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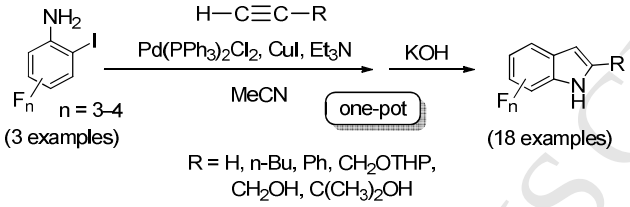

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Synthesis of indoles with a polyfluorinated benzene ring

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ABSTRACT

A two-step sequence consisting of a Sonogashira coupling of polyfluorinated 2-iodoanilines with terminal alkynes, followed by a KOH promoted cyclization of the 2-alkynylanilines thus formed, has been developed as a one–pot synthesis of 2-R-indoles (R = n-Bu, Ph, $CH_2OTHP \rightarrow CH_2OH$, $C(CH_3)_2OH \rightarrow H$) containing a polyfluorinated benzene moiety.

1. Introduction

The indole nucleus is a structural component in a vast number of biologically active natural and synthesized compounds and pharmaceuticals, and so their efficient construction represents an important challenge. Considerable attention is attracted by fluorinated indoles because it is firmly established that fluorine substitution can influence the biological activity of organic molecules.[1,2] There are a number of biologically active functionalized indoles with 1–4 fluorine atoms in the benzene ring.[3–5] In particular, the 4,5,6,7-tetrafluoroindole derivatives exhibit cytotoxic activity,[5] antiandrogenic, gene induction, gene expression, antiproliferative, antibacterial activity,[6] antiviral, anti HIV effects[7] and receptor binding properties.[5,8] For molecular design in this area, it is important to note that polyfluorination affords increased fluorine nucleofugicity.[9] This opens opportunities for nucleophilic substitution in the benzene ring,[10] with the possibility of traditional electrophilic modifications of the pyrrole ring being retained.[11,12] In view of the above reasons, the development of a practical and efficient approach for the construction of an indole skeleton with a polyfluorinated benzene moiety is an important problem for organic synthesis.

The classical Fisher indole synthesis was only sporadically applied to obtain the indoles with a substituted pyrrole moiety,[13] first of all because of difficulties in accessing polyfluoroarylamines unsubstituted *ortho* to an amino group and secondly the difficulty of their transformation into the corresponding polyfluoroarylhydrazines. The latter is implicitly illustrated by the fact that 4,5,6,7-tetrafluoroindole has not been prepared by the Fisher method to date. To synthesize this compound and its substituted analogues, methods involving a nucleophilic heterocyclization of pentafluoroaniline[14] and pentafluorophenylethylamine derivatives[15,16] have been developed. Recently the problem of the inaccessibility of 2-unsubstituted polyfluorinated arylamines was solved by working out methods for the selective *ortho*-hydrodefluorination of polyfluorinated *N*-acetylarylamines[17,18] and dechlorination of polyfluorochloroanilines.[19] Thanks to this favorable prerequisite, modern methods of the indole skeleton construction based on the 2-alkynylanilines cyclizations[20,21] seem more promising. Polyfluorinated 2-alkynylanilines – the potentially universal building blocks to assemble a diversity of polyfluorobenzo azaheterocycles – can be easily prepared by the catalytic cross-condensation of polyfluorinated 2-iodanilines with terminal alkynes.[22]

In this paper, we describe the synthesis of indoles containing a polyfluorinated benzene ring by a cyclization of respective 2-alkynylanilines. In addition, we trialled the possibility of a one-

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pot version of this reaction starting directly from polyfluorinated 2-iodoanilines, without isolation of 2-alkynylanilines thus formed.

2. Results and discussion

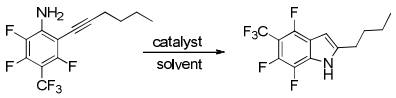
2.1. Cyclization of polyfluorinated 2-alkynylanilines

The cyclization of 2-alkynylanilines is known to be promoted by copper halides,[23,24] $NaAuCl_4 \cdot H_2O$,[25] Pd(II) salts,[26] Lewis acids.[27] The suggested heterocyclization mechanism by transition metal compounds proceeds via the π-coordination of a metal cation to the triple bond, thus providing the electrophilic activation of its terminal carbon atom.[28] One can expect that the introduction of fluorine atoms or a trifluoromethyl group, as electron-withdrawing substituents, into the aniline benzene ring decreases a π-donating function of the triple bond and makes problematic the efficiency of this type of catalysis. Besides, the cyclization of 2-alkynyl-NR-anilines was reported to be promoted by bases such as EtONa (R = CO_2Me),[21] Bu^tOK (R = CO_2Pr^i),[29] Bu_4NF (R = CO_2Et, CO_2Bu^t, CHO, Ac, SO_2Me).[30] Hydrogen bonding with a base increases the nucleophilicity of the amino group and its ability to attack the terminal carbon of the triple bond.[31] Within this mechanism, the indolization can be facilitated by electron withdrawing substituents on the aromatic ring, enhancing the NH acidity of the amino group and, facilitating its deprotonation.[32–34] One can expect, therefore, that the fluorine atoms and CF_3 group on the benzene ring are favourable for the base catalysis in the reaction under study.

2,3,5-Trifluoro-6-(hex-1-yn-1-yl)-4-(trifluoromethyl)aniline (**1aa**) was used as the model substrate to select an appropriate catalyst for the ring closure of the polyfluorinated 2-alkynylanilines **1** into indoles **2** (Table 1). The results of Table 1 show that Cu (I) salts and $AgNO_3$ (entries 1–4) had no catalytic activity and K_2CO_3 (entries 5, 6) had low catalytic activity in the heterocyclization of 2-alkynylaniline **1aa**. When KOH or $Et_4NF \cdot H_2O$, stronger bases than K_2CO_3, (entries 7, 8) and $PdCl_2$ (entries 9, 10), were used as the catalysts, the complete transformation of the aniline into the respective indole **2aa** was observed under reflux conditions. Note also that $Et_4NF \cdot H_2O$ showed good catalytic activity under lowered temperature (entry 12), in contrast to the absence of catalytic activity of KOH and $PdCl_2$ (entries 11, 13) at the same temperature.

The last three catalysts, which promote the cyclization of alkynylaniline **1aa,** were used to test the possibility of the cyclization of polyfluorinated 2-(3-hydroxyalkyne-1-yl)anilines without protection of the hydroxy group. In this regard, the transformations of 4-[2-amino-3,4,6-trifluoro-5-(trifluoromethyl)-phenyl]-2-methylbut-3-yn-2-ol (**1ab**) in the presence of the catalysts were studied (Table 2). $PdCl_2$ was not effective for the aniline **1ab** transformation (entry 1). $Et_4NF \cdot H_2O$ exhibited the high catalytic activity in the transformation and allowed us to obtain 2-(2-hydroxy-2-propyl)-4,6,7-trifluoro-5-(trifluoromethyl)indole (**2ab**) as the only product (entry 2). Aniline **1ab** in the presence of KOH in MeCN medium gave, besides indole **2ab**, the 4,6,7-trifluoro-5-(trifluoromethyl)indole (**2ac**) unsubstituted on the pyrrole ring (entry 2 of Table 2). The precursor of **2ac** is, most likely, 2-ethynyl-4-(trifluoromethyl)-trifluoroaniline (**1ac**) derived from the starting alkynylaniline **1ab** via the retro-Favorsky reaction. The formation of polyfluorinated 2-ethynylanilines was observed in the reaction of the analogues of aniline **1ab** in boiling benzene in the presence of KOH.[22] However, the transformation of **1ab** into **1ac** did not proceed under similar conditions (entry 4), and a higher temperature (boiling toluene) was needed to obtain the latter (along with a small amount of the reported[17] 2,3,5-trifluoro-4-(trifluoromethyl)aniline (**3**)) (entry 5). Apparently, aniline **3** formation is a consequence of **1ac** deprotonation, followed by fragmentation of the arising acetylenide (**1ac**)**–H** with the carbon removal. The latter is believed to be facilitated by the relatively high stability of 2-amino-3,5,6-trifluoro-4-trifluoromethylphenyl anion ((**3**)**–H**) thus formed (Scheme 1).[35]

Table 1. Cyclization of aniline **1aa**

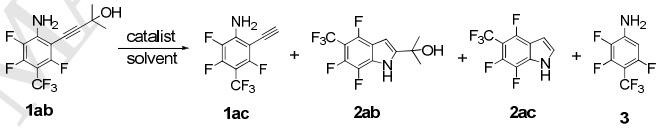


1aa **2aa**

Entry	Catalyst	Solvent	Conditions	Yield[a], mol %
1	CuCl (0.5 equiv)	DMF	110 °C, 3 h	n. r.[b]
2	CuI (0.5 equiv)	DMF	Reflux, 3 h	n. r.
3	CuI (0.5 equiv)	MeCN	Reflux, 3 h	n. r.
4	$AgNO_3$ (0.5 equiv)	MeCN	Reflux, 3 h	n. r.
5	K_2CO_3 (2 equiv)	MeCN	Reflux, 3 h	4
6	K_2CO_3 (2 equiv)	MeCN	Reflux, 24 h	15
7	KOH (5 equiv)	MeCN	Reflux, 3 h	100
8	$Et_4NF \cdot H_2O$ (2 equiv)	MeCN	Reflux, 3 h	100
9	$PdCl_2$ (0.2 equiv)	MeCN	Reflux, 3 h	100
10	$PdCl_2$ (0.2 equiv) $FeCl_3$ (0.2 equiv)	$ClCH_2CH_2Cl$	Reflux, 3 h	100
11	KOH (5 equiv)	MeCN	50 °C, 3 h	n. r.
12	$Et_4NF \cdot H_2O$ (2 equiv)	MeCN	50 °C, 3 h	100
13	$PdCl_2$ (0.2 equiv)	MeCN	50 °C, 3 h	n. r.

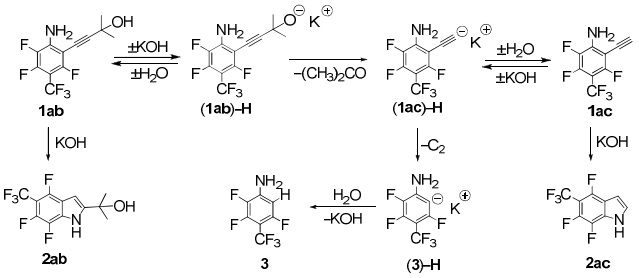
[a]Content in the product mixture (NMR ^{19}F).
[b]**1aa** was recovered.

