A Facile Regiocontrol in the Palladium-Catalyzed Annulation of Fluorine-Containing Internal Alkynes with Variously Substituted 2-Iodoanilines: A New Regioselective Synthesis of 2- or 3-Fluoroalkylated Indole Derivatives

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Treatment of various types of fluoroalkylated alkynes with *o*-iodoaniline in the presence of Pd(PPh_3)$_4$ in DMF at 80 °C for 8 h mainly gave 2-fluoroalkylated indoles in high yields. The use of P(*o*-Tol)$_3$ instead of PPh_3 as a ligand led to the preferential formation of 3-fluoroalkylated indoles in high yields. Interestingly, the reaction of trifluoromethylated alkynes bearing a benzylic substituent afforded 2- or 3-trifluoroethylated indole derivatives in good yields.

Introduction

The indole ring system is present in drug candidates having interesting biological activity and in numerous natural alkaloids that cover a wide range of structural types.[1] Consequently, much effort has been devoted to developing a new methodology for the construction of indole compounds.[2] In the field of medicinal chemistry, on the other hand, introduction of a fluoroalkyl group into lead molecules has been employed as one of the most efficient methods for modification of the lead compounds in view of the biological activity.[3] It is not surprising, therefore, that fluoroalkylated indole derivatives have attracted the attention of many synthetic chemists thus far. There have been several synthetic methods for the fluoroalkylated indole derivatives. For example, fluoroalkylated indoles are prepared by direct fluoroalkylation of indoles with perfluoroalkanoyl peroxides[4] or perfluoroalkyl halides.[5] However, the direct fluoroalkylation very often suffers from poor yields of the desired fluoroalkylindoles. Although the thermolysis of 2-(*N*-trifluoroacetylamino)benzylphosphonium salts[6] or the intramolecular cyclization of *N*-trifluoroacetyl-*p*-benzoquinone[7] gives the corresponding indoles in good yields, multistep preparations are required for the starting substrates. Such drawbacks actually make these methods less attractive. Herein we wish to describe a practical and facile, regioselective synthesis of 2- or 3-fluoroalkylated indole derivatives by the palladium-catalyzed annulation of internal alkynes possessing a fluoroalkyl group.[8,9]

Results and Discussion

Annulation Reaction of Fluoroalkylated Alkynes with *o*-Iodoaniline under the Influence of Palladium Catalyst. The palladium-catalyzed reaction of trifluoromethylated acetylene **1a**[10] (R = *p*-ClC_6H_4) with *o*-iodoaniline was chosen for our initial investigation of the annulation process. Thus, to a solution of 10 mol % of Pd(PPh_3)$_4$ and 1.0 equiv of Et_3N in DMF was added 1.0 equiv each of **1a** and *o*-iodoaniline, and the mixture

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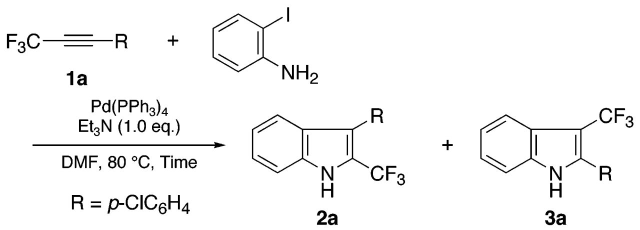
10.1021/jo048872x CCC: $27.50

TABLE 1. Investigation of the Reaction Conditions



entry	aniline (equiv)	$Pd(PPh_3)_4$ (mol %)	time (h)	yield[a] (%) of **2a** + **3a**	ratio[b] (**2a**/**3a**)	recovery[a] (%) of **1a**
1	1	10	4	39	69:31	52
2	2	10	4	51	78:22	37
3	2	20	4	75	77:23	11
4	2	20	8	85 (79)	78:22	0

[a] Determined by ^{19}F NMR. Value in parentheses is the isolated yield. [b] Determined by ^{19}F NMR.

was heated at 80 °C for 4 h. As a result, the regioisomers **2a** and **3a** were obtained in 39% yield in a ratio of 69:31, the starting material **1a** being recovered in 52% yield (Table 1, entry 1). The addition of 2.0 equiv of aniline resulted in the formation of **2a** and **3a** in a higher regioselective manner in 51% yield (entry 2). Additionally, increasing the amount of palladium catalyst gave higher yield (75%), though 11% of **1a** still remained unreacted (entry 3). Eventually, the starting material was completely consumed when the reaction was performed for 8 h, the mixture of **2a** and **3a** being afforded in 85% yield in a ratio of 78:22 (Entry 4). We next examined the effect of ligand on palladium as shown in Table 2.

The use of tri(2-furyl)phosphine as a ligand made the reaction significant reluctant to give **2a** and **3a** in only 20% yield, together with a large amount of unreacted **1a** (entry 2). In sharp contrast to the result in entry 1, the palladium catalyst prepared from $Pd_2(dba)_3{\cdot}CHCl_3$ and PPh_3 gave a low yield of the desired products, strongly suggesting that dba ligand may decrease the efficiency of the reaction (entry 3). In the case of tri(*tert*-butyl)phosphine, the annulation took place smoothly to give the corresponding indole derivatives in excellent yield, but the regioselectivity decreased significantly. Interestingly, **3a** was formed preferentially (**2a**/**3a** = 34:66) when tri(*o*-tolyl)phosphine was employed as a ligand (entry 5). As shown in entries 6−10, trialkylphosphine (entry 6), triaryl phosphite (entry 7), and bidentate ligands (entries 8−10) were all inactive, the desired indoles being produced in very low yields.

Next, the scope and limitations of this annulation reaction were examined. Table 3 summarizes the results of the reactions of a variety of internal alkynes with various 2-iodoanilines under optimized reaction conditions (Table 2, entry 1). As can be seen in entries 1−9, various fluorine-containing internal alkynes could participate nicely in the annulation reaction. Thus, the alkynes bearing an electron-donating group (Me, MeO) on the aromatic ring gave the corresponding indoles in good yields with good regioselectivity. Introduction of an electron-withdrawing group (CO_2Et, NO_2) into the aromatic ring in **1** led to a decrease of the regioselectivity, though the reaction took place smoothly (entries 4 and 5). It should be noted that the position of substituent on the aromatic ring in **1** influenced slightly on the reaction. Thus, the alkyne having a chloro group at *ortho* position of the aromatic ring resulted in formation of the desired product in 64% yield, whereas the corresponding *meta* or *para* isomer afforded the satisfactory results (>80% yield) (entry 6 vs entries 1 and 7). The alkynes bearing an aliphatic side chain as R could also be applied for the annulation reaction successfully (entries 8 and 9). Additionally, changing a fluoroalkyl group from a CF_3 to a CHF_2 group caused the increase of the regioselectivity. We also examined the annulation of **1a** with various 2-iodoaniline derivatives as shown in entries 11−15. It was found that no significant influence of the substituents R^1 and R^2 of the aniline ring was observed for the yield and the regioselectivity, though prolonged reaction times were required.

In almost all cases (except for entries 1, 6, and 7), either the major or the minor isomers (**2** or **3**) could easily be obtained in a pure form by simple silica gel column chromatography.

Interestingly, on treating the alkyne **1b** bearing a benzylic substituent as R with *o*-iodoaniline under the influence of palladium catalyst, *trifluoroethylated* indole derivatives **4b** and **5b** were obtained in 73% combined yield in a ratio of 26:74 (Scheme 1). No 2- or 3-trifluoromethylated products were detected at all. Even when 4-chlorophenylmethyl group was used as R, only **4c** and **5c** were afforded in good yields (Scheme 1).

