Synthesis of 1-Substituted 2-(Trifluoromethyl)indoles via a Palladium-Catalyzed Double Amination Reaction

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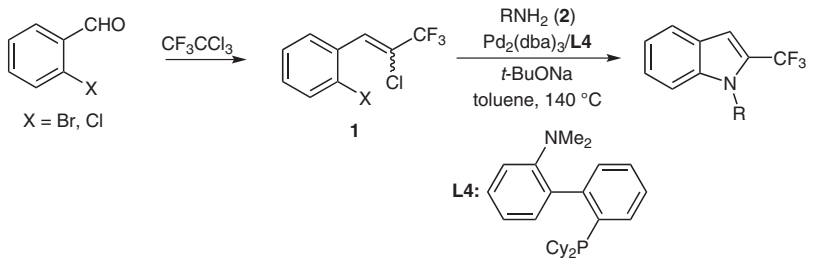
Abstract: A new, selective protocol for the synthesis of 1-substituted 2-(trifluoromethyl)indoles has been developed by palladium-catalyzed double amination reaction of 2-chloro-1-(2-halophenyl)-3,3,3-trifluoroprop-1-enes with primary amines. This route allows the formation of two C–N bonds in one pot from the reaction between 2-chloro-1-(2-halophenyl)-3,3,3-trifluoroprop-1-enes and primary amines using the $Pd_2(dba)_3$/**L4**/*t*-BuONa system.

Key words: palladium, double amination, 2-chloro-1-(2-halophenyl)-3,3,3-trifluoroprop-1-enes, 2-(trifluoromethyl)indoles

A fluorine atom or a fluoroalkyl group presented in an organic molecule produces profound changes in its chemical, physical, and pharmacological properties.[1] Particularly, incorporation of a trifluoromethyl group into lead molecules has been employed as one of the most efficient methods in drug discovery[2] because the resultant products can both retain their original biological activity and have improved pharmacokinetic properties, owing to the unique chemical and physiological stability of the trifluoromethyl group.[3,4] For example, 2-(trifluoromethyl)indoles have been widely employed as core structures for developing pharmaceuticals, such as a general anesthesia inducer,[5] a tyrosine kinase inhibitor,[6] and antitumor compounds.[7] Several methods for the assembly of 2-(trifluoromethyl)indoles have been developed including transition-metal-catalyzed coupling,[8] thermolysis,[9] and Grignard cyclization reactions.[10] Among them, the transition-metal-catalyzed coupling reaction is particularly efficient for this purpose, However, a restriction of these procedures is the use of expensive and unavailable 2-haloanilines as starting materials,[8] Therefore, the development of a direct and concise method for the synthesis of 2-(trifluoromethyl)indoles using inexpensive and readily available materials remains a challenging area for exploration. Recently, the double amination reaction of 1,4-dihalides has been identified as one of the most direct and efficient methods for the synthesis of indoles or pyrroles.[11] To the best of our knowledge, the synthesis of indoles bearing a strong electron-withdrawing substituent at the 2-position by the double amination process has not been reported. 1-Aryl-2-chloro-3,3,3-trifluoroprop-1-enes, which can be readily prepared from the reaction of 2-halobenzaldehyde and Freon-113a in one step (Scheme 1),[12] are versatile trifluoromethyl-containing building blocks.[13] We envisioned that these compounds could participate in a similar double amination reaction. Herein, we report a simple and efficient protocol for the selective synthesis of 1-substituted 2-(trifluoromethyl)indoles via palladium-catalyzed double amination reaction of 2-chloro-1-(2-halophenyl)-3,3,3-trifluoroprop-1-enes with primary amines (Scheme 1).