Table 2. Cyclization of aniline**1ab**



1ab **1ac** **2ab** **2ac** **3**

Entry	Catalyst	Solvent	Condi-tions	Content in the mixture, mol %				
				1ab	**1ac**	**2ab**	**2ac**	**3**
1	$PdCl_2$ (0.2 equiv)	MeCN	Reflux 3 h	100	–	–	–	–
2	$Et_4NF \cdot H_2O$ (2 equiv)	MeCN	Reflux 3 h	–	–	100	–	–
3	KOH (3 equiv)	MeCN	Reflux 3 h	–	–	69	31	–
4	KOH (5 equiv)	Benzene	Reflux 3 h	100	–	–	–	–
5	KOH (5 equiv)	Toluene	Reflux 0.5 h	–	90	–	–	10
6	KOH (5 equiv)	DMF	100 °C 3 h	–	–	–	–	100



Scheme 1

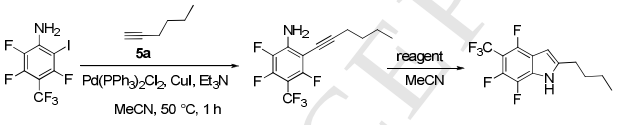
Support for this assumption comes from the following result on the solvent influence on the reaction. The use of a bipolar aprotic solvent (DMF), which effectively solvates anions, instead of toluene led to the predominant formation of aniline **3** (entry 6 of Table 2). It is noteworthy that indole **2ac** (entry 3 of Table 2) and 2-etynylaniline **1ac** (entry 5) were formed in MeCN and toluene solvents, correspondingly, in the presence of KOH as the catalyst. This suggested that the synthesis of the indoles without substituent on the pyrrole ring can be performed.

Based on the above data (entries 2 and 3 of Table 2), $Et_4NF{\cdot}H_2O$ and KOH were found to be the most efficient catalysts for the **1ab** indolization in MeCN solvent.

2.2. One–pot synthesis of polyfluorinated indoles

The above results on the study of the indolization of anilines **1aa** and **1ab** prompted us to attempt the one–pot synthesis of indoles via the sequence of catalytic cross-condensation of 2-iodo-3,5,6-trifluoro-4-(trifluoromethyl)aniline (**4a**) with hex-1-yne (**5a**) and cyclization of aniline **1aa** thus formed without its isolation. We found out that the replacement of NEt_3, which was previously[22] used as the solvent, with MeCN significantly decreases the duration and lowers the temperature of the Sonogashira reaction of polyfluorinated 2-iodoanilines. Besides, $Et_4NF{\cdot}H_2O$ or $PdCl_2$ were not effective in the one–pot synthesis of indole **2aa**, while KOH gave fine result (Table 3). Therefore, KOH was used as the heterocyclization catalyst at the second stage of the synthesis of a series of polyfluorinated indoles.

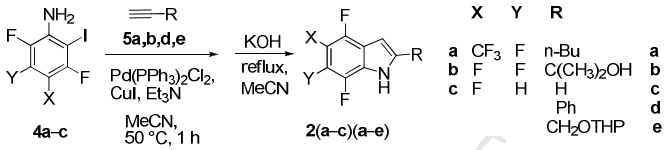
Table 3. One–pot synthesis of indole **2aa**



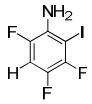
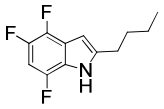
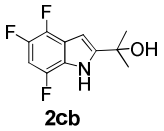
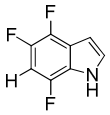
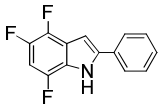
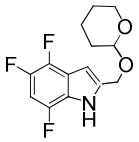
Entry	Catalyst	Conditions	Content in the mixture, mol %	
			1aa	**2aa**
1	$PdCl_2$ (0.2 equiv)	Reflux, 3 h	100	–
2	$Et_4NF{\cdot}H_2O$ (2 equiv)	Reflux, 3 h	100	–
3	KOH (3 equiv)	Reflux, 3 h	–	100
4	KOH (3 equiv)	50 °C, 3 h	100	–
5	KOH (3 equiv)	Reflux, 1 h	40	60

The interaction of anilines **4(a–c)** with alkynes **5a,b,d,e** in the presence of $Pd(PPh_3)_2Cl_2$, CuI and NEt_3 in MeCN medium at 50 ºC for 1 h, followed by the cyclization of 2-alkynylanilines **1** upon addition of 3 equivalents of KOH under reflux conditions for 3 h, resulted in a one–pot synthesis of indoles **2(a–c)(a–e)** (Table 4).

Table 4. One–pot synthesis of indoles **2(a–c)(a–e)**



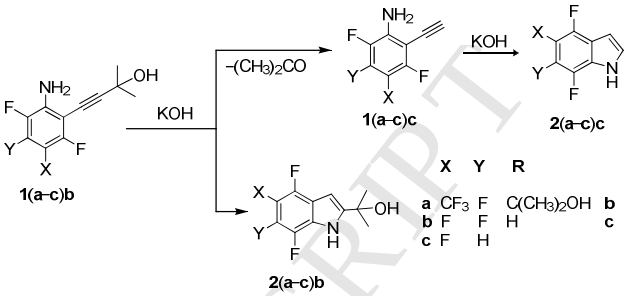
Entry	Substrate	Alkyne	Product	Duration of the second step, h	Yield, %
1	**4a**	**5a**	**2aa**	3	68
2	**4a**	**5b**	**2ab**	2	52
			2ac		45
3	**4a**	**5d**	**2ad**	3	73
4	**4a**	**5e**	**2ae**	3	76
5	**4b**	**5a**	**2ba**	3	85
6	**4b**	**5b**	**2bb**	2	17
			2bc		74
7	**4b**	**5d**	**2bd**	3	90

8	**4b**	**5e**	 **2be**	3	87
9	 **4c**	**5a**	 **2ca**	3	72
10	**4c**	**5b**	 **2cb**	4	8
			 **2cc**		77
11	**4c**	**5e**	 **2cd**	3	85
12	**4c**	**5d**	 **2ce**	3	75

Attempts to increase the yields of indoles **2(b–c)b** by using $Et_4NF{\cdot}H_2O$ as the catalyst in order to cyclize alkynes **1(b–c)b** in MeCN medium, in analogy to the synthesis of **2ab** (entry 2 of Table 2), failed. In this case, as well as in the case of KOH, indoles **2(b–c)c** were the main products, indoles **2bb** and **2cb** having been isolated in 30% and 16% yields based on iodanilines **4b** and **4c**, respectively. Besides, we attempted to selectively prepare indole **2ac** by cyclization of aniline **1ac**, obtained in turn from alkynylaniline **1ab** via the retro-Favorsky reaction in the KOH/toluene system (entry 2 of Table 5). However, probably because of a volatility of aniline **1ac**, causing its loss upon evaporation of toluene, the yield of the target product was low (14% based on aniline **4a**), even compared with the nonselective one–pot synthesis. Thus, it is more effective to obtain indole **2ac** as a side-product of the alkynylaniline **2ab** cyclization in comparison with the synthesis of indole **2ac** via a sequence of three separate reactions.

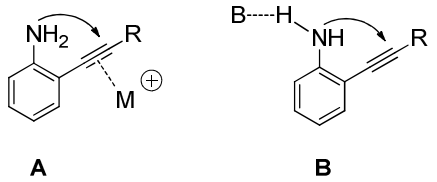
Examining the above data, one can see that the ratio of the formed alcohols **2(a–c)b** and on-pyrrole-unsubstituted indoles **2(a–c)c** changes with the benzene moiety substitution. The question arises, whether this change is associated with a degree of the putative **2(a–c)b** transformation to **2(a–c)c**. Testing the possibility of this transformation to occur, no indole **2bc** was observed to form by heating alcohol **2bb** in MeCN for 3 h under reflux conditions in the presence of 3-fold amount of KOH. This suggests indoles **2(a–c)c** to be derived through the partial retro-Favorsky cleavage of the intermediate anilines **1(a–c)b**, followed by cyclization of 2-ethynylanilines **1(a–c)c** thus formed (Scheme 2).

Presuming the conventional mechanism of the retro-Favorsky reaction (Scheme 2), one can expect that the stability of the incipient acetylenide anions should decrease at the reduction of total electronegativity of substituents in benzene ring in the order **1ab** > **1bb** > **1cb**. Therefore, the retro-Favorsky reaction has to slow down in the order **1ac** > **1bc** > **1cc**. However, contrary to this expectation, the yields of indoles **2(a–c)c** increased in the series 2**ac** < 2**bc** < 2**cc**, and the yields of indoles **2(a–c)b** decreased in the



Scheme 2

series **2ab** > **2bb** > **2cb** (entries 2, 6 and 10 of Table 4). This suggests that, at the reduction of total electronegativity of substituents in benzene ring in the above order, the cyclization of the intermediate 2-alkynylanilines **1(a–c)b** into indoles **2(a-c)b** slows down more progressively than the retro-Favorsky reaction does. As a result, a longer time was necessary to complete the transformation of **1cb** into the respective indoles 2**cb** and 2**cc** (entry 10 of Table 4). Based on the literary data,[16] it can be assumed that, in the course of the 2-alkynylaniline cyclization, two intermediate complexes are formed (structures A and B), depending on the catalyst used. In the complex A, the triple bond, as an electrophilic function, is activated by its π-coordination with a metal cation.[28] In the complex B, the amino group, as a nucleophilic function, is activated by hydrogen bonding with a base.[31] Within these notions, the retardation of cyclization at the reduction of total electron withdrawing effect of substituents in benzene ring is obviously caused by reducing both the triple bond electrophilicity and the N–H acidity.



Figure

*2.3. Hydrolysis of the CH_2OTHP group located in the 2-position of indoles **2(a–c)e***

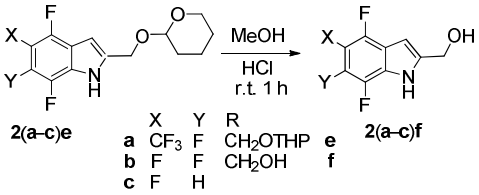
For a molecular design of indoles containing a polyfluorinated benzene moiety, it is interesting to introduce a substituent, which easily undergoes further transformations, into pyrrole ring. In this connection, the indoles **2(a–c)e** containing the CH_2OTHP group in the 2-position were hydrolyzed by HCl in MeOH (by analogy with[36]) to give corresponding 2-hydroxymethylindoles **2(a–c)f** (Table 5).

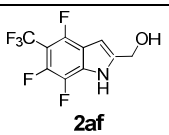
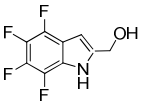
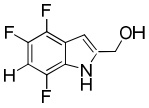
2.4. Spectral data

The structures of all herein prepared polyfluorinated indoles were corroborated by their ^{19}F, ^{1}H and ^{13}C NMR (Tables 6, 7), high resolution mass spectrometry, and IR-spectroscopy data.

Signals in the ^{19}F NMR spectra of indoles **2(a–c)(a–f)** were assigned on the basis of spin coupling constants, which are typical for polyfluorinated benzenes.[37] The ^{1}H and ^{19}F NMR spectra of indoles **2bc** and **2bd** correspond to those reported previously.[38,39] Besides, the ^{19}F NMR characteristics of indoles herein synthesized were in good compliance with those of polyfluorinated on the benzene ring benzothiophens[40] and dibenzofurans.[41] At that, the fluorine resonances showed a high-field shift from benzothiophens through dibenzofurans to indoles, as expected relying on the increase of the heteroatom π-donation along this series.