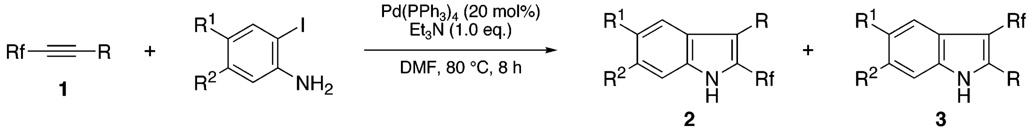
Palladium-Catalyzed Annulation Reaction Using $P(o\text{-}Tol)_3$ as a Ligand. As can be seen in Table 2, the ligand effect was observed significantly in this annulation reaction. Thus, 2-fluoroalkylated indole derivative was obtained preferencially when PPh_3 was employed, while 3-fluoroalkylated counterpart was produced preferentially in the case of $P(o\text{-}Tol)_3$. The interesting phenomena prompted us to investigate the generality of the regiose-

TABLE 2. Screening of Ligand

entry	catalyst (20 mol %)	yield[a] (%) of **2a** + **3a**	ratio[b] (**2a**/**3a**)	recovery[a] (%) of **1a**
1	$Pd(PPh_3)_4$	85 (79)	78:22	0
2	$^1/_2[Pd_2(dba)_3{\cdot}CHCl_3]$ + 4P(2-furyl)$_3$	20	90:10	79
3	$^1/_2[Pd_2(dba)_3{\cdot}CHCl_3]$ + $4PPh_3$	33	88:12	55
4	$^1/_2[Pd_2(dba)_3{\cdot}CHCl_3]$ + 4P(*t*-Bu)$_3$	94	53:47	0
5	$^1/_2[Pd_2(dba)_3{\cdot}CHCl_3]$ + 4P(*o*-Tol)$_3$	90	34:66	0
6	$^1/_2[Pd_2(dba)_3{\cdot}CHCl_3]$ + $4PBu_3$	4	0:100	14
7	$^1/_2[Pd_2(dba)_3{\cdot}CHCl_3]$ + $4P(OPh)_3$	45	73:27	31
8	$Pd(dppe)_2$	4	100:0	64
9	$^1/_2[Pd_2(dba)_3{\cdot}CHCl_3]$ + 2BINAP	1	100:0	68
10	$^1/_2[Pd_2(dba)_3{\cdot}CHCl_3]$ + 2bpy	22	55:45	19

[a] Determined by ^{19}F NMR. Value in parentheses is the isolated yield. [b] Determined by ^{19}F NMR.

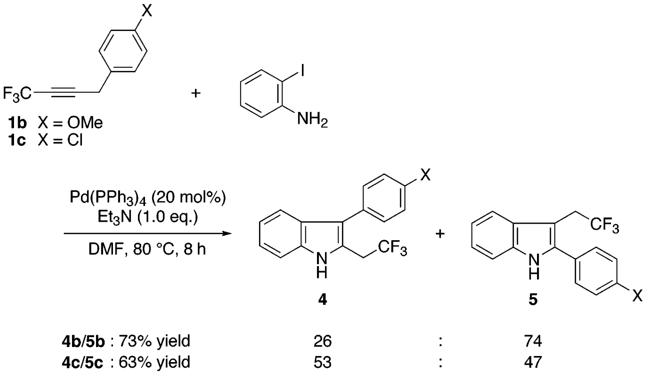
TABLE 3. Scope and Limitations of Palladium-Catalyzed Annulation of Fluorine-Containing Internal Alkynes



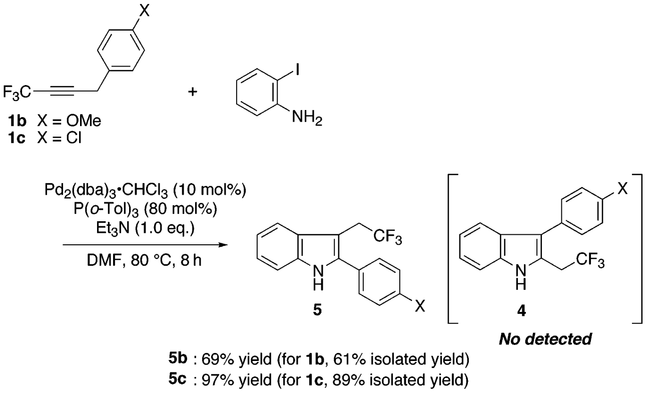
entry	Rf	R	R^1	R^2	product	yield[a] (%) of **2** + **3**	ratio[b] (**2**/**3**)
1	CF_3	*p*-ClC_6H_4	H	H	**2a/3a**	85 (79)	78:22
2[c]	CF_3	*p*-MeC_6H_4	H	H	**2b/3b**	84 (81)	88:12
3[c]	CF_3	*p*-$MeOC_6H_4$	H	H	**2c/3c**	79 (73)	91:9
4	CF_3	*p*-$EtO_2CC_6H_4$	H	H	**2d/3d**	98 (92)	68:32
5	CF_3	*p*-$O_2NC_6H_4$	H	H	**2e/3e**	70 (65)	53:47
6[c]	CF_3	*o*-ClC_6H_4	H	H	**2f/3f**	64 (59)	76:24
7	CF_3	*m*-ClC_6H_4	H	H	**2g/3g**	86 (80)	72:28
8	CF_3	$Ph(CH_2)_3$	H	H	**2h/3h**	53 (47)	81:19
9	CF_3	$PhCH(CH_3)CH_2$	H	H	**2i/3i**	61 (55)	72:28
10	CHF_2	*p*-ClC_6H_4	H	H	**2j**	84 (70)	100:0
11[c]	CF_3	*p*-ClC_6H_4	Cl	H	**2k/3k**	90 (79)	84:16
12	CF_3	*p*-ClC_6H_4	CH_3	H	**2l/3l**	85 (82)	81:19
13[c]	CF_3	*p*-ClC_6H_4	NO_2	H	**2m/3m**	61 (57)	84:16
14[c]	CF_3	*p*-ClC_6H_4	H	OMe	**2n/3n**	68 (65)	88:12
15[d]	CF_3	*p*-ClC_6H_4	Cl	Cl	**2o/3o**	87 (74)	84:16

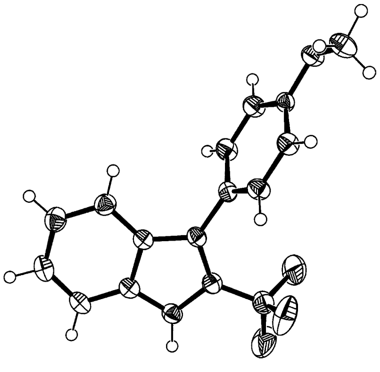
[a] Determined by ^{19}F NMR. Values in parentheses are the isolated yields. [b] Determined by ^{19}F NMR. [c] Stirred for 24 h. [d] Stirred for 48 h.

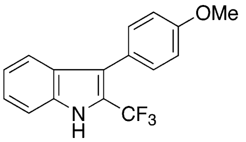
SCHEME 1. Annulation Reaction of the Alkyne Bearing a Benzylic Substituent



SCHEME 2. Annulation Reaction of the Alkyne Bearing a Benzylic Substituent







2c

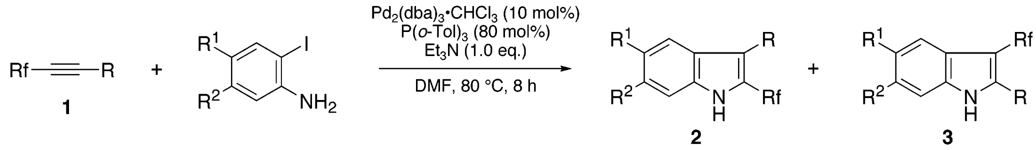
FIGURE 1. ORTEP drawing of **2c**.

lectivity in the catalytic system of $Pd_2(dba)_3{\cdot}CHCl_3$ + P(*o*-Tol)$_3$ in more detail. The results are collected in Table 4. As shown in entries 1−7, various fluorine-containing internal alkynes could participate nicely in the annulation reaction. Thus, the alkynes bearing an electron-donating group (Me, MeO) or an electron-withdrawing group (EtO_2C, NO_2) in the aromatic ring gave the 3-fluoroalkylated indoles as a major isomer in good yields, though a slight decrease of the regioselectivity was observed in the case of an electron-withdrawing group (entries 4 and 5). It is noteworthy that the reaction of the alkynes bearing an alkyl side chain as R resulted in the large decrease of the yield (entries 8 and 9). Surprisingly, no products were obtained in the case of a CF_2H group as Rf, the starting alkyne being not recovered at all in this case. As shown in entries 11−15, it was found that no influence of R^1 or R^2 was observed on the reaction efficiency as well as the regioselectivity.

It should be noted that treatment of **1b** or **1c** with *o*-iodoaniline under the influence of $Pd_2(dba)_3{\cdot}CHCl_3$ and P(*o*-Tol)$_3$ gave the corresponding *3-trifluoroethylated* indole derivatives in good to excellent yields as a single isomer (Scheme 2). Neither 2-trifluoroethylated compounds nor trifluoromethylated indoles were detected.