The reaction between 2-chloro-1-(2-bromophenyl)-3,3,3-trifluoroprop-1-ene (**1a**) and aniline (**2a**) was initially screened to optimize the reaction conditions (Table 1).[14] The results demonstrated that the reaction temperature has a fundamental influence on this tandem reaction (entries 1–4). While treatment of substrate **1a** with aniline **2a** afforded a trace amount of the target product **3** in the presence of $Pd_2(dba)_3$, tricyclohexylphosphine (**L1**) and sodium *tert*-butoxide at 80 °C (entry 1), the yield of **3** increased to 64% yield at 140 °C (entry 4). Prompted by these results, the effect of ligands was subsequently exam-



Scheme 1 Preparation and double amination of 2-chloro-1-(2-halophenyl)-3,3,3-trifluoroprop-1-enes **1**

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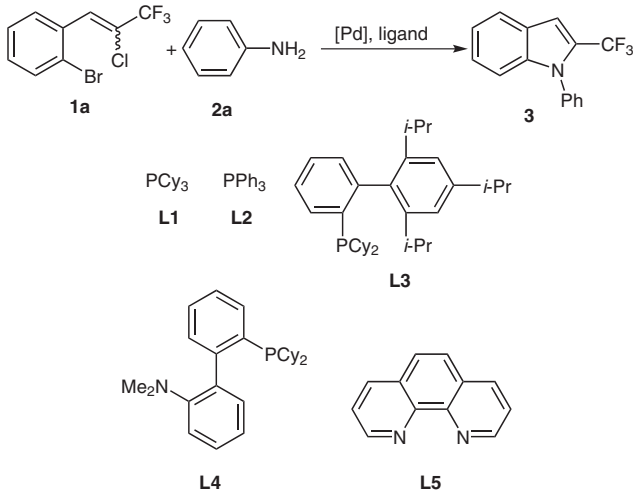
Table 1 Screening Optimal Conditions[a]

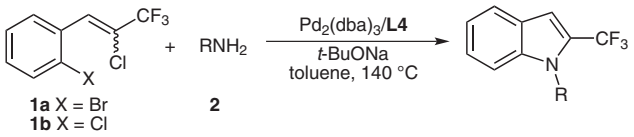


Entry	[Pd]	Ligand	Base	Solvent	Temp (°C)	Yield[b] (%)
1	$Pd_2(dba)_3$	**L1**	*t*-BuONa	toluene	80	trace
2	$Pd_2(dba)_3$	**L1**	*t*-BuONa	toluene	100	33
3	$Pd_2(dba)_3$	**L1**	*t*-BuONa	toluene	120	45
4	$Pd_2(dba)_3$	**L1**	*t*-BuONa	toluene	140	64
5	$Pd_2(dba)_3$	**L2**	*t*-BuONa	toluene	140	<5
6	$Pd_2(dba)_3$	**L3**	*t*-BuONa	toluene	140	76
7	$Pd_2(dba)_3$	**L4**	*t*-BuONa	toluene	140	82
8	$Pd_2(dba)_3$	**L5**	*t*-BuONa	toluene	140	36
9	$Pd_2(dba)_3$	**L4**	Cs_2CO_3	toluene	140	42
10	$Pd_2(dba)_3$	**L4**	K_3PO_4	toluene	140	28
11	$Pd_2(dba)_3$	**L4**	*t*-BuONa	DMF	140	62
12	$Pd_2(dba)_3$	**L4**	*t*-BuONa	DMSO	140	57
13	$Pd(OAc)_2$	**L4**	*t*-BuONa	toluene	140	64
14	$Pd(PPh_3)_4$	**L4**	*t*-BuONa	toluene	140	52
15[c]	$Pd_2(dba)_3$	**L4**	*t*-BuONa	toluene	140	54
16[d]	$Pd_2(dba)_3$	**L4**	*t*-BuONa	toluene	140	80

[a] Reaction conditions: **1a** (0.2 mmol), **2a** (1.2 equiv), [Pd] (5 mol%), ligand (10 mol%), base (4.0 equiv), solvent (2.5 mL), 12 h.
[b] Isolated yield.
[c] $Pd_2(dba)_3$ (2 mol%) and **L4** (4 mol%).
[d] $Pd_2(dba)_3$ (10 mol%) and **L4** (20 mol%).