Table 5. Synthesis of indoles **2(a–c)f**



Entry	Substrate	Product	Yield, %
1	**2ae**	 **2af**	90
2	**2be**	 **2bf**	96
3	**2ce**	 **2cf**	96

The ^{13}C NMR signals were assigned taking into account that the absolute $J_{C,F}$ values change in a sequence $^{1}J_{C,F} >> {}^{2}J_{C,F} > {}^{3}J_{C,F} > {}^{4}J_{C,F}$.[42] The assignment of carbon resonances of the C–F fragments was confirmed by comparing the respective $^{1}J_{C,F}$ values with those observed in satellite signals of the corresponding fluorine resonances in the ^{19}F NMR spectra. The C^{7a} and C^{3a} signals were distinguished by the consecutive C^{7a}–F^{7} and C^{3a}–F^{4} spin decoupling. Indicatively, the relative location of the ^{13}C resonances of indoles **2b(a–f)** is analogous to that reported for the parent indole: $C^{7a} > C^{3a}$, $C^{4} > C^{7}$, $C^{2} > C^{3}$.[43] As one can see from Table 7, the 2-substituent variation does not appreciably influence carbon chemical shifts of the fluorinated benzene ring.

Comparing the ^{13}C NMR spectra of **2bc** and the parent indole exhibits the introduction of four fluorine atoms into the benzene moiety to cause about a 13–14 ppm high-field shift of the C^{3a} and C^{7a} signals. The similar was reported earlier for 3-methyl-4,5,6,7-tetrafluoro-1H-indazole.[44]

3. Conclusion

Thus, we have developed the synthesis of a wide range of the indoles containing a polyfluorinated benzene ring. This makes this class of previously reported (in a small part) but difficultly attainable or unknown (mainly) compounds quite accessible for regular study of their chemistry and molecular design of new potentially biologically active compounds on this ground. A one–pot version of this synthesis have been realized as a sequence of cross-coupling of polyfluorinated 2-iodoanilines with terminal alkynes followed by in situ cyclization of polyfluorinated 2-alkynylanilines thus formed without their isolation. This allowed us to obtain the target indoles in good yields. The possibility has been shown to obtain the indoles of this type with a non-substituted pyrrole moiety in reasonable yields as by-products of the synthesis of their 2-(CMe_2OH)-substituted derivatives.

4. Experimental section

4.1. General methods

All the cross-coupling reactions were carried out in oven-dried glassware under an argon atmosphere. All solvents were purified using standard procedures and dried before use. Et_3N, MeCN, $ClCH_2CH_2Cl$ and DMF were distilled and kept over CaH_2 before to use. Toluene was distilled and used without drying. 2-Iodo-3,5,6-trifluoro-4-(trifluoromethyl)aniline (**4a**).[22] 2-Iodo-3,4,5,6-tetrafluoroaniline (**4b**),[22] 2-iodo-3,4,6-trifluoroaniline (**4c**),[22] 2-(prop-2-in-1-yloxy)oxane (**5e**),[45] $Pd(PPh_3)_2Cl_2$[46] were prepared accoding to literature procedures. CuCl was washed with 0.1% aqueous sulfuric acid, then H_2O, acetone, diethyl ether and air dried.

KOH (≥90 %, flakes) and $Et_4NF{\cdot}H_2O$ (97%) were kept over P_2O_5. Other starting materials were obtained from commercial supplies and used without purification.

The TLC product isolation was carried out on Sorbfil plates (UV 254). Visualization of the developed chromatograms was performed by UV light. Compounds **2(a–c)c** were purified by silica gel (100–300 mesh) column chromatography. To obtain analytically pure samples, the synthesized indoles were sublimed at 100–150 °C under vacuum (~15 Torr).

NMR spectra were recorded on a Bruker Avance-300 (300.13 MHz for ^{1}H and 282.37 MHz for ^{19}F) and Avance-400 (400.13 MHz for ^{1}H, 376.44 MHz for ^{19}F and 100.62 MHz for ^{13}C) spectrometers. Deuterochloroform ($CDCl_3$) was used as solvent, with residual $CHCl_3$ (δ_H = 7.26 ppm) or $CDCl_3$ (δ_C = 77.0 ppm) being employed as internal standards. ^{13}C NMR spectra were registered with C–H spin decoupling. Masses of molecular ions were determined by HRMS on a DFS Thermo scientific instrument (EI, 70 eV). Melting points were recorded on a Melter-Toledo FP81 Thermosystem apparatus. The IR spectra were recorded on a Bruker Vector 22 spectrometer (KBr or thin layer). Elemental analyses were performed on a Euro EA-3000 CHNS analyzer, or on Carlo Erba 1106 CHN elemental analyzer.

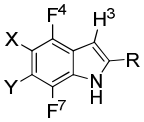
*4.2. General procedure for synthesis 2-alkynylanilines **1aa**, **1ab**, **1bb** and **1cb***

To a stirred solution of aniline **4a** (341 mg, 1 mmol) [or **4b** (291 mg, 1 mmol), or **4c** (273 mg, 1 mmol)], alkyne **5a** (246 mg, 3 mmol) [or **5b** (252 mg, 3 mmol)] in dry MeCN (7 mL) were added $Pd(PPh_3)_2Cl_2$ (28 mg, 0.04 mmol), CuI (17 mg, 0.09 mmol) and Et_3N (1.5 mL) at room temperature under an argon atmosphere. The mixture was heated at 50 °C for 1 h with stirring. The reaction mixture was allowed to cool down to room temperature, and CH_2Cl_2 (10 mL) was added. The mixture was poured into H_2O (20 mL) and extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were washed with H_2O (10 mL) and dried ($MgSO_4$). After evaporation of the solvent *in vacuo*, the crude product was obtained (the ^{1}H and ^{19}F NMR spectra closely agree with the literature data[22]) and used further without purification.

*4.3. 2-Ethynyl-3,5,6-trifluoro-4-(trifluoromethyl)aniline (**1ac**)*

A solution of crude **1ab** in toluene (20 mL) was heated to 70 °C, KOH (168 mg, 3 mmol) was added, and the mixture was heated under reflux with stirring for 45 min. The mixture was cooled to room temperature, diluted with CH_2Cl_2 (10 mL), poured into H_2O (20 mL), neutralized with 5% aqueous AcOH up to pH = 7 and extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were washed with H_2O (10 mL) and dried ($MgSO_4$).

Table 6. ^{1}H and ^{19}F NMR chemical shifts (ppm) and coupling constants (Hz) for indoles **2(a–c)(a–f)** ($CDCl_3$)



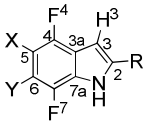
2(a–c)(a–f)

	X	Y	R	
a	CF_3	F	n-Bu	**a**
b	F	F	$C(CH_3)_2OH$	**b**
c	F	H	H	**c**
			Ph	**d**
			CH_2OTHP	**e**
			CH_2OH	**f**