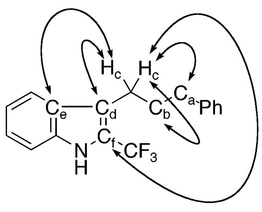
Stereochemistry. The stereochemical assignment of **2** and **3** was carried out as follows. Thus, when the reaction of **1** with *o*-iodoaniline was performed *in the presence of Pd(PPh$_3$)$_4$*, the ^{19}F NMR signal of the major product **2** was observed at the upper field than that of the minor product **3** in all cases. On the other hand, single-crystal X-ray analysis of **2c** could be carried out

TABLE 4. Scope and Limitations of Palladium-Catalyzed Annulation of Fluorine-Containing Internal Alkynes



entry	Rf	R	R^1	R^2	product	yield[a] (%) of **2** + **3**	ratio[b] (**2**/**3**)
1	CF_3	p-ClC_6H_4	H	H	**2a/3a**	90 (85)	34:66
2[c]	CF_3	p-MeC_6H_4	H	H	**2b/3b**	90 (79)	9:91
3	CF_3	p-$MeOC_6H_4$	H	H	**2c/3c**	66 (52)	8:92
4	CF_3	p-$EtO_2CC_6H_4$	H	H	**2d/3d**	91 (85)	34:66
5	CF_3	p-$O_2NC_6H_4$	H	H	**2e/3e**	66 (51)	48:52
6[c]	CF_3	o-ClC_6H_4	H	H	**2f/3f**	61 (56)	16:84
7	CF_3	m-ClC_6H_4	H	H	**2g/3g**	80 (74)	27:73
8	CF_3	$Ph(CH_2)_3$	H	H	**2h/3h**	64 (60)	22:78
9	CF_3	$C_6H_5CH(CH_3)CH_2$	H	H	**2i/3i**	38 (27)	17:83
10	CHF_2	p-ClC_6H_4	H	H		0	
11[c]	CF_3	p-ClC_6H_4	Cl	H	**2k/3k**	99 (89)	22:78
12	CF_3	p-ClC_6H_4	CH_3	H	**2l/3l**	78 (62)	27:73
13	CF_3	p-ClC_6H_4	NO_2	H	**2m/3m**	90 (81)	36:64
14[c]	CF_3	p-ClC_6H_4	H	OMe	**2n/3n**	69 (66)	17:83
15[d]	CF_3	p-ClC_6H_4	Cl	Cl	**2o/3o**	97 (86)	11:89

[a] Determined by ^{19}F NMR. Values in parentheses are the isolated yields. [b] Determined by ^{19}F NMR. [c] Stirred for 24 h. [d] Stirred for 48 h.



2h

FIGURE 2. HMBC analysis of **2h**.

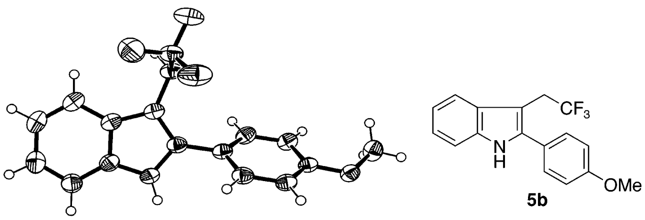


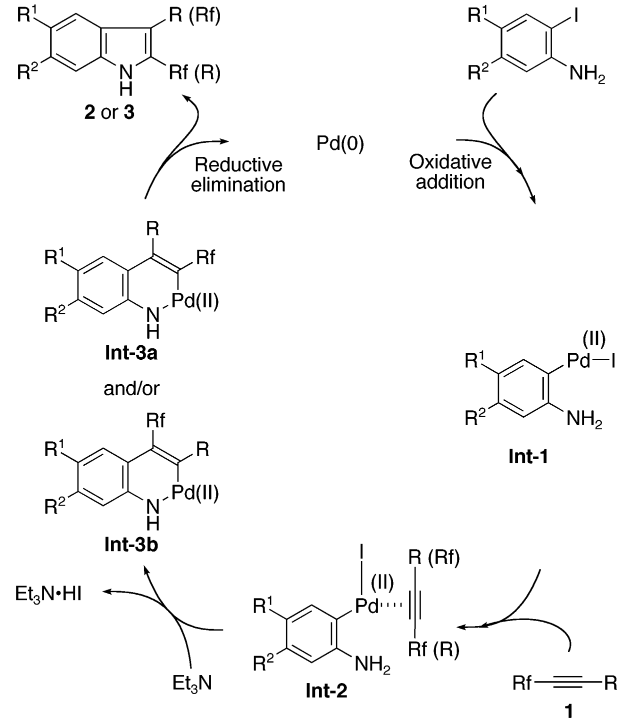
FIGURE 3. ORTEP drawing of **5b**.

successfully, **2c** being unambiguously determined as 2-trifluromethylated indole derivative as shown in Figure 1. Additionally, HMBC analysis of the major compound **2h**, which was obtained via the reaction of **1h** with 2-iodoaniline in the presence of $Pd(PPh_3)_4$, was carried out. As shown in Figure 2, five cross-peaks were observed in H_c-C_a, H_c-C_b, H_c-C_d, H_c-C_e, and H_c-C_f, strongly indicating that the major compound was 2-fluoroalkylated indole derivative. Accordingly, **2** and **3** were determined as 2-fluoroalkylated and 3-fluoroalkylated indoles, respectively.

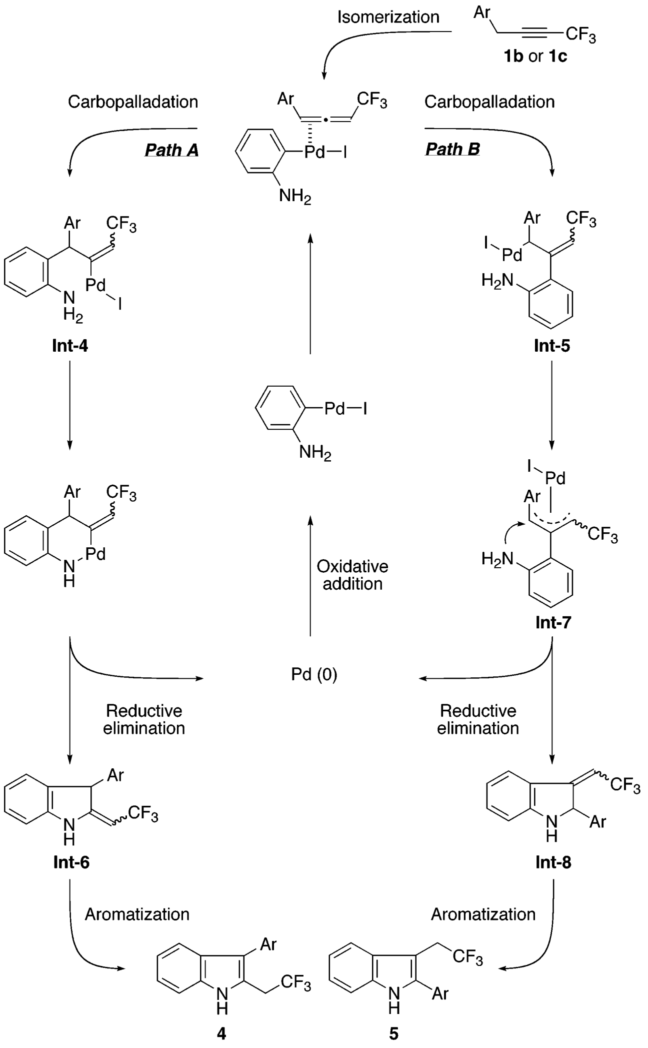
Similarly, the stereochemical determination of **4** and **5** was made on the basis of chemical shifts in ^{19}F NMR and the single-crystal X-ray analysis of **5b** as shown in Figure 3.

Reaction Mechanism. A plausible mechanism of this reaction is outlined in Scheme 3. Thus, the reaction presumably proceeds via (1) oxidative addition of aryl iodide to Pd(0) (**Int-1**), (2) coordination of the alkyne **1** to the metal center of the arylpalladium intermediate (**Int-2**) and subsequent insertion into the Ar−Pd bond, (3) nitrogen displacement of the halide in the resulting vinylic palladium intermediate to form a six-membered heteroatom-containing palladacycle **Int-3**, and (4) reductive elimination to form indoles **2** or **3** to regenerate Pd(0) (Scheme 3).[11] The regioselectivity can be explained as follows. Thus, the palladium(II) may be closer to the carbon attached with a Rf group in the coordination of the alkyne with the palladium complex due to a strong electron-withdrawing effect of a Rf group. Therefore, the reaction may proceed via **Int-3a** preferentially to afford

SCHEME 3. Mechanism I



SCHEME 4. Reaction Mechanisn II



2-fluoroalkylated indoles when PPh_3, a not so bulky ligand on palladium, was employed. In the case of a bulky $P(o\text{-}Tol)_3$, the reaction may take place via **Int-3b** rather than **Int-3a** because of a large steric repulsion between $P(o\text{-}Tol)_3$ and a Rf group, 3-fluoroalkylated indoles being afforded preferentially.