ined (entries 4–8). We were pleased to observe that ligand **L4** was the most efficient for the reaction, affording the desired product **3** in 82% yield (entry 7). Examining the bases and solvents (entries 9–12), it turned out that sodium *tert*-butoxide combined with toluene was the most effective (entry 7). Two other palladium catalysts, $Pd(OAc)_2$ and $Pd(PPh_3)_4$, were also examined, and they were less efficient than $Pd_2(dba)_3$ (entries 13 and 14). Finally, the amount of the catalytic system was evaluated (entries 15 and 16). The results showed that identical results were observed in the presence of 10 mol% $Pd_2(dba)_3$ and 20 mol% of **L4** (entry 16), but the yield decreased using 2 mol% $Pd_2(dba)_3$ combined with 4 mol% of **L4** (entry 15). It is noteworthy that the yield of indole **3** did not depend on the *Z*/*E* ratio of **1a**; the same yield was observed when using either the mixtures of **1a** (*Z*/*E* 82:18)[12b] or **1a** (*Z*/*E* 96:4).[12c]

Table 2 Palladium-Catalyzed Double Amination Reactions[a]



Entry	Substrate **1**	RNH_2		Time (h)	Product	Yield[b] (%)
		2	R			
1	**1a**	**2b**	1-naphthyl	16	**4**	67
2	**1a**	**2c**	4-Tol	18	**5**	94
3[c]	**1a**	**2c**	4-Tol	26	**5**	96
4	**1a**	**2d**	2-Tol	12	**6**	76
5	**1a**	**2e**	2,6-$Me_2C_6H_3$	6	**7**	62
6	**1a**	**2f**	4-$MeOC_6H_4$	10	**8**	84
7	**1a**	**2g**	4-FC_6H_4	14	**9**	87
8	**1a**	**2h**	4-ClC_6H_4	32	**10**	64
9	**1a**	**2i**	4-$O_2NC_6H_4$	36	**11**	41
10	**1a**	**2j**	4-$F_3CC_6H_4$	16	**12**	68
11	**1a**	**2k**	4-pyridyl	24	**13**	24
12	**1a**	**2l**	CH_2CH_2Ph	10	**14**	44
13	**1a**	**2m**	Bu	26	**15**	36
14	**1a**	**2n**	Bz	48	trace	trace
15	**1b**	**2a**	Ph	18	**3**	83
16	**1b**	**2b**	1-naphthyl	36	**4**	71
17	**1b**	**2c**	4-Tol	16	**5**	76
18	**1b**	**2d**	2-Tol	18	**6**	72
19	**1b**	**2g**	4-FC_6H_4	12	**9**	87
20	**1b**	**2j**	4-$F_3CC_6H_4$	24	**12**	57
21	**1b**	**2m**	Bu	14	**15**	32

[a] Reaction conditions: **1** (0.2 mmol), **2** (1.2 equiv), $Pd_2(dba)_3$ (5 mol%), **L4** (10 mol%), *t*-BuONa (4.0 equiv), toluene (2.5 mL), 140 °C.
[b] Isolated yield.
[c] 1 mmol of **1a** was used.

With the optimal conditions in hand, we explored the scope of the double amination reactions (Table 2). Initially, the reactions of substrate **1a** with various primary amines were investigated (entries 1–13). The results demonstrated that the reaction conditions were compatible with a wide range of primary arylamines (entries 1–10), but less efficiency was displayed for heteroaryl amines and aliphatic amines (entries 11–13). Moreover, several functional groups, such as methyl, methoxy, fluoro, chloro, nitro, and trifluoromethyl groups, on the aryl moiety were tolerated, and the properties of the functional groups affected the reaction to some extent. Amine **2c** bearing a 4-methylphenyl group, for instance, successfully underwent the reaction with substrate **1a**, $Pd_2(dba)_3$, **L4**, and sodium *tert*-butoxide to give **5** in 94% yield (entry 2), but bulky amines **2d** and **2e** provided the corresponding products **6** and **7** in moderate yields under the same conditions (entries 4 and 5). Arylamines **2i**, bearing a strong electron-withdrawing nitro group, also reduced the yield of **11** to 41% (entry 9). We found that low yields of **14** and **15** were obtained from the reaction between substrate **1a** with aliphatic amines **2l** or **2m**, respectively, under the standard conditions, partly because of electronic effect (entries 12 and 13). Unfortunately, attempted amination of substrate **1a** with amide **2n** failed (entry 14). Subsequently, another 1,4-dichloride, 2-chloro-1-(2-chlorophenyl)-3,3,3-trifluoroprop-1-ene (**1b**), was examined in this reaction under optimized conditions (entries 15–21). It was found that moderate to good yields were achieved from the reactions of substrate **1b** with arylamines **2b–d**, **1g**, and **2j** (entries 15–20). However, **15** was isolated in only 32% yield from the reaction between **1b** and butylamine (**2m**) (entry 21).