Compound	NH	H^3	F^4	X	Y	F^7	R
2aa	8.34 (1H, bs)	6.36 (1H, ddt) $J_{H}3,_{F}4 = 2.4$ $J_{H}3,_{F}7 = 3.2$ $J_{H}3,_{CH2} \approx 1$	–126.2 (1F, qddd) $J_{F}4,_{CF3} = 24.4$ $J_{F}4,_{F}7 = 17.9$ $J_{F}4,_{F}6 = 5.4$ $J_{F}4,_{H}3 = 2.4$	–56.0 (3F, dd) $J_{CF3,F}4 = 24.4$ $J_{CF3,F}6 = 20.7$	–151.4 (1F, qdd) $J_{F}7,_{CF3} = 20.7$ $J_{F}6,_{F}7 = 19.8$ $J_{F}6,_{F}4 = 5.4$	–164.7 (1F, ddd) $J_{F}7,_{F}4 = 17.9$ $J_{F}7,_{F}6 = 19.8$ $J_{F}7,_{H}3 = 3.2$	0.95 (3H, t, CH_3) $J_{H,H} = 7.3$; 1.41 (2H, qt, CH_2CH_3), $J_{CH2,CH3} = 7.3$, $J_{CH2,CH2} \approx 7.5$; 1.70 (2H, tt, $CH_2CH_2CH_3$), $J_{CH2,CH2} \approx 7.5$; 2.75 (2H, t, CH_2C_{ar}) $J_{H,H} \approx 7.5$
2ab	8.97 (1H, bs)	6.42 (1H, dd) $J_{H}3,_{F}4 = 2.3$, $J_{H}3,_{F}7 = 3.1$	–125.6 (1F, qddd) $J_{F}4,_{CF3} = 24.5$, $J_{F}4,_{F}7 = 18.1$, $J_{F}4,_{F}6 = 5.0$, $J_{F}4,_{H}3 = 2.3$	–56.0 (3F, dd) $J_{CF3,F}4 = 24.5$ $J_{CF3,F}6 = 20.6$	–150.0 (1F, qdd) $J_{F}7,_{CF3} = 20.6$ $J_{F}6,_{F}7 = 19.8$ $J_{F}6,_{F}4 = 5.0$	–164.1 (1F, ddd) $J_{F}7,_{F}4 = 18.1$ $J_{F}7,_{F}6 = 19.8$ $J_{F}7,_{H}3 = 3.1$	1.68 (s, 6H, CH_3); 1.95 (1H, s, OH)
2ac	8.81 (1H, bs)	6.71 (1H, ddd) $J_{H}3,_{F}4 = 2.3$ $J_{H}3,_{F}7 = 3.2$ $J_{H}3,_{H}2 = 3.3$	–124.5 (1F, qddd) $J_{F}4,_{CF3} = 24.7$ $J_{F}4,_{F}7 = 18.3$ $J_{F}4,_{F}6 = 4.8$ $J_{F}4,_{H}3 = 2.3$	–56.1 (3F, dd) $J_{CF3,F}4 = 24.7$ $J_{CF3,F}6 = 20.5$	–149.8 (1F, qdd) $J_{F}6,_{CF3} = 20.5$ $J_{F}6,_{F}7 = 19.5$ $J_{F}6,_{F}4 = 4.8$	–164.0 (1F, ddd) $J_{F}7,_{F}4 = 18.3$ $J_{F}7,_{F}6 = 19.5$ $J_{F}7,_{H}3 = 3.2$	7.27 (1H, dd, H^2) $J_{H}2,_{H}3 = 3.3$ $J_{H}2,_{H}1 = 2.3$
2ad	8.75 (1H, bs)	6.91 (1H, dd) $J_{H}3,_{F}4 = 2.3$ $J_{H}3,_{F}7 = 3.0$	–124.9 (1F, qddd) $J_{F}4,_{CF3} = 24.6$ $J_{F}4,_{F}7 = 18.3$ $J_{F}4,_{F}6 = 5.0$ $J_{F}4,_{H}3 = 2.3$	–56.1 (3F, dd) $J_{CF3,F}4 = 24.6$ $J_{CF3,F}6 = 20.6$	–149.0 (1F, qdd) $J_{F}6,_{CF3} = 20.6$ $J_{F}6,_{F}7 \approx 20$ $J_{F}6,_{F}4 = 5.0$	–163.8 (1F, ddd) $J_{F}7,_{F}4 = 18.3$ $J_{F}7,_{F}6 \approx 20$ $J_{F}7,_{H}3 = 3.0$	7.37–7.52 (3H, m, Ph); 7.62–7.67 (2H, m, Ph)
2ae	9.30 (1H, bs)	6.53 (1H, ddm) $J_{H}3,_{F}4, = 2.4$ $J_{H}3,_{F}7 = 3.2$	–122.0 (1F, qddd) $J_{F}4,_{CF3} = 24.6$ $J_{F}4,_{F}7 = 18.2$ $J_{F}4,_{F}6 = 5.0$ $J_{F}4,_{H}3 = 2.4$	–53.0 (3F, dd) $J_{CF3,F}4 = 24.6$ $J_{CF3,F}6 = 20.5$	–146.8 (1F, qdd) $J_{F}6,_{CF3} = 20.5$ $J_{F}6,_{F}7 = 19.5$ $J_{F}6,_{F}4 = 5.0$	–161.2 (1F, ddd) $J_{F}7,_{F}4 = 18.2$ $J_{F}7,_{F}6 \approx 19.5$ $J_{F}7,_{H}3 = 3.2$	1.50–1.90 (6H, m, $CH_2CH_2CH_2$); 3.55–3.63 (1H, m, OCH_2); 3.94–4.01 (1H, m, OCH_2); 4.66 – 4.69 (1H, m, CH); 4.80 (2H, s, CH_2C_{ar})
2af	9.30 (1H, bs)	6.51 (1H, ddm) $J_{H}3,_{F}4 = 2.4$ $J_{H}3,_{F}7 = 3.3$	–125.0 (1F, qddd) $J_{F}4,_{CF3} = 24.6$ $J_{F}4,_{F}7 = 18.2$ $J_{F}4,_{F}6 = 5.0$ $J_{F}4,_{H}3 = 2.4$	–56.1 (3F, dd) $J_{CF3,F}4 = 24.6$ $J_{CF3,F}6 = 20.7$	–149.4 (1F, qdd) $J_{F}6,_{CF3} = 20.7$ $J_{F}6,_{F}7 = 19.5$ $J_{F}6,_{F}4 = 5.0$	–164.0 (1F, ddd) $J_{F}7,_{F}4 = 18.2$ $J_{F}7,_{F}6 = 19.5$ $J_{F}7,_{H}3 = 3.3$	2.44 (1H, bs, OH); 4.84 (2H, s, CH_2C_{ar})
2ba	8.25 (1H, bs)	6.35 (1H, dd) $J_{H}3,_{F}4 = 2.4$ $J_{H}3,_{F}7 = 3.3$	–152.4 (1F, ddd) $J_{F}4,_{F}5 = 20.4$ $J_{F}4,_{F}7 = 16.1$ $J_{F}4,_{F}6 = 2.2$ $J_{F}4,_{H}3 = 2.4$	–171.7 (1F, ddd) $J_{F}5,_{F}4 = 20.4$ $J_{F}5,_{F}6 = 19.6$ $J_{F}5,_{F}7 = 4.1$	–169.3 (1F, ddd) $J_{F}6,_{F}5 = 19.6$ $J_{F}6,_{F}7 = 19.9$ $J_{F}6,_{F}4 = 2.2$	–163.8 (1F, dddd) $J_{F}7,_{F}6 = 19.9$ $J_{F}7,_{F}4 = 16.1$ $J_{F}7,_{F}5 = 4.1$ $J_{F}7,_{H}3 = 3.3$	0.99 (3H, t, CH_3) $J_{H,H} = 7.3$; 1.45 (2H, qt, CH_2CH_3) $J_{CH2,CH3} = 7.3$, $J_{CH2,CH2} \approx 7.5$; 1.74 (2H, tt, $CH_2CH_2CH_3$) $J_{CH2,CH2} \approx 7.5$; 2.77 (2H, t, CH_2C_{ar}) $J_{H,H} \approx 7.5$
2bb	8.76 (1H, bs)	6.37 (1H, dd) $J_{H}3,_{F}4 = 2.3$ $J_{H}3,_{F}7 = 3.1$	–151.9 (1F, ddd) $J_{F}4,_{F}5 = 20.3$ $J_{F}4,_{F}7 = 16.3$ $J_{F}4,_{H}3 = 2.3$ $J_{F}4,_{F}6 = 2.0$	–170.9 (1F, ddd) $J_{F}5,_{F}4 = 20.3$ $J_{F}5,_{F}6 = 19.7$ $J_{F}5,_{F}7 = 4.0$	–167.7 (1F, ddd) $J_{F}6,_{F}7$, $J_{F}6,_{F}5 = 19.7$ $J_{F}6,_{F}4 = 2.0$	–163.2 (1F, ddm) $J_{F}7,_{F}6 = 19.7$ $J_{F}7,_{F}4 = 16.3$ $J_{F}7,_{F}5 = 4.0$ $J_{F}7,_{H}3 = 3.1$	1.67 (6H, s, CH_3); 1.96 (1H, s, OH)