In the case of the reaction of alkyne bearing a benzylic substituent as R, on the other hand, the reaction may proceed via carbopalladation of the in-situ generated fluoroalkylated allene, as shown in Scheme 4. Thus, the first step is thermal isomerization of fluoroalkylated alkyne into allene due to highly acidic benzylic proton. The allene coordinates with the palladium complex which was produced via oxidative addition of aryl halide to palladium(0) followed by carbopalladation to afford two different complexes **Int-4** and **Int-5**.[12] The vinylic palladium **Int-4** is transformed to **Int-6** via the same mechanism as described in Scheme 3 (path A). Finally, aromatization of **Int-6** results in 2-trifluoroethylated indole derivative **4**. On the other hand, **Int-5** is known to produce π-allylpalladium compound **Int-7**, which readily undergo intramolecular nucleophilic substitution at the allylic carbon distal to a bulky CF_3 group. Consequently, trifluoroethylidene compound **Int-8** is formed, which finally aromatizes to form 3-trifluoroethylated indole derivatives **5**.

Summary

In conclusion, we have accomplished the convenient synthesis of fluoroalkylated indoles via palladium-catalyzed annulation reaction of fluorine-containing alkynes. In particular, it should be noted that the reaction in the presence of $Pd(PPh_3)_4$ gave 2-fluoroalkylated indole derivatives preferentially, while the use of $P(o\text{-}Tol)_3$ resulted in the preferential formation of 3-fluoroalkylated indoles. We have also found that the trifluoromethylated alkynes bearing a benzylic substituent as R produced 2- or 3-trifluoroethylated indoles instead of 2- or 3-trifluoromethylated ones via the carbopalladation reaction of the in-situ generated trifluoromethylated allenes.

Experimental Section

General Methods. ^1H NMR or ^{13}C NMR spectra were measured with a 500.13 or 125.77 MHz spectrometer in a chloroform-*d* ($CDCl_3$) solution with tetramethylsilane (Me_4Si) as an internal reference, and 84.1 and 282.29 MHz spectrometers were used for determining ^{19}F NMR yield with internal C_6F_6, as well as for taking ^{19}F NMR spectra in a $CDCl_3$ solution with $CFCl_3$ as an internal standard.

Reagents. 2-Iodoaniline was commercially available. DMF and Et_3N were freshly distilled from calcium hydride (CaH_2). All chemicals were of reagent grade and, if necessary, were purified in the usual manner prior to use. Thin-layer chromatography (TLC) was done with silica gel 60 F_{254} plates, and column chromatography was carried out with silica gel (200~300 mesh). All alkynes were prepared according to a previous literature procedure.[10] The substituted *o*-iodoanilines were prepared according to a literature procedure.[13]

3-(4-Chlorophenyl)-2-(trifluoromethyl)indole (2a): mp 83−85 °C; ^1H NMR ($CDCl_3$) δ 7.26 (1H, t, J = 8.0 Hz), 7.43 (1H, d, J = 7.1 Hz), 7.45 − 7.50 (5H, m), 7.65 (1H, d, J = 7.5 Hz), 8.54 (1H, s, br); ^{13}C NMR ($CDCl_3$) δ 111.8, 118.5 (q, J = 3.0 Hz), 120.8, 121.3 (q, J = 37.0 Hz), 121.5, 121.5 (q, J = 268.9 Hz), 125.3, 127.1, 128.7, 130.6, 131.2, 133.6, 134.9; ^{19}F NMR ($CDCl_3$) δ −57.36 (3F, s); IR (KBr) 3421, 3150, 1602, 1566, 1492 cm^{-1}; HRMS (EI) calcd for $C_{15}H_9ClF_3N$ 295.0376, found 295.0376. Anal. Calcd for $C_{15}H_9ClF_3N$: C, 60.93; H, 3.07; N, 4.74. Found: C, 60.80; H, 3.18; N, 4.61.

2-(4-Chlorophenyl)-3-(trifluoromethyl)indole (3a): mp 91−93 °C; ^1H NMR ($CDCl_3$) δ 7.25 (1H, t, J = 7.0 Hz), 7.30 (1H, t, J = 7.0 Hz), 7.40 (1H, d, J = 8.0 Hz), 7.45 (2H, d, J = 6.5 Hz), 7.51 (2H, d, J = 8.5 Hz), 7.81 (1H, d, J = 8.0 Hz), 8.32 (1H, s, br); ^{13}C NMR ($CDCl_3$) δ 104.0 (q, J = 36.3 Hz), 111.1, 120.1, 121.9, 123.7, 124.6 (q, J = 267.6 Hz), 125.5 (q, J = 1.5 Hz), 129.0, 129.5, 130.3, 134.9, 135.6, 137.1 (q, J = 3.6 Hz); ^{19}F NMR ($CDCl_3$) δ −53.46 (3F, s); IR (KBr) 3404, 3100, 1602, 1490 cm^{-1}; HRMS (EI) calcd for $C_{15}H_9ClF_3N$ 295.0376, found 295.0373.

3-(4-Methylphenyl)-2-(trifluoromethyl)indole (2b): mp 101−103 °C; ^1H NMR ($CDCl_3$) δ 2.45 (3H, s), 7.21 (1H, t, J = 7.90 Hz), 7.30 (2H, d, J = 7.8 Hz), 7.38 (1H, t, J = 8.25 Hz),

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[11] The opposite regioselectivity in the case of $P(o\text{-}Tol)_3$ may be derived from the large repulsion between a bulky fluoroalkyl group and a bulky $P(o\text{-}Tol)_3$ in **Int-2**.

[12] For the palladium-catalyzed annulation reaction of allenes, see: (a) Zenner, J. M.; Larock, R. C. *J. Org. Chem.* **1999**, *64*, 7312−7322. (b) Larock, R. C.; Zenner, J. M. *J. Org. Chem.* **1995**, *60*, 482−483. (c) Larock, R. C.; Berrios-Peña, N. G.; Fried, C. A. *J. Org. Chem.* **1991**, *56*, 2615−2617.

[13] Ma, C.; Liu, X.; Li, X.; F.-Anderson, J.; Yu, S.; M. Cook, J. *J. Org. Chem.* **2001**, *66*, 4525−4542.

7.43 − 7.47 (3H, m), 7.67 (1H, d, $J = 8.15$ Hz), 8.45 (1H, s, br); ^{13}C NMR (CDCl$_3$) δ 21.3, 111.6, 119.8 (q, $J = 2.5$ Hz), 121.0 (q, $J = 36.5$ Hz), 121.1, 121.2, 121.7 (q, $J = 269.0$ Hz), 125.1, 127.4, 129.0, 129.1, 129.7, 134.9, 137.3; ^{19}F NMR (CDCl$_3$) δ −57.33 (3F, s); IR (KBr) 3402, 3080, 1618, 1508 cm^{-1}; HRMS (EI) calcd for $C_{16}H_{12}F_3N$ 275.0922, found 275.0922.

2-(4-Methylphenyl)-3-(trifluoromethyl)indole (3b): mp 81−83 °C; ^{1}H NMR (CDCl$_3$) δ 2.41 (3H, s), 7.22−7.27 (4H, m), 7.37 (1H, d, $J = 7.95$ Hz), 7.46 (2H, d, $J = 7.75$ Hz), 7.81 (1H, d, $J = 7.6$ Hz), 8.30 (1H, s, br); ^{13}C NMR (CDCl$_3$) δ 21.3, 104.1 (q, $J = 35.7$ Hz), 111.0, 119.9, 121.6, 123.3, 124.8 (q, $J = 267.4$ Hz), 125.6 (q, $J = 1.5$ Hz), 128.1, 128.8, 129.4, 134.8, 138.7 (q, $J = 3.9$ Hz), 139.5; ^{19}F NMR (CDCl$_3$) δ −53.33 (3F, s); IR (KBr) 3386, 3100, 1616, 1508, 1438 cm^{-1}; HRMS (EI) calcd for $C_{16}H_{12}F_3N$ 275.0922, found 275.0915. Anal. Calcd for $C_{16}H_{12}F_3N$: C, 69.81; H, 4.39; N, 5.09. Found: C, 70.20; H, 4.69; N, 4.71.