In summary, we have developed a new, practical protocol for the preparation of 1-substituted 2-(trifluoromethyl)indoles by a $Pd_2(dba)_3$-catalyzed double amination reaction. In the presence of $Pd_2(dba)_3$, **L4**, and sodium *tert*-butoxide, 2-chloro-1-(2-halophenyl)-3,3,3-trifluoroprop-1-enes smoothly underwent the double amination reaction with a wide range of primary amines to afford the desired 2-(trifluoromethyl)indoles in moderate to good yields. Importantly, this new route allows the use of the less active 1,4-dichloride as the starting substrate. Work to extend the reaction in organic synthesis is currently underway.

Chemicals were either purchased or purified by standard techniques. ^{1}H NMR and ^{13}C NMR were determined in $CDCl_3$ soln with a Bruker Avance 300 (300 MHz) spectrometer using TMS as the internal standard. ^{19}F NMR spectra also were obtained in a $CDCl_3$ soln on a Bruker Avance 300 (282.2 MHz) spectrometer using TFA as external standard. All reactions under an N_2 atmosphere were conducted using standard Schlenk techniques. Column chromatography was performed using EM silica gel 60 (300–400 mesh). Melting points are uncorrected.

2-Chloro-3,3,3-trifluoro-1-(2-halophenyl)prop-1-enes 1a,b[12b]

A mixture of 2-chlorobenzaldehyde or 2-bromobenzaldehyde (1 mmol), CCl_3CF_3 (2 mmol), Zn powder (5 mmol), and Ac_2O (1.5 mmol) in DMF (2 mL) was stirred at 50 °C for 7 h until complete consumption of the starting material (TLC). 5% HCl (10 mL) was then added and the mixture was extracted with Et_2O (3 × 10 mL). The combined organic layers were washed with sat. Na_2CO_3 soln and brine, dried (Na_2SO_4), and evaporated under vacuum. The residue was purified by flash column chromatography (hexane–EtOAc) to afford **1a** (67%, *Z*/*E* 82:18) or **1b** (72%, *Z*/*E* 83:17).

Palladium-Catalyzed Double Amination Reaction; General Procedure

A mixture of 1-(2-bromophenyl)-2-chloro-3,3,3-trifluoroprop-1-ene (**1a**, 57 mg, 0.2 mmol) or 2-chloro-1-(2-chlorophenyl)-3,3,3-trifluoroprop-1-ene (**1b**, 48 mg, 0.2 mmol), aniline **2** (0.24 mmol), $Pd_2(dba)_3$ (8.1 mg, 0.01 mmol), **L4** (7.9 mg, 0.02 mmol), and *t*-BuONa (7.7 mg, 0.8 mmol) in toluene (2.5 mL) was stirred at 140 °C for 6–36 h until complete consumption of the starting material (TLC and GC-MS analysis). The mixture was poured into Et_2O and this was washed with brine. The aqueous layer was extracted with Et_2O and the combined organic layers were dried (anhyd Na_2SO_4) and evaporated under vacuum. The residue was purified by flash column chromatography (hexane–EtOAc) to afford **3–15**.

1-Phenyl-2-(trifluoromethyl)-1*H*-indole (3)

Pale solid; mp 52.9–53.8 °C.

IR (KBr): 1498, 1267, 1193, 1163, 1115 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.76 (d, *J* = 7.4 Hz, 1 H), 7.57–7.55 (m, 3 H), 7.46–7.44 (m, 2 H), 7.31–7.25 (m, 2 H), 7.14–7.10 (m, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 139.8, 136.7, 129.0, 128.5, 127.9, 125.5, 124.8, 122.4 (q, J_{C-F} = 266.8 Hz), 122.0, 121.3, 112.2, 105.7, 105.6.

^{19}F NMR (283 MHz): δ = –57.45.

LRMS (EI, 70 eV): *m*/*z* (%) = 261 (M^+, 100), 240 (16), 222 (17), 77 (13), 51 (16).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{15}H_{11}F_3N$: 261.0760; found: 261.0763.