2bc	8.14 (1H, bs)	6.07 (1H, dddd), $J_{H}3,_{F}4$ = 2.2, $J_{H}3,_{F}7$ = 3.1 $J_{H}3,_{H}2$ = 3.0 $J_{H}3,_{H}1$ = 3.0	–148.7 (1F, dddd) $J_{F}4,_{F}5$ = 20.2 $J_{F}4,_{F}7$ = 16.1 $J_{F}4,_{F}6 \approx 2$ $J_{F}4,_{H}3$ = 2.2	–168.0 (1F, ddd) $J_{F}5,_{F}4$ = 20.2 $J_{F}5,_{F}6$ = 19.7 $J_{F}5,_{F}7$ = 4.1	–164.4 (1F, ddd) $J_{F}6,_{F}7$, $J_{F}6,_{F}5$ = 19.7 $J_{F}6,_{F}4 \approx 2$	–160.7 (1F, dddd) $J_{F}7,_{F}6$ = 19.7 $J_{F}7,_{F}4$ = 16.1 $J_{F}7,_{F}5$ = 4.1 $J_{F}7,_{H}3$ = 3.1	6.41 (1H, dd, H^2) $J_{H}2,_{H}3$ = 3.0 $J_{H}2,_{H}1$ = 2.5
2bd	8.51 (1H, bs)	6.87 (1H, dd) $J_{H}3,_{F}4$ = 2.3 $J_{H}3,_{F}7$ = 3.0	–151.3 (1F, dddd) $J_{F}4,_{F}5$ = 20.1 $J_{F}4,_{F}7$ = 16.4 $J_{F}4,_{F}6$ = 1.8 $J_{F}4,_{H}3$ = 2.3	–170.1 (1F, ddd) $J_{F}5,_{F}4$ = 20.1 $J_{F}5,_{F}6$ = 19.8 $J_{F}5,_{F}7$ = 3.7	–163.6 (1F, ddd) $J_{F}6,_{F}5$ = 19.8 $J_{F}6,_{F}7$ = 19.6 $J_{F}6,_{F}4$ = 1.8	–162.9 (1F, dddd) $J_{F}7,_{F}6$ = 19.6 $J_{F}7,_{F}4$ = 16.4 $J_{F}7,_{F}5$ = 3.7 $J_{F}7,_{H}3$ = 3.0	7.31–7.41 (1H, m, Ph); 7.43–7.53 (2H, m, Ph); 7.61–7.66 (2H, m, Ph)
2be	8.96 (1H, bs)	6.49 (1H, dd) $J_{H}3,_{F}4$ = 2.2 $J_{H}3,_{F}7$ = 3.4	–151.4 (1F, dddd) $J_{F}4,_{F}5$ = 20.2 $J_{F}4,_{F}7$ = 16.3 $J_{F}4,_{F}6$ = 1.8 $J_{F}4,_{H}3$ = 2.2	–171.0 (1F, ddd) $J_{F}5,_{F}4$ = 20.2 $J_{F}5,_{F}6$ = 19.7 $J_{F}5,_{F}7$ = 4.0	–167.3 (1F, ddd) $J_{F}6,_{F}5$ = 19.7 $J_{F}6,_{F}7$ = 19.7 $J_{F}6,_{F}4$ = 1.8	–163.2 (1F, dddd) $J_{F}7,_{F}6$ = 19.7 $J_{F}7,_{F}4$ = 16.3 $J_{F}7,_{F}5$ = 4.0 $J_{F}7,_{H}3$ = 3.4	1.54–1.84 (6H, m, $CH_2CH_2CH_2$); 3.54–3.62, (1H, m, OCH_2); 3.92–3.99 (1H, m, OCH_2); 4.67–4.69 (1H, m, CH); 4.76 and 4.80 (2H, AB-system, CH_2C_{ar}) J_{AB} = 13.3
2bf	8.66 (1H, bs)	6.47 (1H, ddm) $J_{H}3,_{F}4$ = 2.0 $J_{H}3,_{F}7$ = 3.3	–151.3 (1F, dddd) $J_{F}4,_{F}5$ = 20.3 $J_{F}4,_{F}7$ = 16.4 $J_{F}4,_{F}6$ = 1.8 $J_{F}4,_{H}3$ = 2.0	–170.5 (1F, ddd) $J_{F}5,_{F}4$ = 20.3 $J_{F}5,_{F}6$ = 19.8 $J_{F}5,_{F}7$ = 3.8	–167.0 (1F, ddd) $J_{F}6,_{F}5$ = 19.8 $J_{F}6,_{F}7$ = 19.6 $J_{F}6,_{F}4$ = 1.8	–163.0 (1F, dddd) $J_{F}7,_{F}6$ = 19.6 $J_{F}7,_{F}4$ = 16.4 $J_{F}7,_{F}5$ = 3.8 $J_{F}7,_{H}3$ = 3.3	2.26 (1H, bs, OH); 4.82 (2H, s, CH_2C_{ar})
2ca	8.25 (1H, bs)	6.34 (1H, dd) $J_{H}3,_{F}4$ = 2.2 $J_{H}3,_{F}7$ = 3.3	–155.5 (1F, dddd) $J_{F}4,_{F}5$ = 20.6 $J_{F}4,_{F}7$ = 19.4 $J_{F}4,_{H}6$ = 5.6 $J_{F}4,_{H}3$ = 2.2	–150.8 (1F, ddd) $J_{F}5,_{F}4$ = 20.6 $J_{F}5,_{H}6$ = 10.8 $J_{F}5,_{F}7$ = 1.4	6.67 (1H, ddd) $J_{H}6,_{F}5$ = 10.8 $J_{H}6,_{F}7$ = 10.1 $J_{H}6,_{F}4$ = 5.6	–139.2 (1F, dddd) $J_{F}7,_{F}4$ = 19.4 $J_{F}7,_{H}6$ = 10.1 $J_{F}7,_{H}3$ = 3.3 $J_{F}7,_{F}5$ = 1.4	0.95 (3H, t, CH_3) $J_{H,H}$ = 7.4; 1.40 (2H, qt, CH_2CH_3) J_{CH_2,CH_3} = 7.4, $J_{CH_2,CH_2} \approx 7.5$; 1.69 (2H, tt, $CH_2CH_2CH_3$) $J_{CH_2,CH_2} \approx 7.5$; 2.73 (2H, t, CH_2C_{ar}) $J_{CH_2,CH_2} \approx 7.5$
2cb	8.73 (1H, bs)	6.40 (1H, dd) $J_{H}3,_{F}4$ = 2.3 $J_{H}3,_{F}7$ = 3.2	–152.2 (1F, dddd) $J_{F}4,_{F}5$ = 20.4 $J_{F}4,_{F}7$ = 19.7 $J_{F}4,_{H}6$ = 5.7 $J_{F}4,_{H}3$ = 2.3	–147.3 (1F, ddd) $J_{F}5,_{F}4$ = 20.4 $J_{F}5,_{H}6$ = 10.8 $J_{F}5,_{F}7$ = 1.3	6.73 (1H, ddd) $J_{H}6,_{F}5$ = 10.8 $J_{H}6,_{F}7$ = 10.0 $J_{H}6,_{F}4$ = 5.7	–135.8 (1F, dddd) $J_{F}7,_{F}4$ = 19.7 $J_{F}7,_{H}6$ = 10.0 $J_{F}7,_{H}3$ = 3.2 $J_{F}7,_{F}5$ = 1.3	1.67 (6H, s, CH_3); 2.05 (1H, s, OH)
2cc	8.37 (1H, bs)	6.67 (1H, ddd) $J_{H}3,_{F}4$ = 2.2 $J_{H}3,_{F}7$ = 3.2 $J_{H}3,_{H}2$ = 3.2	–154.0 (1F, dddd) $J_{F}4,_{F}5$ = 20.3 $J_{F}4,_{F}7$ = 19.9 $J_{F}4,_{H}6$ = 5.7 $J_{F}4,_{H}3$ = 2.2	–149.8 (1F, ddd) $J_{F}5,_{F}4$ = 20.3 $J_{F}5,_{H}6$ = 10.7 $J_{F}5,_{F}7$ = 1.3	6.79 (1H, ddd) $J_{H}6,_{F}5$ = 10.7 $J_{H}6,_{F}7$ = 10.0 $J_{H}6,_{F}4$ = 5.7	–138.1 (1F, dddd) $J_{F}7,_{F}4$ = 19.9 $J_{F}7,_{H}6$ = 10.0 $J_{F}7,_{H}3$ = 3.2 $J_{F}7,_{F}5$ = 1.3	7.23 (1H, dd, H^2) $J_{H}2,_{H}3$ = 3.2 $J_{H}2,_{H}1$ = 2.3
2cd	8.47 (1H, bs)	6.91 (1H, dd) $J_{H}3,_{F}4$ = 2.2 $J_{H}3,_{F}7$ = 3.1	–154.5 (1F, dddd) $J_{F}4,_{F}5$ = 20.3 $J_{F}4,_{F}7$ = 19.8 $J_{F}4,_{H}6$ = 5.7 $J_{F}4,_{H}3$ = 2.2	–149.4 (1F, ddd) $J_{F}5,_{F}4$ = 20.3 $J_{F}5,_{H}6$ = 10.7 $J_{F}5,_{F}7$ = 1.2	6.78 (1H, ddd) $J_{H}6,_{F}5$ = 10.7 $J_{H}6,_{F}7$ = 10.0 $J_{H}6,_{F}4$ = 5.7	–138.5 (1F, dddd) $J_{F}7,_{F}4$ = 19.8 $J_{F}7,_{H}6$ = 10.0 $J_{F}7,_{H}3$ = 3.1 $J_{F}7,_{F}5$ = 1.2	7.34–7.41 (1H, m, Ph); 7.43–7.50 (2H, m, Ph); 7.63–7.68 (2H, m, Ph)
2ce	8.86 (1H, bs)	6.51 (1H, dd) $J_{H}3,_{F}4$ = 2.3 $J_{H}3,_{F}7$ = 3.2	–154.6 (1F, dddd) $J_{F}4,_{F}5$ = 20.4 $J_{F}4,_{F}7$ = 19.7 $J_{F}4,_{H}6$ = 5.7 $J_{F}4,_{H}3$ = 2.3	–150.3 (1F, ddd) $J_{F}5,_{F}4$ = 20.4 $J_{F}5,_{H}6$ = 10.8 $J_{F}5,_{F}7$ = 1.5	6.75 (1H, ddd) $J_{H}6,_{F}5$ = 10.8 $J_{H}6,_{F}7$ = 10.1 $J_{H}6,_{F}4$ = 5.7	–138.7 (1F, ddd) $J_{F}7,_{F}4$ = 19.7 $J_{F}7,_{H}6$ = 10.1 $J_{F}7,_{H}3$ = 3.2 $J_{F}7,_{F}5$ = 1.5	1.30–1.90 (6H, m, $CH_2CH_2CH_2$); 3.51–3.61, (1H, m, OCH_2); 3.91–4.02 (1H, m, OCH_2); 4.67–4.70 (1H, m, CH); 4.76 and 4.82 (2H, AB-system, CH_2C_{ar}) J_{AB} = 13.4
2cf	8.90 (1H, bs)	6.48 (1H, dd) $J_{H}3,_{F}4$ = 2.1 $J_{H}3,_{F}7$ = 3.1	–154.2 (1F, dddd) $J_{F}4,_{F}5$ = 20.4 $J_{F}4,_{F}7$ = 19.8 $J_{F}4,_{H}6$ = 5.7 $J_{F}4,_{H}3$ = 2.1	–149.7 (1F, ddd) $J_{F}5,_{F}4$ = 20.4 $J_{F}5,_{H}6$ = 10.7 $J_{F}5,_{F}7$ = 1.4	6.75 (1H, ddd) $J_{H}6,_{F}5$ = 10.7 $J_{H}6,_{F}7$ = 10.0 $J_{H}6,_{F}4$ = 5.7	–138.7 (1F, dddd) $J_{F}7,_{F}4$ = 19.8 $J_{F}7,_{H}6$ = 10.0 $J_{F}7,_{H}3$ = 3.1 $J_{F}7,_{F}5$ = 1.4	1.92 (1H, bs, OH); 4.84 (2H, s, CH_2C_{ar})

Table 7. ^{13}C NMR chemical shifts (ppm) and coupling constants (Hz) for indoles **2(a–c)(a–f)** ($CDCl_3$)



2(a–c)(a–f)

	X	Y	R	
a	CF_3	F	n-Bu	**a**
b	F	F	$C(CH_3)_2OH$	**b**
c	F	H	H	**c**
			Ph	**d**
			CH_2OTHP	**e**
			CH_2OH	**f**

