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General and efficient synthesis of polyfluorinated 2-aminotolans and 2-arylindoles

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ABSTRACT

It was established here that cross-coupling of polyfluorinated 2-iodoanilines with arylacetylenes in MeCN in the presence catalytic amounts of $Pd(PPh_3)_2Cl_2$, CuI and Et_3N produces the corresponding 2-aminotolans although their yields are decreased from 98% to 40% with increasing fluorination of the substrates. It was shown that the 2-aminotolans with six or fewer fluorine atoms in their rings can be heterocyclised by heating in ethanol containing *p*-TSA to produce the corresponding polyfluorinated indoles. Cyclisation of tolans containing larger numbers of fluorine atoms in their rings proceeds most efficiently in the presence of KOH, resulting in 2-phenylindoles containing the current maximum of eight fluorine atoms.

1. Introduction

An indole moiety is present in numerous substances produced naturally in living organisms and in a vast array of biologically active compounds and pharmaceutical agents. For this reason, indole is referred to as one of the so-called privileged structures, whose presence in more complex systems means a high probability that such compounds will have well-pronounced and targeted biological effects [1]. Accordingly, increased attention is given to research on the synthesis of various polyfunctional indole derivatives and on their biological and pharmaceutical activities. According to the 'Web of Science', more than 23000 articles were published only in the last five years on the subject of production of biologically active compounds of the indole series. Because it is not practical to cite all the works deserving attention, we can mention a few selected publications illustrating the range of biological effects of some indole derivatives. For example, it is worthwhile to consider the series of substituted 2-arylindoles [2], considering that it contains effective antineoplastic agents [3–7] and modulators of tubulin dynamics [7,8] together with progesterone receptors [9], antioxidants [10], antibacterial [11–14] and antimicrobial [15] drugs, anti-inflammatory, analgesic and antipyretic medicines [16] as well as selective cyclooxygenase (COX-2) inhibitors [17–19]. It is also obvious that despite much interest in the chemistry of indole, its polyfluorinated derivatives remain a poorly studied class of compounds. Meanwhile, it is known that introduction of a fluorine atom into biologically active substances is an effective way to alter their therapeutic potency [20–22]. Additionally, the presence of several fluorine atoms in an indole nucleus and its substituents opens up new opportunities to obtain polyfluorinated indole derivatives and heterocyclic systems containing indole moieties. All these observations motivated us to conduct the present study on the synthesis of a large series of polyfluorinated 2-arylindoles, including the syntheis of octafluorophenylindole with the current maximal extent of fluorination.

2. Results and discussion

The basic methods for synthesis of the indole nucleus comprise heterocyclisation of 2-aminotolans [23,24]; this reaction, in the case of polyfluorinated compounds, may be promoted specifically by $NaAuCl_4 \cdot H_2O$ [25], Pd(II) salts [26] or *p*-TSA [27] as well as by bases such as KOH, Et_4NF [26] and EtONa [28]. To construct aminotolans, it is best to use the well-known reaction of cross-coupling of terminal acetylenes and iodo-arenes [29]. Thus, this approach involves the retrosynthesis of polyfluorinated 2-arylindoles (compound **1**, Scheme 1) from 2-aminotolans (compound **2**) prepared from fluorinated 2-iodoanilines (compound **3**) and ethynylarenes (compound **4**, Scheme 1). Acetylene derivatives **5** may serve as precursors of the latter, which are produced by cross-coupling of iodo-arenes **6** and 2-methylbut-3-yn-2-ol (Scheme 1).

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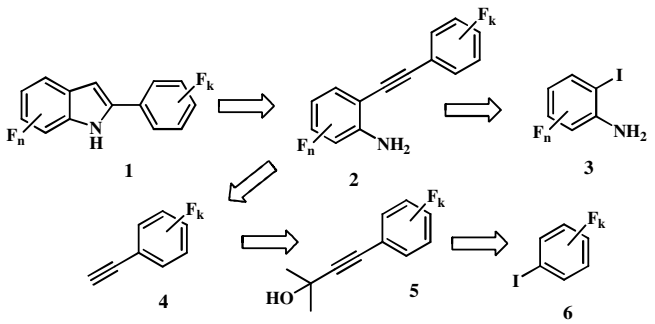


Scheme 1. Retrosynthesis of polyfluorinated 2-arylindoles.

This strategy to obtain polyfluoroindoles **1** seemed fairly reliable. Nevertheless, before the experiments were carried out, there had been some doubts about the feasibility of smooth cleavage of acetylenic alcohols **5** bearing polyfluorinated aromatic rings and about heterocyclisation of polyfluorinated 2-aminotolans **2**.