2-(Trifluoromethyl)-3-(4-methoxyphenyl)indole (2c): mp 165−167 °C; ^{1}H NMR (CDCl$_3$) δ 3.89 (3H, s), 7.03 (2H, d, $J = 8.7$ Hz), 7.20 (1H, t, $J = 7.25$ Hz), 7.37 (1H, t, $J = 7.85$ Hz), 7.44 − 7.47 (3H, m), 7.65 (1H, d, $J = 8.05$ Hz), 8.47 (1H, s, br); ^{13}C NMR (CDCl$_3$) δ 55.3, 111.6, 113.9, 119.5 (q, $J = 3.5$ Hz), 120.9 (q, $J = 37.3$ Hz), 121.1, 121.1, 121.7 (q, $J = 269.0$ Hz), 124.3, 125.1, 127.5, 131.0, 134.9, 159.1; ^{19}F NMR (CDCl$_3$) δ −57.36 (3F, s); IR (KBr) 3317, 3062, 1616, 1512 cm^{-1}; HRMS (EI) calcd for $C_{16}H_{12}F_3NO$ 291.0871, found 291.0872. Crystal data: $C_{16}H_{12}F_3NO$, $M = 291.27$, triclinic, $P1$ (no. 2), $a = 10.280(5)$ Å, $b = 13.653(6)$ Å, $c = 9.689(3)$ Å, $\alpha = 95.33(3)°$, $\beta = 98.28(3)°$, $\gamma = 90.18(4)°$, $V = 1339.7(9)$ Å^3, $Z = 4$, $D_c = 1.444$ g/cm^{-3}, μ(Cu Kα) = 10.21 cm^{-1}, $T = 198$ K, colorless; 12 880 independent measured reflections, F^2 refinement, $R_1 = 0.051$, w$R_2 = 0.141$, 4662 independent observed absorption corrected reflections, $2\theta_{\max} = 133.6°$.

3-(Trifluoromethyl)-2-(4-methoxyphenyl)indole (3c): mp 178−180 °C; ^{1}H NMR (CDCl$_3$) δ 3.87 (3H, s), 7.00 (2H, d, $J = 8.65$ Hz), 7.23−7.29 (2H, m), 7.40 (1H, d, $J = 7.9$ Hz), 7.63 (2H, d, $J = 8.6$ Hz), 7.81 (1H, d, $J = 7.65$ Hz), 8.32 (1H, s, br); ^{13}C NMR (CDCl$_3$) δ 55.4, 102.9 (q, $J = 36.1$ Hz), 111.0, 114.1, 119.9 (q, $J = 1.4$ Hz), 121.6, 123.2, 123.3, 124.9 (q, $J = 267.0$ Hz), 125.7, 130.3 (q, $J = 1.2$ Hz), 134.7, 138.6 (q, $J = 4.2$ Hz), 160.4; ^{19}F NMR (CDCl$_3$) δ −53.38 (3F, s); IR (KBr) 3313, 3060, 1614, 1506 cm^{-1}; HRMS (EI) calcd for $C_{16}H_{12}F_3NO$ 291.0871, found 291.0865.

3-(4-Ethoxycarbonylphenyl)-2-(trifluoromethyl)indole (2d): mp 143−145 °C; ^{1}H NMR (CDCl$_3$) δ 1.43 (3H, t, $J = 7.25$ Hz), 4.43 (2H, q, $J = 7.25$ Hz), 7.23 (1H, t, $J = 7.65$ Hz), 7.39 (1H, t, $J = 7.3$ Hz), 7.49 (1H, d, $J = 8.25$ Hz), 7.61−7.64 (3H, m), 8.17 (2H, d, $J = 8.3$ Hz), 8.77 (1H, s, br); ^{13}C NMR (CDCl$_3$) δ 14.3, 61.1, 111.9, 118.6 (q, $J = 3.0$ Hz), 120.4, 121.5 (q, $J = 269.3$ Hz), 121.6 (q, $J = 37.4$ Hz), 121.6, 125.3, 126.9, 129.5, 129.6, 129.8, 134.9, 137.0, 165.6; ^{19}F NMR (CDCl$_3$) δ −57.31 (3F, s); IR (KBr) 3298, 3060, 1697, 1612 cm^{-1}; HRMS (EI) calcd for $C_{18}H_{14}F_3NO_2$ 333.0977, found 333.0977.

2-(4-Ethoxycarbonylphenyl)-3-(trifluoromethyl)indole (3d): mp 164−166 °C; ^{1}H NMR (CDCl$_3$) δ 1.42 (3H, t, $J = 7.1$ Hz), 4.42 (2H, q, $J = 7.1$ Hz), 7.27 (1H, t, $J = 7.7$ Hz), 7.32 (1H, t, $J = 7.2$ Hz), 7.45 (1H, d, $J = 8.05$ Hz), 7.66 (2H, d, $J = 8.1$ Hz), 7.84 (1H, d, $J = 7.85$ Hz), 8.12 (2H, d, $J = 8.2$ Hz), 8.70 (1H, s, br); ^{13}C NMR (CDCl$_3$) δ 14.3, 61.4, 104.2 (q, $J = 35.8$ Hz), 111.3, 120.1, 121.8, 123.8, 124.6 (q, $J = 267.5$ Hz), 125.5 (q, $J = 1.4$ Hz), 129.0, 129.7, 130.8, 135.2, 135.4, 137.1 (q, $J = 3.8$ Hz), 166.3; ^{19}F NMR (CDCl$_3$) δ −53.33 (3F, s); IR (KBr) 3311, 3060, 1689, 1614 cm^{-1}; HRMS (EI) calcd for $C_{18}H_{14}F_3NO_2$ 333.0977, found 333.0977.

2-(Trifluoromethyl)-3-(4-nitrophenyl)indole (2e): mp 185−187 °C; ^{1}H NMR (CDCl$_3$) δ 7.16 (1H, t, $J = 7.6$ Hz), 7.32 (1H, t, $J = 7.45$ Hz), 7.42 (1H, d, $J = 8.25$ Hz), 7.51 (1H, d, $J = 8.1$ Hz), 7.60 (2H, d, $J = 8.6$ Hz), 8.24 (2H, d, $J = 8.7$ Hz), 8.63 (1H, s, br); ^{13}C NMR (CDCl$_3$) δ 112.0, 117.3 (q, $J = 2.3$ Hz), 120.4, 121.3 (q, $J = 268.7$ Hz), 122.0 (q, $J = 36.5$ Hz), 122.1, 123.7, 125.7, 126.6, 130.6, 134.9, 139.3, 147.1; ^{19}F NMR (CDCl$_3$) δ −56.58 (3F, s); IR (KBr) 3315, 3060, 1600, 1514 cm^{-1}; HRMS (EI) calcd for $C_{15}H_9F_3N_2O_2$ 306.0616, found 306.0624.

3-(Trifluoromethyl)-2-(4-nitrophenyl)indole (3e): mp 151−153 °C; ^{1}H NMR (CDCl$_3$) δ 7.30 (1H, t, $J = 7.3$ Hz), 7.35 (1H, t, $J = 7.35$ Hz), 7.47 (1H, d, $J = 8.1$ Hz), 7.78 (2H, d, $J = 8.65$ Hz), 7.85 (1H, d, $J = 8.0$ Hz), 8.32 (2H, d, $J = 8.65$ Hz), 8.65 (1H, s, br); ^{13}C NMR (CDCl$_3$) δ 104.3 (q, $J = 36.3$ Hz), 111.4, 122.3, 123.8, 124.3 (q, $J = 267.6$ Hz), 124.4, 125.3 (q, $J = 2.3$ Hz), 125.4, 129.9, 135.3 (q, $J = 3.2$ Hz), 135.4, 137.3, 148.0; ^{19}F NMR (CDCl$_3$) δ −53.28 (3F, s); IR (KBr) 3355, 3060, 1600, 1506, 1446 cm^{-1}; HRMS (EI) calcd for $C_{15}H_9F_3N_2O_2$ 306.0616, found 306.0624.