Compound	C^2	C^3	C^4	C^5	C^6	C^7	C^{3a}	C^{7a}	R, CF_3
2aa	142.8	97.4	147.8 $J_{C}4,_{F}4$ = 257.0 $J_{C}4,_{F}6$ = 5.7	99.4 $J_{C}5,_{CF3}$ = 33.3 $J_{C}5,_{F}4$, $J_{C}5,_{F}6$ = 13.9	142.4 $J_{C}6,_{F}6$ = 248.4 $J_{C}6,_{F}7$ = 13.3 $J_{C}6,_{F}4$ = 5.5 $J_{C}6,_{CF3}$ = 1.8	134.4 $J_{C}7,_{F}7$ = 242.7 $J_{C}7,_{F}6$ = 16.4 $J_{C}7,_{F}4$ = 4.2	116.3 $J_{C}3a,_{F}4$ = 24.1 $^{3}J_{C}9,_{F}7$ = 4.2	127.3 $J_{C}7a,_{F}7$ = 14.6	13.9 (CH_3), 22.5 (CH_2), 27.8 (CH_2), 31.1 (CH_2), 122.8 (CF_3) $^{1}J_{CF3,F}$ = 272.9
2ab	148.4	95.0	148.6 $J_{C}4,_{F}4$ = 257.1	99.5 $J_{C}5,_{CF3}$ = 33.7 $J_{C}5,_{F}4$, $J_{C}5,_{F}6$ = 14.3	142.7 $J_{C}6,_{F}6$ = 249.0 $J_{C}6,_{F}7$ = 13.0	134.7 $J_{C}7,_{F}7$ = 243.5 $J_{C}7,_{F}6$ = 16.5 $J_{C}7,_{F}4$ = 4.5	116.1 $J_{C}3a,_{F}4$ = 24.1	127.0 $J_{C}7a,_{F}7$ = 14.0	31.1 (CH_3), 69.9 ($C(CH_3)_2OH$), 122.7 (CF_3) $^{1}J_{CF3,F}$ = 273.6
2ac	126.5	100.9	148.7 $J_{C}4,_{F}4$ = 258.9	100.0 $J_{C}5,_{CF3}$ = 33.2 $J_{C}5,_{F}4$, $J_{C}5,_{F}6$ ≈ 14	142.9 $J_{C}6,_{F}6$ = 249.6 $J_{C}6,_{F}7$ = 13.2 $J_{C}6,_{F}4$ = 5.3	134.9 $J_{C}7,_{F}7$ = 243.8 $J_{C}7,_{F}6$ = 16.5 $J_{C}7,_{F}4$ = 4.5	115.7 $J_{C}3a,_{F}4$ = 24.3	127.5 $J_{C}7a,_{F}7$ = 13.8	122.4 (CF_3) $^{1}J_{CF3,F}$ = 273.0
2ad	140.5	97.2	148.4 $J_{C}4,_{F}4$ = 258.5	100.2 $J_{C}5,_{CF3}$ = 33.4 $J_{C}5,_{F}4$, $J_{C}5,_{F}6$ ≈ 14	142.9 $J_{C}6,_{F}6$ = 250.0 $J_{C}6,_{F}7$ = 13.0 $J_{C}6,_{F}4$ ≈ 5	134.5 $J_{C}7,_{F}7$ = 243.6 $J_{C}7,_{F}6$ = 16.5 $J_{C}7,_{F}4$ = 4.3	116.7 $J_{C}3a,_{F}4$ = 24.1	127.8 $J_{C}7a,_{F}7$ = 13.9	125.5 (Ph), 129.2 (Ph), 129.4 (Ph), 130.3 (Ph), 122.4 (CF_3) $^{1}J_{CF3,F}$ = 273.0
2ae	138.5	99.0	148.4 $J_{C}4,_{F}4$ = 258.0	99.8 $J_{C}5,_{CF3}$ =33.5	142.8 $J_{C}6,_{F}6$ = 248.7 $J_{C}6,_{F}7$ = 13.1 $J_{C}6,_{F}4$ = 5.2	134.7 $J_{C}7,_{F}7$ = 243.7 $J_{C}7,_{F}6$ = 16.4 $J_{C}7,_{F}4$ = 4.3	115.8 $J_{C}3a,_{F}4$ = 23.8	127.9 $J_{C}7a,_{F}7$ = 14.2	30.8, 25.3, 20.2 ($CH_2CH_2CH_2$) 64.0, 63.1 (OCH_2), 100.3 (OCHO), 122.6 (CF3) $^{1}J_{CF3,F}$ = 272.7
2af	140.3	98.0	148.5 $J_{C}4,_{F}4$ = 258.8	99.9 $J_{C}5,_{CF3}$ = 33.5 $J_{C}5,_{F}4$, $J_{C}5,_{F}6$ = 14.5	142.9 $J_{C}6,_{F}6$ = 250.0 $J_{C}6,_{F}7$ = 13.0	134.7 $J_{C}7,_{F}7$ = 243.7 $J_{C}7,_{F}6$ = 16.5 $J_{C}7,_{F}4$ = 4.6	115.8 $J_{C}3a,_{F}4$ = 23.9	127.8 $J_{C}7a,_{F}7$ = 14.3	58.2 (CH_2OH), 122.6 (CF_3) $^{1}J_{CF3,F}$ = 273.0
2ba	142.4	96.6	139.1 $J_{C}4,_{F}4$ = 244.9 $J_{C}4,_{F}5$ = 11.6 $J_{C}4,_{F}6$, $J_{C}4,_{F}7$ = 3.7, 3.1	135.1 $J_{C}5,_{F}5$ = 240.0 $J_{C}5,_{F}4$, $J_{C}5,_{F}6$ = 15.6, 14.5 $J_{C}5,_{F}7$ = 2.1	136.2 $J_{C}6,_{F}6$ = 241.3 $J_{C}6,_{F}5$, $J_{C}6,_{F}7$ = 15.1, 13.7 $J_{C}6,_{F}4$ = 3	134.1 $J_{C}7,_{F}7$ = 243.0 $J_{C}7,_{F}6$ = 13.8 $J_{C}7,_{F}5$ = 4.4 $J_{C}7,_{F}4$ = 2.6	114.9 $J_{C}3a,_{F}4$ = 20.2	120.4 $J_{C}7a,_{F}7$ = 11.5	13.9 (CH_3), 22.5 (CH_2), 27.9 (CH_2), 31.2 (CH_2)
2bb	148.0	94.3	139.6 $J_{C}4,_{F}4$ = 245.7 $J_{C}4,_{F}5$ = 11.7	135.2 $J_{C}5,_{F}5$ = 241.0 $J_{C}5,_{F}4$, $J_{C}5,_{F}6$ ≈ 15	136.7 $J_{C}6,_{F}6$ ≈ 243 $J_{C}6,_{F}5$, $J_{C}6,_{F}7$ ≈ 14.5	134.4 $J_{C}7,_{F}7$ = 244.0 $J_{C}7,_{F}6$ ≈ 11.5	114.7 $J_{C}3a,_{F}4$ = 20.2	120.2 $J_{C}7a,_{F}7$ = 11.8	31.1 (CH_3), 69.9 ($C(CH_3)_2OH$)
2bc	126.0	100.3	139.8 $J_{C}4,_{F}4$ = 246.5 $J_{C}4,_{F}5$ = 11.5	135.3 $J_{C}5,_{F}5$ = 241.2 $J_{C}5,_{F}4$, $J_{C}5,_{F}6$ = 14.8	137.0 $J_{C}6,_{F}6$ = 243.2 $J_{C}6,_{F}5$, $J_{C}6,_{F}7$ = 14.3	134.5 $J_{C}7,_{F}7$ = 244.1 $J_{C}7,_{F}6$ ≈ 14	114.3 $J_{C}3a,_{F}4$ = 20.6	120.8 $J_{C}7a,_{F}7$ = 12.0	
2bd	140.2	96.8	139.8 $J_{C}4,_{F}4$ = 246.8 $J_{C}4,_{F}5$ = 11.6	135.6 $J_{C}5,_{F}5$ = 242.0 $J_{C}5,_{F}4$, $J_{C}5,_{F}6$	137.1 $J_{C}6,_{F}6$ = 243.5 $J_{C}6,_{F}5$, $J_{C}6,_{F}7$	134.4 $J_{C}7,_{F}7$ = 244.0 $J_{C}7,_{F}6$ ≈ 14	115.5 $J_{C}3a,_{F}4$ = 20.4	121.4 $J_{C}7a,_{F}7$ ≈ 11	125.6 (Ph), 129.0 (Ph), 129.5 (Ph),

			$J_C4,_F6$, $J_C4,_F7$ ≈ 3	≈ 15	= 14.0, 15.0 $J_C6,_F4$ = 3	$J_C7,_F5$ = 4.4 $J_C7,_F4$ = 2.4			130.9 (Ph)
2be	137.9	98.3	139.6 $J_C4,_F4$ = 246.0 $J_C4,_F5$ = 11.6 $J_C4,_F6$, $J_C4,_F7$ ≈ 3.5	135.1 $J_C5,_F5$ = 240.7 $J_C5,_F4$, $J_C5,_F6$ ≈ 15	136.8 $J_C6,_F6$ = 242.7 $J_C6,_F5$, $J_C6,_F7$ ≈ 14.5	134.3 $J_C7,_F7$ = 244.5 $J_C7,_F6$ = 13.7	114.4 $J_C3a,_F4$ = 20.2	121.1 $J_C7a,_F7$ = 11.3	20.2 (CH_2), 25.4 (CH_2), 30.8 (CH_2), 63.1 (OCH_2), 63.8 (OCH_2), 100.0 (OCHO)
2bf	139.9	97.3	139.6 $J_C4,_F4$ = 246.2 $J_C4,_F5$ = 11.6 $J_C4,_F6$, $J_C4,_F7$ ≈ 3.5	135.3 $J_C5,_F5$ = 241.3 $J_C5,_F4$, $J_C5,_F6$ ≈ 15	136.9 $J_C6,_F6$ = 242.7 $J_C6,_F5$, $J_C6,_F7$ ≈ 14.5	134.4 $J_C7,_F7$ = 244.5 $J_C7,_F6$ = 14.0	114.4 $J_C3a,_F4$ = 20.2	121.5 $J_C7a,_F7$ = 11.3	58.3 (CH_2OH)
2ca	142.8	97.0	139.0 $J_C4,_F4$ = 242.0 $J_C4,_F5$ = 14.1 $J_C4,_F7$ = 4.1	142.8 $J_C5,_F5$ = 236.2 $J_C5,_F4$ = 13.2 $J_C5,_F7$ = 10.7	96.7 $J_C6,_F5$, $J_C6,_F7$ = 25.2, 22.7	143.4 $J_C7,_F7$ = 241.4 $J_C7,_F5$ = 11.6 $J_C7,_F4$ = 2.8	120.9 $J_C3a,_F4$ = 20.3	121.6 $J_C7a,_F7$ = 14.9	13.9 (CH_3), 22.5 (CH_2), 27.9 (CH_2), 31.2 (CH_2)
2cb	148.3	94.7	139.5 $J_C4,_F4$ = 243.1 $J_C4,_F5$ = 14.1 $J_C4,_F7$ = 4.2	142.9 $J_C5,_F5$ = 237.0 $J_C5,_F4$ = 13.1 $J_C5,_F7$ = 10.5	97.8 $J_C6,_F5$, $J_C6,_F7$ = 25.2, 22.6	143.8 $J_C7,_F7$ = 242.3 $J_C7,_F5$ = 11.5 $J_C7,_F4$ = 2.9	120.7 $J_C3a,_F4$ = 20.0	121.4 $J_C7a,_F7$ = 15.2	31.1 (CH_3) 69.9 ($\underline{C}(CH_3)_2OH$)
2cd	140.4	97.2	139.6 $J_C4,_F4$ = 243.7 $J_C4,_F5$ = 14.1 $J_C4,_F7$ = 4.1	143.2 $J_C5,_F5$ = 237.8 $J_C5,_F4$ = 13.0 $J_C5,_F7$ = 10.7	98.4 $J_C6,_F5$, $J_C6,_F7$ = 25.3, 22.6	143.8 $J_C7,_F7$ = 242.4 $J_C7,_F5$ = 11.4 $J_C7,_F4$ = 3.0	121.5 $J_C3a,_F4$ = 20.2	122.6 $J_C7a,_F7$ = 15.0	125.7 (Ph), 129.0 (Ph), 129.5 (Ph), 131.2 (Ph)
2ce	138.1	98.6	139.5 $J_C4,_F4$ = 243.3 $J_C4,_F5$ = 14.1 $J_C4,_F7$ = 4.2	142.8 $J_C5,_F5$ = 237.0 $J_C5,_F4$ = 13.1 $J_C5,_F7$ = 10.5	98.0 $J_C6,_F5$, $J_C6,_F7$ = 25.2, 22.6	143.8 $J_C7,_F7$ = 242.4 $J_C7,_F5$ = 11.3 $J_C7,_F4$ = 3.0	120.5 $J_C3a,_F4$ = 20.3	122.3 $J_C7a,_F7$ = 15.1	20.1 (CH_2), 25.4 (CH_2), 30.8 (CH_2), 63.0 (OCH_2), 63.7 (OCH_2), 99.9 (OCHO)
2cf	140.2	97.6	139.5 $J_C4,_F4$ = 243.4 $J_C4,_F5$ = 14.1 $J_C4,_F7$ = 4.1	142.9 $J_C5,_F5$ = 237.2 $J_C5,_F4$ = 13.2 $J_C5,_F7$ = 10.5	98.1 $J_C6,_F5$, $J_C6,_F7$ = 25.2, 22.5	143.8 $J_C7,_F7$ = 242.6 $J_C7,_F5$ = 11.6 $J_C7,_F4$ = 3.0	120.4 $J_C3a,_F4$ = 20.1	122.2 $J_C7a,_F7$ = 15.1	58.4 (CH_2OH)

The solvent was evaporated *in vacuo* to give the crude product, which was purified by TLC (hexane/ethyl acetate, 5:1) to give the *title compound* **1ac** (84 mg, 35%) as a colourless oil; R_f (hexane/ethyl acetate, 5:1, three times) 0.45; ν_{max} (liquid film): 3514 (br) and 3410 (NH_2), 3308 (C–H), 2116 (C(C), 1643, 1504, 1337, 1236, 1177, 1132, 922, 854, 706, 619 cm^{-1}; d_H (300.13 MHz, $CDCl_3$) 4.88 (2H, s, NH_2), 3.64 (1H, s, C(C)H); d_C (100.62 MHz, $CDCl_3$) 157.0 ($^1J_C3,_F3$ = 258.2, $^3J_C3,_{CF3}$ = 2.2 Hz, C^3), 148.4 ($^1J_C5,_F5$ = 259.7, $^2J_C5,_F6$ = 13.3, $^3J_C5,_{CF3}$ = 1.7 Hz, C^5), 141.9 ($^2J_C1,_F6$ = 11.7 Hz, C^1), 135.4 ($^1J_C6,_F6$ = 238.6, $^2J_C6,_F5$ = 15.2 Hz, C^6), 121.6 ($^1J_{CF3,F}$ = 273.0 Hz, CF_3), 96.9 ($^2J_C4,_{CF3}$ = 34.5, $^2J_C4,_F3$ = 15.8, $^2J_C4,_F5$ = 12.6 Hz, C^4), 93.6 ($^2J_C2,_F3$ = 21.6 Hz, C^2), 89.2 (C^8), 71.2 (C^7); d_F (282.37 MHz, $CDCL_3$) –56.4 (3F, dd, $J_{CF3,F}3$, $J_{CF3,F}5 \approx 21$ Hz, CF_3), –114.2 (1F, dq, $J_F3,_{CF3}$ = 21.7, $J_F3,_F6$ = 11.4 Hz, F^3), –136.7 (1F, dq, $J_F5,_{CF3}$, $J_F5,_F6 \approx 21$ Hz, F^5), –164.8 (1F, dd, $J_F6,_F5$ = 20.1, $J_F6,_F3$ = 11.4 Hz, F^6); HRMS (EI): M^+, found 239.0162. $C_9H_3F_6N$ requires 239.0164.

