.4, 27.5, 28.8, 31.6, 107.6, 110.8, 116.0, 119.9, 121.1, 122.2, 126.5, 135.0, 141.0, 142.1, 163.4.

Anal. Calcd for $C_{16}H_{18}N_2S$: C, 71.07; H, 6.71; N, 10.36. Found: C, 70.99; H, 6.70, N, 10.33.

2-Phenylindole-3-carboxaldehyde
Mp 248–250 °C (Lit.[8] 249–253 °C)

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