2.1. Synthesis of polyfluorinated 4-iodoanilines and 4-ethynylanilines

A decision was made to generate a series of 4-iodoanilines fluorinated to various degrees: 3-fluoro- (**6a**), 2,5-difluoro- (**6b**) and 2,3,5,6-tetrafluoro-4-iodoaniline (**6c**). Mono-fluoro-derivative **6a** was described earlier [30]. Compound **6b** was synthesised here with a 91% yield via iodination of 2,5-difluoroaniline in an I_2/$NaHCO_3$/water system. Tetrafluorinated substrate **6c** was produced as shown in Scheme 2: by amination of pentafluoro(trifluoromethyl)benzene, removal of the trifluoromethyl group in 2,3,5,6-tetrafluoro-4-(trifluoromethyl)aniline (**7**) and iodination of the resulting 2,3,5,6-tetrafluoroaniline (**8**).

4-Iodoanilines **6** were cross-coupled with 2-methyl-3-butyn-2-ol in MeCN in the presence of $Pd(PPh_3)_2Cl_2$ (4 mol%), CuI (9 mol%) and Et_3N as catalysts to obtain acetylenic alcohols **5a–c** with the yield of 54–83% (Scheme 3). The resulting compounds (**5a–c**) were cleaved via the retro-Favorsky reaction by the action of KOH in benzene as described previously [31], thus producing fluorinated ethynylarenes **4a–c** with yields of 67–91%. The use of toluene in this reaction resulted in a significant decrease in the yield of the target products because of losses at the stage of isolation of volatile compounds **4a–c**.

2.2. Synthesis of polyfluorinated 2-(arylethynyl)anilines and 2-arylindoles

In this work, a representative series of polyfluorinated 2-iodoanilines **3a–d** was used. It appeared that compounds **3a–d** smoothly entered into the Sonogashira cross-coupling reaction with fluorinated ethynylarenes **4a–c**, producing the target polyfluorinated 2-aminotolans **2**(**a–d**)(**a–c**). Meanwhile, small amounts of the corresponding diynes (**9a–c**, Scheme 4) were always detected among the reaction products. The yields of the 2-aminotolans are presented in Table 1.

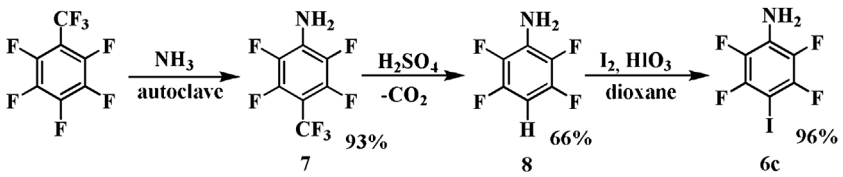
Table 1 shows that the lowest yields of 2-aminotolans **2** were obtained in the reaction between 2-iodoanilines **3b–d** and ethynyltetrafluoroaniline (**4c**). This result is due to the low reactivity of **4c**, which prevents the full extent of conversion of the initial compound, even when the reaction time is doubled. The fact that the polyfluorination of substrates decreases the reactivity was confirmed by an attempt to perform the opposite type of the cross-coupling reaction between 4-iodoaniline **6c** and 2-ethynyl-3,5,6-trifluoro-4-(trifluoromethyl)aniline (**4d**). In this case, even after 6 h, we achieved only 25% conversion of ethynylarene **4d** into the target 2-aminotolan (**2dc**), with a yield of 19% after isolation. 2,3,5,6-Tetrafluoroaniline (**8**) was a by-product with a yield of ~20%, while unreacted compounds **4d** and **6c** were isolated from the reaction mixture with yields of 25% and 33%, respectively (Scheme 5). Therefore, the cross-coupling of polyfluorinated compounds **4d** and **6c** is noticeably slower than that of the less fluorinated substrates, and this reaction is complicated by parallel processes such as deiodination of compound **6c**.

The successful synthesis of polyfluorinated 2-aminotolans **2** allowed us to proceed to the main task of the study, i.e., investigation of the heterocyclisation of tolans **2** into indoles. It is known that this process may be implemented through activation of either electrophilic or nucleophilic functions of the molecule. The first type of heterocyclisation mentioned can be induced by transition metal compounds (method *A*, Fig. 1), e.g. $PdCl_2$ [26], or proton donor acids (method *B*), e.g. *p*-TSA [27], due to formation of a partial positive charge on the carbon atom of the substrate's triple bond. The second type heterocyclisation involves activation of the amine group under the influence of bases (method C, Fig. 1) [32].