1-(Naphthalen-1-yl)-2-(trifluoromethyl)-1*H*-indole (4)

Yellow oil.

IR (KBr): 1271, 1202, 1163, 1120, 773 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.97 (m, 1 H), 7.94 (m, 1 H), 7.78 (d, *J* = 7.2 Hz, 1 H), 7.60–7.58 (m, 2 H), 7.50 (m, 1 H), 7.23 (m, 1 H), 7.23–7.20 (m, 3 H), 7.03 (m, 1 H), 6.76 (m, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 140.4, 134.2, 133.0, 129.9, 127.4, 127.3, 126.7, 126.6 (q, J_{C-F} = 253.5 Hz), 125.3, 125.2, 122.9, 122.8, 122.0, 111.5, 105.7, 105.6, 105.5.

^{19}F NMR (283 MHz): δ = –58.64.

LRMS (EI, 70 eV): *m*/*z* (%) = 311 (M^+, 20), 242 (12), 120 (38), 77 (9), 51 (3).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{19}H_{12}F_3N$: 311.0916; found: 311.0917.

1-(4-Tolyl)-2-(trifluoromethyl)-1*H*-indole (5)

A mixture of 1-(2-bromophenyl)-2-chloro-3,3,3-trifluoroprop-1-ene (**1a**, 284 mg, 1 mmol), 4-methylaniline (**2c**, 128 mg, 1.2 mmol), $Pd_2(dba)_3$ (46 mg, 0.05 mmol), **L4** (39.4 mg, 0.1 mol), and *t*-BuONa (384 mg, 4 mmol) in toluene (10 mL) was stirred at 140 °C for 26 h until complete consumption of the starting material (TLC and GC-MS analysis). The mixture was poured into Et_2O and this was washed with brine. The aqueous layer was extracted with Et_2O and the combined organic layers were dried (anhyd Na_2SO_4) and evaporated under vacuum. The residue was purified by flash column chromatography (hexane–EtOAc) to afford **5** (96% yield) as a pale yellow oil.

IR (KBr): 1268, 1193, 1162, 1121, 1098 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.74 (d, *J* = 7.3 Hz, 1 H), 7.36–7.26 (m, 3 H), 7.25–7.10 (m, 3 H), 7.07 (m, 2 H), 2.48 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 139.9, 138.9, 134.0, 129.9, 128.4, 128.2, 125.4, 124.7, 124.6 (q, J_{C-F} = 266.3 Hz), 121.9, 121.1, 111.2, 105.4, 21.2.

^{19}F NMR (283 MHz): δ = –57.58.

LRMS (EI, 70 eV): *m*/*z* (%) = 275 (M^+, 17), 240 (3), 206 (3), 165 (5), 91 (8), 65 (12).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{16}H_{12}F_3N$: 275.0916; found: 275.0919.

1-(2-Tolyl)-2-(trifluoromethyl)-1*H*-indole (6)
Yellow oil.

IR (KBr): 1266, 1190, 1163, 1120 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.73 (d, *J* = 7.1 Hz, 1 H), 7.41–7.20 (m, 6 H), 7.10 (s, 1 H), 6.85 (d, *J* = 8.2 Hz, 1 H), 1.89 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 139.2, 137.7, 135.3, 130.9, 128.0, 127.5, 125.4, 124.9, 124.4 (q, J_{C-F} = 266.9 Hz), 122.1, 121.1, 111.0, 105.2, 16.9.

^{19}F NMR (283 MHz): δ = –59.01.

LRMS (EI, 70 eV): *m*/*z* (%) = 275 (M^+, 12), 206 (16), 204 (16), 102 (14), 65 (16).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{16}H_{12}F_3N$: 275.0916; found: 275.0919.

1-(2,6-Dimethylphenyl)-2-(trifluoromethyl)-1*H*-indole (7)
Yellow oil.

IR (KBr): 1201, 1162, 1119, 1120, 798 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.76–7.73 (m, 1 H), 7.32–7.18 (m, 5 H), 7.13 (s, 1 H), 6.82 (d, *J* = 8.0 Hz, 1 H), 1.88 (s, 6 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 138.2, 138.1, 134.3, 129.2, 128.3, 127.5, 127.0, 125.5, 124.9, 124.3 (q, J_{C-F} = 249.0 Hz), 122.1, 110.6, 105.2, 17.0.