3-(2-Chlorophenyl)-2-(trifluoromethyl)indole (2f): ^{1}H NMR (CDCl$_3$) δ 7.20 (1H, t, $J = 7.9$ Hz), 7.35−7.44 (5H, m), 7.48 (1H, d, $J = 8.45$ Hz), 7.54 (1H, d, $J = 7.2$ Hz), 8.52 (1H, s, br); ^{13}C NMR (CDCl$_3$) δ 111.7, 117.0 (q, $J = 3.0$ Hz), 121.2, 121.3 (q, $J = 269.1$ Hz), 121.3, 122.2 (q, $J = 36.8$ Hz), 125.2, 126.4, 127.2, 129.4, 129.6, 130.9, 131.1, 132.6, 134.8; ^{19}F NMR (CDCl$_3$) δ −58.86 (3F, s); IR (neat) 3408, 3064, 1706, 1604 cm^{-1}; HRMS (EI) calcd for $C_{15}H_9ClF_3N$ 295.0376, found 295.0378.

2-(2-Chlorophenyl)-3-(trifluoromethyl)indole (3f): mp 99−101 °C; ^{1}H NMR (CDCl$_3$) δ 7.27 (1H, t, $J = 8.5$ Hz), 7.32 (1H, t, $J = 8.5$ Hz), 7.34−7.53 (5H, m), 7.82 (1H, d, $J = 8.0$ Hz), 8.38 (1H, s, br); ^{13}C NMR (CDCl$_3$) δ 105.5 (q, $J = 34.6$ Hz), 111.2, 119.9, 121.7, 123.7, 124.2 (q, $J = 267.4$ Hz), 124.6 (q, $J = 1.7$ Hz), 126.6, 129.8, 130.0, 130.9, 132.5, 133.9, 134.9 (q, $J = 3.7$ Hz); ^{19}F NMR (CDCl$_3$) δ −55.08 (3F, s); IR (KBr) 3375, 3058, 1616, 1568 cm^{-1}; HRMS (EI) calcd for $C_{15}H_9ClF_3N$ 295.0376, found 295.0381.

3-(3-Chlorophenyl)-2-(trifluoromethyl)indole (2g): ^{1}H NMR (CDCl$_3$) δ 7.22 (1H, t, $J = 7.0$ Hz), 7.37−7.42 (4H, m), 7.47 (1H, d, $J = 8.5$ Hz), 7.52 (1H, s), 7.62 (1H, d, $J = 8.0$ Hz), 8.57 (1H, s, br); ^{13}C NMR (CDCl$_3$) δ 111.8, 118.3 (q, $J = 2.8$ Hz), 120.7, 121.4 (q, $J = 269.4$ Hz), 121.5 (q, $J = 37.0$ Hz), 121.6, 125.4, 127.0, 127.7, 128.1, 129.7, 129.8, 133.9, 134.2, 134.8; ^{19}F NMR (CDCl$_3$) δ −57.36 (3F, s); IR (neat) 3425, 3100, 1602, 1562 cm^{-1}; HRMS (EI) calcd for $C_{15}H_9ClF_3N$ 295.0376, found 295.0373.

2-(3-Chlorophenyl)-3-(trifluoromethyl)indole (3g): ^{1}H NMR (CDCl$_3$) δ 7.26 (1H, t, $J = 8.0$ Hz), 7.30 (1H, t, $J = 7.0$ Hz), 7.39−7.45 (3H, m), 7.48 (1H, d, $J = 7.5$ Hz), 7.57 (1H, s), 7.82 (1H, d, $J = 8.0$ Hz), 8.34 (1H, s, br); ^{13}C NMR (CDCl$_3$) δ 104.2 (q, $J = 35.8$ Hz), 111.2, 120.1, 121.9, 123.8, 124.5 (q, $J = 267.5$ Hz), 125.4 (q, $J = 1.4$ Hz), 127.4 (q, $J = 1.4$ Hz), 128.9, 129.5, 129.9, 132.7, 134.6, 134.9, 136.7 (q, $J = 4.4$ Hz); ^{19}F NMR (CDCl$_3$) δ −53.46 (3F, s); IR (neat) 3406, 3100, 1558, 1440 cm^{-1}; HRMS (EI) calcd for $C_{15}H_9ClF_3N$ 295.0376, found 295.0372.

2-(Trifluoromethyl)-3-(3-phenylpropyl)indole (2h): ^{1}H NMR (CDCl$_3$) δ 2.00 (2H, quint, $J = 8.00$ Hz), 2.70 (2H, t, $J = 7.5$ Hz), 2.92 (2H, t, $J = 8.0$ Hz), 7.14−7.31 (7H, m), 7.36 (1H, d, $J = 8.0$ Hz), 7.58 (1H, d, $J = 8.0$ Hz), 8.14 (1H, s, br); ^{13}C NMR (CDCl$_3$) δ 23.6, 32.4, 35.8, 111.7, 118.7 (q, $J = 2.6$ Hz), 120.3, 120.5, 121.3 (q, $J = 36.7$ Hz), 122.1 (q, $J = 268.7$ Hz), 124.7, 125.8, 127.4, 128.3, 128.4, 135.2, 142.1; ^{19}F NMR (CDCl$_3$) δ −57.73 (3F, s); IR (neat) 3406, 2937, 1591, 1452 cm^{-1}; HRMS (EI) calcd for $C_{18}H_{16}F_3N$ 303.1235, found 303.1236.

3-(Trifluoromethyl)-2-(3-phenylpropyl)indole (3h): ^{1}H NMR (CDCl$_3$) δ 2.05 (2H, quint, $J = 7.8$ Hz), 2.70 (2H, t, $J = 7.5$ Hz), 2.93 (2H, t, $J = 7.5$ Hz), 7.16−7.22 (5H, m), 7.28−7.31 (3H, m), 7.69 (1H, d, $J = 7.4$ Hz), 8.04 (1H, s, br); ^{13}C NMR (CDCl$_3$) δ 26.5, 31.2, 35.3, 104.5 (q, $J = 32.6$ Hz), 110.7, 119.2, 121.2, 122.6, 125.2, 126.1, 127.1 (q, $J = 266.8$ Hz), 128.4, 128.5, 134.3, 139.7 (q, $J = 3.3$ Hz), 141.2; ^{19}F NMR (CDCl$_3$) δ −54.81 (3F, s); IR (neat) 3402, 2937, 1722, 1566 cm^{-1}; HRMS (FAB) calcd for $C_{18}H_{16}F_3N$ 303.1235, found 303.1234.

2-(Trifluoromethyl)-3-(2-phenylpropyl)indole (2i): ^{1}H NMR (CDCl$_3$) δ 1.25 (3H, d, $J = 7.00$ Hz), 3.04−3.19 (3H, m), 7.15 (1H, t, $J = 7.0$ Hz), 7.19 (1H, t, $J = 7.0$ Hz), 7.24−7.31 (5H, m), 7.37 (1H, d, $J = 8.5$ Hz), 7.58 (1H, d, $J = 8.0$ Hz), 8.17 (1H, s, br); ^{13}C NMR (CDCl$_3$) δ 20.7, 33.2, 40.9, 111.6, 117.5 (q, J = 2.8 Hz), 120.4, 120.6, 121.9 (q, J = 35.2 Hz), 124.2 (q, J = 264.1 Hz), 124.7, 126.2, 126.9, 127.6, 128.4, 135.2, 147.0; ^{19}F NMR (CDCl$_3$) δ −58.44 (3F, s); IR (neat) 3408, 3028, 2964, 1724, 1591 cm^{-1}; HRMS (FAB) calcd for $C_{18}H_{16}F_3N$ 303.1235, found 303.1227.

3-(Trifluoromethyl)-2-(2-phenylpropyl)indole (3i): ^{1}H NMR (CDCl$_3$) δ 1.35 (3H, d, J = 6.7 Hz), 3.05−3.24 (3H, m), 7.14−7.32 (8H, m), 7.60 (1H, s, br), 7.68−7.69 (1H, m); ^{13}C NMR (CDCl$_3$) δ 21.4, 35.9, 40.5, 103.5 (q, J = 36.2 Hz), 110.6, 119.2, 121.1 122.5, 124.8, 125.2 (q, J = 267.1 Hz), 126.8, 126.8, 128.8, 134.3 138.5 (q, J = 3.7 Hz), 145.6; ^{19}F NMR (CDCl$_3$) δ −54.46 (3F, s); IR (neat) 3409, 3030, 2966, 1755, 1566 cm^{-1}; HRMS (FAB) calcd for $C_{18}H_{16}F_3N$ 303.1235, found 303.1240.