*4.4. General procedure for synthesis of indoles **2(a–c)a,d,e***

To a stirred solution of aniline **4** (1 mmol) and alkyne **5** (3 mmol) in MeCN (9 mL) were added $Pd(PPh_3)_2Cl_2$ (28 mg, 0.04 mmol), CuI (17 mg, 0.09 mmol) and Et_3N (1.5 mL) at room temperature under an argon atmosphere. The reaction mixture was stirred at 50 °C for 1 h. Then the mixture was heated to reflux, and KOH (168 mg, 3 mmol) was added. The reaction mixture was maintained under reflux for 3 h with stirring. After the mixture was cooled to room temperature, diluted with CH_2Cl_2 (10 mL), poured into H_2O (20 mL), neutralized with 5% aqueous AcOH up to pH = 7 and extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were washed with H_2O (10 mL) and dried ($MgSO_4$). After evaporation of solvent *in vacuo*, the residue was purified by TLC (hexane/ethyl acetate) to give the *title product*.

*4.4.1. 2-Butyl-4,6,7-trifluoro-5-(trifluoromethyl)-indole (**2aa**)*

The reaction of **4a** (341 mg, 1 mmol) and **5a** (246 mg, 3 mmol), conducted according to the above general procedure, afforded the *title compound* (**2aa**) (201 mg, 68 %) as a yellow liquid; [found: C, 52.71; H, 3.97; N, 4.76. $C_{13}H_{11}F_6N$ requires C, 52.89; H, 3.76; N 4.74 %]; R_f (hexane/ethyl acetate, 7:1, then 10:1) 0.55; ν_{max} (liquid film): 3473 (NH), 2962, 2935, 2873, 1660, 1568, 1521, 1464, 1358, 1277, 1169, 1132, 999, 877, 793, 744, 702, 654, 511 sm^{-1}; HRMS (EI): M^+, found 295.0791. $C_{13}H_{11}F_6N$ requires 295.0790.

*4.4.2. 4,6,7-Trifluoro-2-phenyl-5-(trifluoromethyl)-indole (**2ad**)*

The reaction of **4a** (341 mg, 1 mmol) and **5d** (306 mg, 3 mmol), conducted according to the above general procedure,

afforded the *title compound* (**2ad**) (230 mg, 73%) as a colourless solid; m.p. 127–128 °C; [Found: C, 57.23; H, 2.22; N, 4.34. $C_{15}H_7F_6N$ requires C, 57.16; H, 2.24; N 4.44%]; R_f (hexane/ethyl acetate, 7:1, three times) 0.72; ν_{max} (KBr): 3470 (NH), 1660, 1520, 1452, 1354, 1295, 1180, 1144, 996, 870, 793, 765, 744, 525 cm^{-1}; HRMS (EI): M^+, found 315.0479. $C_{15}H_7F_6N$ requires 315.0477.

*4.4.3. 4,6,7-Trifluoro-2-[(oxan-2-yloxy)methyl]-5-(trifluoromethyl)indole (**2ae**)*

The reaction of **4a** (341 mg, 1 mmol) and **5e** (420 mg, 3 mmol), conducted according to the above general procedure, afforded the *title compound* (**2ae**) (268 mg, 76%) as a colourless solid; m.p. 146–148 °C; [Found: C, 50.97; H, 3.76; N, 3.93. $C_{15}H_{13}F_6NO_2$ requires C, 51.00; H, 3.71; N 3.96%]; R_f (hexane/ethyl acetate, 7:1, four times) 0.50; ν_{max} (KBr): 3421 (br) (NH), 3217, 2945, 1661, 1524, 1464, 1366, 1308, 1167, 1135, 1022, 1000, 880, 810, 793, 681, 507 cm^{-1}; HRMS (EI): M^+, found 353.0843. $C_{15}H_{13}F_6NO_2$ requires 353.0845.

*4.4.4. 2-Butyl-4,5,6,7-tetrafluoroindole (**2ba**)*

The reaction of **4a** (341 mg, 1 mmol) and **5e** (420 mg, 3 mmol), conducted according to the above general procedure, afforded the *title compound* (**2ba**) (208 mg, 85%) as a yellow liquid; [Found: C, 58.73; H, 4.73; N, 5.68. $C_{12}H_{11}F_4N$ requires C, 58.78; H, 4.52; N 5.71%]; R_f (hexane/ethyl acetate, 7:1, then 10:1) 0.60; ν_{max} (liquid film): 3474 (NH), 2961, 2872, 1661, 1539, 1491, 1338, 1199, 1117, 995, 794, 727, 657, 466 cm^{-1}; HRMS (EI): M^+, found 245.0821. $C_{12}H_{11}F_4N$ requires 245.0822.

*4.4.5. 4,5,6,7-Tetrafluoro-2-phenylindole (**2bd**)*

The reaction of **4b** (291 mg, 1 mmol) and **5d** (306 mg, 3 mmol), conducted according to the above general procedure, afforded the *title compound* (**2bd**) (238 mg, 90%) as a colourless solid; m.p. 126–129 °C (lit. data[13]); R_f (hexane/ethyl acetate, 10:1, two times) 0.40; ν_{max} (KBr): 3482 (NH), 1724, 1539, 1481, 1334, 1268, 996, 796, 761, 726, 688, 560 cm^{-1}.

*4.4.6. 4,5,6,7-Tetrafluoro-2-[(oxan-2-yloxy)-methyl]indole (**2be**)*

The reaction of **4b** (291 mg, 1 mmol) and **5e** (420 mg, 3 mmol), conducted according to the above general procedure, afforded the *title compound* (**2be**) (263 mg, 87%) as a colourless solid; m.p. 117–120 °C; [Found: C, 55.49; H, 4.33; N, 4.42. $C_{14}H_{13}F_4NO_2$ requires C, 55.45; H, 4.32; N 4.62%]; R_f (hexane/ethyl acetate, 7:1, three times) 0.56; ν_{max} (KBr): 3428 (br) (NH), 3226 (br), 2945, 1725, 1543, 1492, 1341, 1264, 1113, 999, 940, 900, 871, 807, 728, 689, 518 cm^{-1}; HRMS (EI): M^+, found 303.0875. $C_{14}H_{13}F_4NO_2$ requires 303.0877.

*4.4.7. 2-Butyl-4,5,7-trifluoroindole (**2ca**)*

The reaction of **4c** (273 mg, 1 mmol) and **5a** (246 mg, 3 mmol), conducted according to the above general procedure, afforded the *title compound* (**2ca**) (163 mg, 72%) as a yellow liquid; [Found: C, 63.72; H, 5.53; N, 5.59. $C_{12}H_{12}F_3N$ requires C, 63.43; H, 5.32; N 6.16%]; R_f (hexane/ethyl acetate, 7:1, two times) 0.60; ν_{max} (liquid film): 3470 (NH), 3369 (br), 2961, 2934, 2872, 1715, 1666, 1531, 1436, 1333, 1269, 1200, 1113, 959, 812, 781, 731, 702 cm^{-1}; HRMS (EI): M^+, found 227.0917. $C_{12}H_{12}F_3N$ requires 227.0916.

*4.4.8. 4,5,7-Trifluoro-2-phenylindole (**2cd**)*

The reaction of (273 mg, 1 mmol) and **5d** (306 mg, 3 mmol), conducted according to the above general procedure, afforded the *title compound* (**2cd**) (210 mg, 85%) as a colourless solid; m.p. 105–106 °C; [Found: C, 68.21; H, 3.17; N, 5.66. $C_{14}H_8F_3N$ requires C, 68.02; H, 3.26; N 5.67%]; R_f (hexane/ethyl acetate, 15:1, three times) 0.42; ν_{max} (KBr): 3481 (NH), 1662, 1535, 1487, 1454, 1406, 1325, 1265, 1178, 1119, 1076, 964, 814, 754, 721, 680, 488 cm^{-1}; HRMS (EI): M^+, found 247.0604. $C_{14}H_8F_3N$ requires 247.0603.

*4.4.9. 4,5,7-Trifluoro-2-[(oxan-2-yloxy)methyl]-indole (**2ce**)*

The reaction of **4c** (273 mg, 1 mmol) and **5e** (420 mg, 3 mmol), conducted according to the above general procedure, afforded the *title compound* (**2ce**) (214 mg, 75%) as a colourless solid; m.p. 119–120 °C; [Found: C, 59.12; H, 4.92; N, 5.31. $C_{14}H_{14}F_3NO_2$ requires C, 58.95; H, 4.95; N 4.91%]; R_f (hexane/ethyl acetate, 7:1, three times) 0.51; ν_{max} (KBr): 3422 (br) and 3233 (br) (NH), 2947, 1726, 1666, 1535, 1441, 1340, 1265, 1202, 1113, 1022, 961, 901, 804, 714, 496 cm^{-1}; HRMS (EI): M^+, found 285.0968. $C_{14}H_{14}F_3NO_2$ requires 285.0971.

*4.5. General procedure for synthesis of indoles **2(a–c)b,c***

To a stirred solution of aniline **4** (1 mmol), 2-methyl-3-butyn-2-ol **5b** (252 mg, 3 mmol) in dry MeCN (9 mL) were added $Pd(PPh_3)_2Cl_2$ (28 mg, 0.04 mmol), CuI (17 mg, 0.09 mmol) and Et_3N (1.5 mL) at room temperature under an argon atmosphere. The reaction mixture was stirred at 50 °C for 1 h. Then the mixture was heated up to boiling, and KOH (168 mg, 3 mmol) was added. The mixture was maintained under reflux with stirring, cooled to room temperature and diluted with CH_2Cl_2 (5 mL). The suspension was placed into a chromatography column filled with silica gel (to minimize volatilization of indoles **2(a–c)c**). The column was washed with hexane/ethyl acetate (15:1) and then with hexane/ethyl acetate (5:1) under the TLC control to isolate indoles **2(a–c)c** and **2(a–c)b**, respectively, after evaporation of solvents *in vacuo*.