^{19}F NMR (283 MHz): δ = –60.62.

LRMS (EI, 70 eV): *m*/*z* (%) = 289 (M^+, 16), 220 (18), 204 (28), 102 (13), 77 (5).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{17}H_{14}F_3N$: 289.1073; found: 289.1077.

1-(4-Methoxyphenyl)-2-(trifluoromethyl)-1*H*-indole (8)
Yellow solid; mp 99.3–102.9 °C.

IR (KBr): 1271, 1202, 1162, 1119, 798 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.75 (d, *J* = 7.8 Hz, 1 H), 7.37–7.27 (m, 2 H), 7.27–7.21 (m, 2 H), 7.11–7.04 (m, 4 H), 3.92 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.8, 140.1, 129.6, 128.5, 128.0, 125.3, 124.7, 124.3 (q, J_{C-F} = 266.7 Hz), 121.9, 121.1, 114.4, 111.2, 105.3, 55.5.

^{19}F NMR (283 MHz): δ = –57.71.

LRMS (EI, 70 eV): *m*/*z* (%) = 291 (M^+, 18), 276 (7), 222 (2), 178 (6).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{16}H_{12}F_3NO$: 291.0866; found: 291.0868.

1-(4-Fluorophenyl)-2-(trifluoromethyl)-1*H*-indole (9)
Yellow oil.

IR (KBr): 1512, 1269, 1194, 1165, 1120 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.75 (d, *J* = 7.6 Hz, 1 H), 7.74–7.39 (m, 2 H), 7.32–7.21 (m, 4 H), 7.13 (s, 1 H), 7.1 (m, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 162.6 (d, J_{C-F} = 247.5 Hz), 139.9, 132.5, 130.4, 125.4, 125.0, 124.8 (q, J_{C-F} = 266.9 Hz), 122.0, 121.4, 116.5, 116.2, 111.0, 105.8.

^{19}F NMR (283 MHz): δ = –57.58 (3 F), –111.73 (1 F).

LRMS (EI, 70 eV): *m*/*z* (%) = 279 (M^+, 17), 258 (12), 240 (3), 183 (4), 139 (5), 75 (12).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{15}H_9F_4N$: 279.0666; found: 279.0667.

1-(4-Chlorophenyl)-2-(trifluoromethyl)-1*H*-indole (10)
Yellow oil.

IR (KBr): 2159, 1269, 1194, 1165, 1122 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.74 (m, 1 H), 7.53–7.47 (m, 3 H), 7.33–7.14 (m, 3 H), 7.12 (m, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 139.6, 137.8, 135.0, 130.3, 129.3, 128.2, 126.9 (q, J_{C-F} = 268.6 Hz), 126.8, 125.5, 122.7, 122.1, 110.9, 106.2.

^{19}F NMR (283 MHz): δ = –57.38.

LRMS (EI, 70 eV): *m*/*z* (%) = 295 (M^+, 17), 240 (10), 191 (3), 120 (1), 75 (16).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{15}H_9ClF_3N$: 295.0370; found: 295.0370.

1-(4-Nitrophenyl)-2-(trifluoromethyl)-1*H*-indole (11)
Yellow oil.

IR (KBr): 1271, 1201, 1162, 1119, 772 cm^{-1}.

^{1}H NMR (300 MHz,$CDCl_3$): δ = 8.43 (d, *J* = 8.8 Hz, 2 H), 7.75 (m, 1 H), 7.64 (d, *J* = 8.8 Hz, 2 H), 7.34–7.19 (m, 2 H), 7.19 (s, 1 H), 7.10 (m, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 147.7, 142.4, 139.2, 129.2, 125.8, 125.6, 124.9, 124.2 (q, J_{C-F} = 253.1 Hz), 122.4, 122.1, 110.6, 107.5, 107.4.

^{19}F NMR (283 MHz): δ = –56.98.

LRMS (EI, 70 eV): *m*/*z* (%) = 306 (M^+, 16), 276 (4), 240 (4), 191 (10), 120 (8), 50 (9).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{15}H_9F_3N_2O_2$: 306.0611; found: 306.0615.