3-(4-Chlorophenyl)2-(difluoromethyl)indole (2j): mp 92−94 °C; ^{1}H NMR (CDCl$_3$) δ 6.66 (1H, t, J = 53.76 Hz), 7.13 (1H, t, J = 7.3 Hz), 7.28 (1H, t, J = 7.8 Hz), 7.35−7.40 (5H, m), 7.61 (1H, d, J = 8.0 Hz), 8.49 (1H, s, br); ^{13}C NMR (CDCl$_3$) δ 109.8 (t, J = 233.7 Hz), 111.8, 118.7 (t, J = 8.0 Hz), 120.3, 121.1, 124.8, 125.9 (t, J = 22.4 Hz), 126.2, 129.1, 130.8, 131.0, 133.4, 135.6; ^{19}F NMR (CDCl$_3$, CFCl$_3$) δ −104.48 (2F, d, J = 51.97 Hz); IR (KBr) 3394, 3060, 1600, 1560, 1492 cm^{-1}; HRMS (EI) calcd for $C_{15}H_{10}ClF_2N$ 277.0470, found 277.0464. Anal. Calcd for $C_{15}H_{10}ClF_3N$: C, 64.88; H, 3.63; N, 5.04. Found: C, 64.51; H, 4.15; N, 4.87.

5-Chloro-3-(4-chlorophenyl)-2-(trifluoromethyl)indole (2k): ^{1}H NMR (CDCl$_3$) δ 7.31 (1H, dd, J = 8.75, 1.8 Hz), 7.38 (1H, d, J = 8.8 Hz), 7.40 (2H, d, J = 8.45 Hz), 7.45 (2H, d, J = 8.5 Hz), 7.55 (1H, s), 8.59 (1H, s, br); ^{13}C NMR (CDCl$_3$) δ 112.9, 118.1 (q, J = 2.8 Hz), 120.2, 121.2 (q, J = 269.4 Hz), 122.6 (q, J = 37.1 Hz), 125.9, 127.4, 128.1, 128.8, 129.8, 131.0, 133.1, 133.9; ^{19}F NMR (CDCl$_3$) δ −57.06 (3F, s); IR (neat) 3436, 3070, 1604, 1581 cm^{-1}; HRMS (EI) calcd for $C_{15}H_8Cl_2F_3N$ 328.9986, found 328.9988.

5-Chloro-2-(4-chlorophenyl)-3-(trifluoromethyl)indole (3k): mp 132−134 °C; ^{1}H NMR (CDCl$_3$) δ 7.21 (1H, dd, J = 8.6, 1.9 Hz), 7.27 (1H, d, J = 8.6 Hz), 7.42 (2H, d, J = 8.5 Hz), 7.46 (2H, d, J = 8.5 Hz), 7.76 (1H, s), 8.39 (1H, s, br); ^{13}C NMR (CDCl$_3$) δ 103.6 (q, J = 36.2 Hz), 112.2, 119.5 (q, J = 1.4 Hz), 124.1, 124.2 (q, J = 267.6 Hz), 126.4 (q, J = 1.4 Hz), 127.6, 128.8, 129.0, 130.1, 133.2, 135.9, 138.4 (q, J = 4.1 Hz); ^{19}F NMR (CDCl$_3$) δ −53.50 (3F, s); IR (KBr) 3415, 1575, 1446, 1328 cm^{-1}; HRMS (EI) calcd for $C_{15}H_8Cl_2F_3N$ 328.9986, found 328.9988. Anal. Calcd for $C_{15}H_8Cl_2F_3N$: C, 54.57; H, 2.44; N, 4.24. Found: C, 54.19; H, 2.84; N, 4.31.

3-(4-Chlorophenyl)-2-(trifluoromethyl)-5-methylindole (2l): ^{1}H NMR (CDCl$_3$) δ 2.42 (3H, s), 7.19 (1H, d, J = 8.4 Hz), 7.33 (1H, d, J = 8.5 Hz), 7.35 (1H, s), 7.43 (4H, s), 8.39 (1H, s, br); ^{13}C NMR (CDCl$_3$) δ 21.4, 111.4, 118.0 (q, J = 2.6 Hz), 120.0, 121.3 (q, J = 36.9 Hz), 121.6 (q, J = 269.3 Hz), 127.1, 127.3, 128.6, 130.8, 131.0, 131.2, 133.2, 133.5; ^{19}F NMR (CDCl$_3$) δ −57.33 (3F, s); IR (neat) 3438, 2925, 1494, 1377, 1328 cm^{-1}; HRMS (EI) calcd for $C_{16}H_{11}ClF_3NO$ 309.0532, found 309.0531.

2-(4-Chlorophenyl)-3-(trifluoromethyl)-5-methylindole (3l): ^{1}H NMR (CDCl$_3$) δ 2.48 (3H, s), 7.11 (1H, d, J = 8.5 Hz), 7.28 (1H, d, J = 8.5 Hz), 7.44 (2H, d, J = 9.0 Hz), 7.50 (2H, d, J = 8.5 Hz), 7.59 (1H, s), 8.21 (1H, s, br); ^{13}C NMR (CDCl$_3$) δ 21.6, 103.4 (q, J = 36.1 Hz), 110.8, 119.6 (q, J = 1.3 Hz), 124.7 (q, J = 276.9 Hz), 125.3, 125.7 (q, J = 1.8 Hz), 128.9, 129.6, 130.2, 131.4, 133.3, 135.5, 135.05 (q, J = 3.9 Hz); ^{19}F NMR (CDCl$_3$) δ −53.41 (3F, s); IR (neat) 3411, 3047, 2925, 1600 cm^{-1}; HRMS (EI) calcd for $C_{16}H_{11}F_3NO$ 309.0532, found 309.0531.

3-(4-Chlorophenyl)-2-(trifluoromethyl)-5-nitroindole (2m): mp 206−208 °C; ^{1}H NMR (CDCl$_3$) δ 7.44 (2H, d, J = 8.5 Hz), 7.51 (2H, d, J = 8.0 Hz), 7.57 (1H, d, J = 9.0 Hz), 8.28 (1H, dd, J = 9.0, 2.0 Hz), 8.55 (1H, s), 9.19 (1H, s, br); ^{13}C NMR (CDCl$_3$) δ 112.3, 118.3, 120.6, 120.7 (q, J = 3.0 Hz), 120.7 (q, J = 270.4 Hz), 124.4 (q, J = 37.6 Hz), 126.6, 128.8, 129.1, 131.0, 134.7, 137.6, 143.2; ^{19}F NMR (CDCl$_3$) δ −58.00 (3F, s); IR (KBr) 3338, 2927, 1720, 1585, 1512 cm^{-1}; HRMS (EI) calcd for $C_{15}H_8ClF_3N_2O_2$ 340.0226, found 340.0226.

2-(4-Chlorophenyl)-3-(trifluoromethyl)-5-nitroindole (3m): mp 166−168 °C; ^{1}H NMR (CDCl$_3$) δ 7.50−7.52 (3H, m), 7.56 (2H, d, J = 8.5 Hz), 8.21 (1H, dd, J = 9.0, 2.0 Hz), 8.75 (1H, s), 8.97 (1H, s, br); ^{13}C NMR (CDCl$_3$) δ 105.9 (q, J = 37.7 Hz), 111.6, 117.2 (q, J = 1.2 Hz), 119.2, 123.8 (q, J = 267.5 Hz), 124.9 (q, J = 1.6 Hz), 128.1, 129.2, 130.2, 136.5, 137.8, 140.6 (q, J = 3.8 Hz), 143.2; ^{19}F NMR (CDCl$_3$) δ −53.83 (3F, s); IR (KBr) 3357, 1625, 1492, 1323 cm^{-1}; HRMS (EI) calcd for $C_{15}H_8ClF_3N_2O_2$ 340.0226, found 340.0222.

3-(4-Chlorophenyl)-2-(trifluoromethyl)-6-methoxyindole (2n): mp 142−144 °C; ^{1}H NMR (CDCl$_3$) δ 3.86 (3H, s), 6.85−6.88 (2H, m), 7.43 (4H, s), 7.45 (1H, d, J = 8.5 Hz), 8.39 (1H, s, br); ^{13}C NMR (CDCl$_3$) δ 55.6, 94.1, 112.3, 118.7 (q, J = 3.2 Hz), 119.9 (q, J = 37.4 Hz), 121.3, 121.5, 121.6 (q, J = 268.6 Hz), 128.6, 130.7, 131.1, 133.5, 135.8, 158.7; ^{19}F NMR (CDCl$_3$) δ −57.12 (3F, s); IR (KBr) 3355, 3070, 1635, 1600, 1506, 1490 cm^{-1}; HRMS (EI) calcd for $C_{16}H_{11}ClF_3NO$ 325.0481, found 325.0488.