*4.5.1. 2-[4,6,7-Trifluoro-5-(trifluoromethyl)indol-2-yl]propan-2-ol (**2ab**); 4,6,7-trifluoro-5-(trifluoromethyl)indole (**2ac**)*

The above general procedure was followed using **4a** (341 mg, 1 mmol) and **5b** (252 mg, 3 mmol), stirring the reaction mixture after addition of KOH (168 mg, 3 mmol) under reflux condition for 2 h, and separating the products by column chromatography (hexane/ethyl acetate, 15:1) to afford **2ac** (107 mg, 45%) as a colourless solid; m.p. 73–75 °C; [Found: C, 45.32; H, 1.47; N, 5.64. $C_9H_3F_6N$ requires C, 45.21; H, 1.26; N 5.86%]; R_f (hexane/ethyl acetate, 10:1 → 10:1) 0.33; ν_{max} (KBr): 3484 (NH), 3256 (br), 2962, 2934, 2876, 1660, 1529, 1462, 1363, 1304, 1215, 1175, 1130, 992, 852, 793, 732, 696 cm^{-1}; HRMS (EI): M^+, found 239.0165. $C_9H_3F_6N$ requires 239.0164. The further elution of the chromatography column (hexane/ethyl acetate, 5:1) afforded **2ab** (154 mg, 52%) as a colourless solid; m.p. 149–151 °C; [Found: C, 48.71; H, 3.18; N, 4.61. $C_{12}H_9F_6NO$ requires C, 48.50; H, 3.05; N 4.71%]; R_f (hexane/ethyl acetate, 5:1, three times) 0.55; ν_{max} (KBr): 3611 (NH), 3280 (br) (OH), 2988, 2939, 1660, 1523, 1467, 1392, 1355, 1279, 1146, 998, 952, 879, 791, 716, 649, 520 cm^{-1}; HRMS (EI): M^+, found 297.0585. $C_{12}H_9F_6NO$ requires 297.0583.

*4.5.2. 2-(4,5,6,7-Tetrafluoroindol-2-yl)propan-2-ol (**2bb**); 4,5,6,7-tetrafluoro-1H-indole (**2bc**)*

The above general procedure was followed using **4b** (291 mg, 1 mmol) and **5b** (252 mg, 3 mmol), stirring the reaction mixture after addition of KOH (168 mg, 3 mmol) under reflux condition for 2 h, and separating the products by column chromatography (hexane/ethyl acetate, 15:1) to afford **2bc** (140 mg, 74%) as a colourless solid; m.p. 86–89 °C (lit. data[10,15,16]); R_f (hexane/ethyl acetate, 7:1, three times) 0.56; ν_{max} (KBr): 3434 (br) (NH), 2960, 2857, 1725, 1578, 1456, 1408, 1368, 1264, 1097, 1037, 898, 730, 505 cm^{-1}. The further elution of chromatography column (hexane/ethyl acetate, 5:1) afforded **2bb** (42 mg, 17%) as a colourless solid; m.p. 137–140 °C; [Found: C, 53.76; H, 3.71; N, 5.56. $C_{11}H_9F_4NO$ requires C, 53.45; H, 3.67; N 5.67%]; R_f (hexane/ethyl acetate, 7:1 → 7:1 → 7:1) 0.21; n_{max} (KBr): 3603 (NH), 3245 (br) (OH), 2985, 2938, 1546, 1487, 1431, 1343,

1267, 1221, 1174, 1127, 997, 946, 844, 791, 726, 642, 535 cm^{-1}; HRMS (EI): M^+, found 247.0613. $C_{11}H_9F_4NO$ requires 247.0615.

*4.5.3. 2-(4,5,7-Trifluoroindol-2-yl)propan-2-ol (**2cb**); 4,5,7-trifluoroindole (**2cc**)*

The above general procedure was followed using **4c** (273 mg, 1 mmol) and **5b** (0.25 g, 3 mmol), stirring the reaction mixture after addition of KOH (168 mg, 3 mmol) under reflux condition for 4 h, and separating the products by column chromatography (hexane/ethyl acetate, 15:1) to afford **2cc** (132 mg, 77%) as a colourless oil; [Found: C, 56.02; H, 2.56; N, 8.07. $C_8H_4F_3N$ requires C, 56.15; H, 2.36; N 8.19%]; R_f (hexane/ethyl acetate, 5:1, three times) 0.81; ν_{max} (liquid film): 3479 (NH), 3306 (br), 2924, 2853, 1713, 1537, 1503, 1346, 1132, 955, 716 cm^{-1}; HRMS (EI): M^+, found 171.0288. $C_8H_4F_3N$ requires 171.0290. The further elution of chromatography column (hexane/ethyl acetate, 5:1) to afford **2cb** (18 mg, 8%) as a colourless solid; m.p. 132–134 °C; [Found: C, 57.91; H, 4.49; N, 5.80. $C_{11}H_{10}F_3NO$ requires C, 57.64; H, 4.40; N 6.11%]; R_f (hexane/ethyl acetate, 5:1 → 5:1 → 5:1) 0.25; n_{max} (KBr): 3595 (NH), 3398 (br), 3265 (br) (OH), 2976, 2928, 2855, 1661, 1533, 1439, 1371, 1340, 1254, 1177, 1130, 945, 785, 729, 694, 498 cm^{-1}; HRMS (EI): M^+, found 229.0707. $C_{11}H_{10}F_3NO$ requires 229.0709.

*4.6. General procedure for synthesis of indoles **2(a–c)b** from alkynes **1(a–c)b***

The crude **1(a–c)b**, obtained in the experiment *4.2***,** was dissolved in MeCN (10 mL), $Et_4NF{\cdot}H_2O$ (370 mg, 3 mmol) was added, and the mixture was refluxed for 3 h. The mixture was cooled to room temperature, diluted with CH_2Cl_2 (10 mL), poured into H_2O (20 mL), neutralized with 5% aqueous AcOH up to pH = 7 and extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were washed with H_2O (10 mL) and dried ($MgSO_4$). After evaporation of solvent *in vacuo*, the residue was purified by TLC (hexane/ethyl acetate, 5:1, three times) to give the *title product*.

*4.6.1. 2-[4,6,7-Trifluoro-5-(trifluoromethyl)indol-2-yl]propan-2-ol (**2ab**)*

Conducting the reaction of crude **1ab** according the above general procedure, the standard workup and TLC separation (hexane/ethyl acetate, R_f = 0.55) gave the *title compound* **2ab** (220 mg, 74%) as a colourless solid.

*4.6.2. 2-(4,5,6,7-Tetrafluoroindol-2-yl)propan-2-ol (**2bb**)*

Conducting the reaction of crude **1bb** according the above general procedure, the standard workup and TLC separation (hexane/ethyl acetate, R_f = 0.35) gave the *title compound* **2bb** (74 mg, 30%) as a colourless solid.

*4.6.3. 2-(4,5,7-Trifluoroindol-2-yl)propan-2-ol (**2cb**)*

Conducting the reaction of crude **1cb** according the above general procedure, the standard workup and TLC separation (hexane/ethyl acetate, R_f = 0.25) gave the *title compound* **2cb** (37 mg, 16%) as a colourless solid.

*4.7. General procedure for synthesis of indoles **2(a–c)f***

To a stirred solution of indole **2(a–c)e** (0.1 mmol) in MeOH (5 mL) was added 15% aqueous HCl (6 drops) at room temperature. After stirring for 1 h the mixture was diluted with CH_2Cl_2 (5 mL), poured into H_2O (5 mL), neutralized by addition of an aqueous solution of $NaHCO_3$ up to pH = 7 and extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were washed with H_2O (10 mL) and dried ($MgSO_4$). After evaporation of solvent *in vacuo*, the residue was purified by TLC (hexane/ethyl acetate) to give the *title product*.

*4.7.1. [4,6,7-Trifluoro-5-(trifluoromethyl)indol-2-yl]methanol (**2af**)*

Conducting the reaction of **2ae** (35 mg, 0.1 mmol) according the above general procedure, the standard workup and TLC separation (hexane/ethyl acetate, 5:1) afforded the *title compound* (**2af**) (24 mg, 90%) as a colourless solid; m.p. 123–125 °C; [Found: C, 44.90; H, 2.05; N, 5.19. $C_{10}H_5F_6NO$ requires C, 44.63; H, 1.87; N 5.20%]; R_f (hexane/ethyl acetate, 5:1, three times) 0.25; ν_{max} (KBr): 3626 (NH), 3248 (br) (OH), 2922, 2851, 1718, 1660, 1523, 1467, 1365, 1288, 1132, 999, 878, 798, 743, 709, 511 cm^{-1}; HRMS (EI): M^+, found 269.0267. $C_{10}H_5F_6NO$ requires 269.0270.

*4.7.2. (4,5,6,7-Tetrafluoroindol-2-yl)methanol (**2bf**)*

Conducting the reaction of **2be** (30 mg, 0.1 mmol) according the above general procedure, the `standard workup and TLC separation (hexane/ethyl acetate, 5:1) afforded the *title compound* (**2bf**) (21 mg, 96%) as a colourless solid; m.p. 136–138 °C; [Found: C, 49.54; H, 2.41; N, 6.39. $C_9H_5F_4NO$ requires C, 49.33; H, 2.30; N 6.39%]; R_f (hexane/ethyl acetate, 5:1, three times) 0.23; ν_{max} (KBr): 3607 (NH), 3420 (br), 3248 (br) (OH), 2924, 2853, 1724, 1610, 1543, 1490, 1435, 1383, 1342, 1267, 1202, 1123, 995, 797, 727, 523 cm^{-1}; HRMS (EI): M^+, found 219.0303. $C_9H_5F_4NO$ requires 219.0302.

*4.7.3. (4,5,7-Trifluoroindol-2-yl)methanol (**2cf**)*

Conducting the reaction of **2ce** (29 mg, 0.1 mmol) according the above general procedure, the standard workup and TLC separation (hexane/ethyl acetate) afforded the *title compound* (**2cf**) (19 mg, 96%) as a colourless solid; m.p. 105–107 °C; [Found: C, 53.88; H, 3.05; N, 6.88. $C_9H_6F_3NO$ requires C, 53.74; H, 3.01; N 6.96%]; R_f (hexane/ethyl acetate, 5:2, two times, then 4:1, two times) 0.45; ν_{max} (KBr): 3597 (NH), 3307 (br) (OH), 2926, 2855, 1713, 1666, 1537, 1441, 1337, 1252, 1203, 1163, 1115, 1015, 962, 806, 708, 498 cm^{-1}; HRMS (EI): M^+, found 201.0393. $C_9H_6F_3NO$ requires 201.0396.

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