2-(Trifluoromethyl)-1-[4-(trifluoromethyl)phenyl]-1*H*-indole (12)
Yellow oil.

IR (KBr): 1271, 1202, 1163, 1120, 773 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.84 (d, *J* = 8.2 Hz, 2 H), 7.76 (d, *J* = 7.4 Hz, 1 H), 7.58 (d, *J* = 8.2 Hz, 2 H), 7.33–7.27 (m, 2 H), 7.17 (s, 1 H), 7.09 (d, *J* = 8.2 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 140.0, 139.6, 130.1, 127.7, 127.1 (q, J_{C-F} = 269.3 Hz), 126.7, 125.7, 125.5, 124.7 (q, J_{C-F} = 277.4 Hz), 122.3, 121.9, 115.7, 110.9, 106.7.

^{19}F NMR (283 MHz): δ = –57.24, –62.58.

LRMS (EI, 70 eV): *m*/*z* (%) = 329 (M^+, 19), 260 (2), 240 (7), 191 (1), 95 (4).

HRMS(EI): *m*/*z* $[M]^+$ calcd for $C_{16}H_9F_6N$: 329.0634; found: 329.0638.

1-(Pyridin-4-yl)-2-(trifluoromethyl)-1*H*-indole (13)
Yellow oil.

IR (KBr): 2159, 2028, 1979, 1163, 1122 cm^{-1}.

^{1}H NMR (300 MHz,$CDCl_3$): δ = 8.83 (d, *J* = 5.8 Hz, 2 H), 7.75 (d, *J* = 7.8 Hz, 1 H), 7.42 (d, *J* = 5.8 Hz, 2 H), 7.36–7.24 (m, 2 H), 7.18–7.15 (m, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 151.4, 150.1, 144.6, 138.7, 127.8, 125.6, 124.3 (q, J_{C-F} = 267.0 Hz), 122.7, 122.4, 122.0, 110.7, 107.6.

^{19}F NMR (283 MHz): δ = –56.89.

LRMS (EI, 70 eV): *m*/*z* (%) = 262 (M^+, 16), 241 (10), 193 (2), 165 (7), 78 (12), 51 (33).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{14}H_9F_3N_2$: 262.0712; found: 262.0713.

1-Phenethyl-2-(trifluoromethyl)-1*H*-indole (14)
Yellow oil.

IR (KBr): 1267, 1193, 1162, 1118, 1096 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.55–7.18 (m, 8 H), 6.66–6.61 (m, 2 H), 3.49–3.41 (m, 2 H), 2.95 (t, *J* = 6.8 Hz, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 150.0, 138.5, 133.3, 130.4, 128.8, 126.7, 125.1 (q, J_{C-F} = 279.2 Hz), 122.4, 116.7, 116.4, 113.3, 110.1, 102.1, 44.4, 36.3.

^{19}F NMR (283 MHz): δ = –58.4.

LRMS (EI, 70 eV): *m*/*z* (%) = 289 (M^+, 22), 198 (100), 178 (34), 128 (20), 91 (12).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{17}H_{14}F_3N$: 289.1073; found: 289.1075.

1-Butyl-2-(trifluoromethyl)-1*H*-indole (15)
Yellow oil.

IR (KBr): 1266, 1190, 1164, 1121, 752 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.65 (d, *J* = 8.0 Hz, 1 H), 7.38–7.29 (m, 2 H), 7.18–7.13 (m, 1 H), 6.90 (s, 1 H), 4.22–4.16 (m, 2 H), 1.84–1.74 (m, 2 H), 1.44–1.36 (m, 2 H), 0.95 (t, *J* = 7.3 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 137.8, 127.0, 125.8, 124.9 (q, J_{C-F} = 266.5 Hz), 124.2, 122.3, 120.6, 110.3, 104.4, 44.7, 32.0, 20.2, 13.7.

^{19}F NMR (283 MHz): δ = –56.82.

LRMS (EI, 70 eV): *m*/*z* (%) = 241 (M^+, 7), 198 (24), 172 (24), 128 (24), 77 (4), 57 (3).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{13}H_{14}F_3N$: 241.1073; found: 241.1075.

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