2-(4-Chlorophenyl)-3-(trifluoromethyl)-6-methoxyindole (3n): mp 176−178 °C; ^{1}H NMR (CDCl$_3$) δ 3.38 (3H, s), 6.85 (1H, d, J = 2.0 Hz), 6.91 (1H, dd, J = 9.0, 2.5 Hz), 7.43 (2H, d, J = 8.5 Hz), 7.49 (2H, d, J = 8.5 Hz), 7.67 (1H, d, J = 9.0 Hz), 8.24 (1H, s, br); ^{13}C NMR (CDCl$_3$) δ 55.6, 94.3, 103.8 (q, J = 35.8 Hz), 111.9, 119.7 (q, J = 1.1 Hz), 120.8, 124.6 (q, J = 267.5 Hz), 128.9, 129.9, 129.6, 130.1, 135.3, 135.9 (q, J = 4.1 Hz), 157.4; ^{19}F NMR (CDCl$_3$) δ −53.30 (3F, s); IR (KBr) 3292, 3060, 1633, 1573 cm^{-1}; HRMS (EI) calcd for $C_{16}H_{11}ClF_3NO$ 325.0481, found 325.0482.

5,6-Dichloro-3-(4-chlorophenyl)-2-(trifluoromethyl)indole (2o): mp 119−121 °C; ^{1}H NMR (CDCl$_3$) δ 7.39 (2H, d, J = 8.4 Hz), 7.46 (2H, d, J = 8.5 Hz), 7.58 (1H, s), 7.65 (1H, s), 8.57 (1H, s, br); ^{13}C NMR (CDCl$_3$) δ 113.3, 118.2 (q, J = 3.1 Hz), 121.0 (q, J = 269.8 Hz), 121.9, 123.0 (q, J = 37.6 Hz), 126.1, 126.7, 128.9, 129.3, 129.6, 131.0, 133.4, 134.2; ^{19}F NMR (CDCl$_3$) δ −57.79 (3F, s); IR (KBr) 3415, 1560, 1494 cm^{-1}; HRMS (EI) calcd for $C_{15}H_7Cl_3F_3N$ 362.9596, found 362.9595. Anal. Calcd for $C_{15}H_7Cl_3F_3N$: C, 49.42; H, 1.94; N, 3.84. Found: C, 49.09; H, 2.18; N, 3.80.

5,6-Dichloro-2-(4-chlorophenyl)-3-(trifluoromethyl)indole (3o): mp 169−171 °C; ^{1}H NMR (CDCl$_3$) δ 7.47 (2H, d, J = 8.6 Hz), 7.51 (2H, d, J = 8.5 Hz), 7.51 (1H, s), 7.87 (1H, s), 8.39 (1H, s, br); ^{13}C NMR (CDCl$_3$) δ 103.7 (q, J = 36.5 Hz), 112.6, 121.1 (q, J = 1.6 Hz), 123.9 (q, J = 267.8 Hz), 125.1 (q, J = 1.6 Hz), 126.3, 127.8, 128.5, 129.2, 130.2, 133.6, 136.2, 139.1 (q, J = 4.0 Hz); ^{19}F NMR (CDCl$_3$) δ −53.76 (3F, s); IR (KBr) 3413, 1550, 1456, 1338 cm^{-1}; HRMS (EI) calcd for $C_{15}H_7Cl_3F_3N$ 362.9596, found 362.9602.

2-(2,2,2-Trifluoroethyl)-3-(4-methoxyphenyl)indole (4b). This compound could not be purified by silica gel column chromatography. Only observed peaks are shown below: ^{1}H NMR (CDCl$_3$) δ 3.62 (2H, q, J = 10.6 Hz), 3.87 (3H, s), 7.01 (2H, d, J = 8.3 Hz), 8.20 (1H, s, br); ^{19}F NMR (CDCl$_3$) δ −64.77 (3F, t, J = 11.84 Hz) ppm.

3-(2,2,2-Trifluoroethyl)-2-(4-methoxyphenyl)indole (5b): mp 128−130 °C; ^{1}H NMR (CDCl$_3$) δ 3.56 (2H, q, J = 10.50 Hz), 3.86 (3H, s), 7.01 (2H, d, J = 8.5 Hz), 7.18 (1H, t, J = 7.0 Hz), 7.22 (1H, t, J = 8.5 Hz), 7.36 (1H, d, J = 8.0 Hz), 7.47 (2H, d, J = 9.0 Hz), 7.64 (1H, d, J = 8.0 Hz), 8.14 (1H, s, br); ^{13}C NMR (CDCl$_3$) δ 30.2 (q, J = 31.1 Hz), 55.4, 101.2 (q, J = 3.5 Hz), 110.8, 114.4, 119.3, 120.3, 122.5, 124.4, 126.7 (q, J = 278.0 Hz), 128.9, 129.8, 135.4, 137.8, 159.8; ^{19}F NMR (CDCl$_3$) δ −64.90 (3F, t, J = 11.26 Hz); IR (KBr) 3344, 3100, 1614, 1506 cm^{-1}; HRMS (EI) calcd for $C_{17}H_{14}F_3NO$ 305.1027, found 305.1022. Crystal data $C_{17}H_{14}F_3NO$, M = 305.30, triclinic, $P1$ (no. 2), a = 9.386(3) Å, b = 10.943(2) Å, c = 7.482(2) Å, α = 100.20(2)°, β = 104.51(2)°, γ = 91.21(2)°, V = 730.5(3) Å^3, Z = 2, D_c = 1.388 g/cm^{-3}, μ(Cu Kα) = 9.62 cm^{-1}, T = 198 K, colorless block; 7112 independent measured reflections, F^2 refinement, R_1 = 0.038, wR_2 = 0.113, 2589 independent observed absorption corrected reflections, $2\theta_{\max}$ = 133.4°.

2-(2,2,2-Trifluoroethyl)-3-(4-chlorophenyl)indole (4c): mp 118−120 °C; ^{1}H NMR (CDCl$_3$) δ 3.60 (2H, q, J =

10.5 Hz), 7.15 (1H, t, $J = 8.0$ Hz), 7.27 (1H, t, $J = 7.5$ Hz), 7.38−7.41 (3H, m), 7.45 (2H, d, $J = 8.5$ Hz), 7.56 (1H, d, $J = 8.0$ Hz), 8.25 (1H, s, br); ^{13}C NMR ($CDCl_3$) δ 31.7 (q, $J = 31.1$ Hz), 110.9, 118.0, 119.4, 120.6, 123.1 (q, $J = 2.9$ Hz), 123.3, 125.3 (q, $J = 277.5$ Hz), 127.0, 129.0, 131.0, 132.3, 132.9, 135.8; ^{19}F NMR ($CDCl_3$) δ −64.76 (3F, t, $J = 10.71$ Hz); IR (KBr) 3409, 3058, 2925, 1494 cm^{-1}; HRMS (FAB) Calcd for $C_{17}H_{13}ClF_3N$ (M + H) 309.0580, found 309.0648.

3-(2,2,2-Trifluoroethyl)-2-(4-chlorophenyl)indole (5c): mp 126−128 °C; ^{1}H NMR ($CDCl_3$) δ 3.55 (2H, q, $J = 10.6$ Hz), 7.19 (1H, t, $J = 7.2$ Hz), 7.25 (1H, t, $J = 7.15$ Hz), 7.36 (1H, d, $J = 8.0$ Hz), 7.44−7.48 (4H, m), 7.66 (1H, d, $J = 7.9$ Hz), 8.12 (1H, s, br); ^{13}C NMR ($CDCl_3$) δ 30.2 (q, $J = 31.2$ Hz), 102.2 (q, $J = 3.0$ Hz), 110.9, 119.5 (q, $J = 1.4$ Hz), 120.6, 123.1, 126.5 (q, $J = 277.7$ Hz), 128.7, 129.3, 129.7, 130.4, 134.7, 135.7, 136.5; ^{19}F NMR ($CDCl_3$) δ −64.88 (3F, t, $J = 10.15$ Hz); IR (KBr) 3408, 3049, 1664, 1456 cm^{-1}; HRMS (FAB) calcd for $C_{17}H_{13}ClF_3N$ (M + H) 309.0580, found 309.0653.

Supporting Information Available: Characterization data, ^{1}H NMR and ^{13}C NMR spectra of **2a**−**o**, **3a**−**o**, **4b**,**c**, and **5b**,**c**, and X-ray data of **2c** and **5b**. This material is available free of charge via the Internet at http://pubs.acs.org.

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