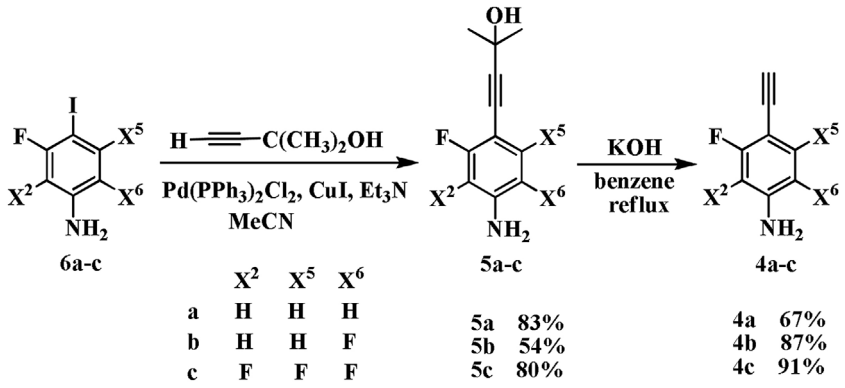
In our study, the initial emphasis was on heterocyclisation method *B*, which, judging by our experience [27], ensured a good yield of 2-phenylindoles. Nevertheless, the experiments we conducted revealed that an increased number of fluorine atoms in the tolan scaffold significantly decreased the yield, whereas in the case of substrates with the highest fluorine content, the heterocyclisation did not occur at all. Therefore, we tested alternative methods, *A* and *C*, to obtain polyfluorinated indoles, using the systems of $PdCl_2$/MeCN and KOH/MeCN, respectively. The data on the structure and yields of the reaction products under various experimental conditions are summarised in Table 2.

Table 2 shows that the cyclisation of polyfluorinated 2-aminotolans **2** containing six or fewer fluorine atoms proceeds smoothly in the *p*-TSA/AlkOH system and in the $PdCl_2$/MeCN system, producing the target 2-arylindoles (**1**) with yields of 45–81%. In addition, the acid-catalysed cyclisation of compounds containing one or two fluorine atoms in the peripheral ring proceeded more effectively than the reaction catalysed by the transition metal cation (the yield of **1** is higher with *p*-TSA than the yield in the case of $PdCl_2$; reaction 1 versus 2; reaction 3 vs. 4 in Table 2). On the other hand, as soon as the number of fluorine atoms is increased, the situation is reversed. In the presence of *p*-TSA, 2-aminotolans with four fluorine atoms in the peripheral ring cyclised with a lower yield than in the presence of $PdCl_2$ (reaction 5 vs. 6; reaction 9 vs. 10 in Table 2), or the heterocyclisation reaction did not occur at all (reaction 13 vs. 14; reaction 19 vs. 21, Table 2).

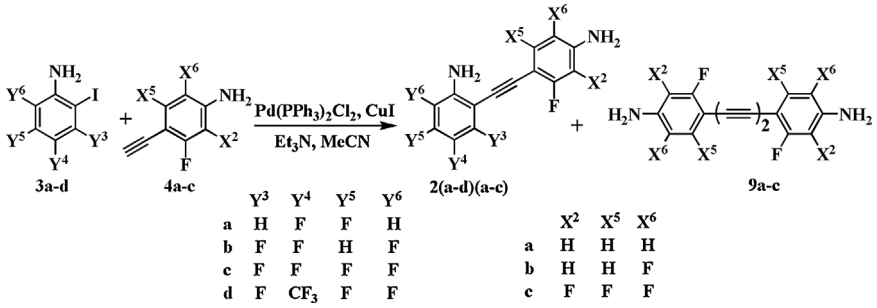
With a larger number of fluorine atoms on both aromatic fragments of a tolane, strong deactivation of the triple bond takes



Scheme 2. Preparation of 4-iodoaniline **6c**.



Scheme 3. Synthesis of 4-ethynylanilines **4a–c**.



Scheme 4. Sonogashira cross-coupling of iodoanilines **3a–d** with ethynylarenes **4a–c**.

place toward its interaction with a cation. This outcome is especially well-pronounced in the case of conversion of **2dc** into **1dc**, which, under the influence of *p*-TSA, takes place only when the reaction is carried out at the boiling point of *n*-BuOH, whereas even boiling the reaction mixture in EtOH for 6 h yielded no detectable production of **1dc** (reactions 19 and 20, Table 2). The method that was found to be effective in this case consisted in carrying out the reaction in the presence of $PdCl_2$ or, even better, in KOH; both of these approaches ensured production of polyfluoroindoles with an acceptable yield (reactions 21 and 22, Table 2). For cyclisation of 2-aminotolan **2cc**, which contains eight fluorine atoms, base catalysis appeared to be the most effective (reactions 13–15).

3. Conclusion

We demonstrated feasibility of the synthesis of a wide spectrum of polyfluorinated aromatic moieties of 2-aminotolans and 2-arylindoles. This work may open up new opportunities for the synthesis of novel biologically active compounds. It was established that with the increased number of fluorine atoms in the peripheral ring of 2-aminotolans, it is preferable to use $PdCl_2$ rather than *p*-TSA as the cyclising agent. Cyclisation of 2-aminotolans **2dc** and **2cc** (containing the greatest numbers of fluorine atoms) proceeds efficiently only under the conditions of base catalysis (KOH/MeCN). The latter finding is a valuable contribution to the field of synthesis of perfluoroindoles (currently, a challenge for researchers).

4. Experimental section

4.1. General methods

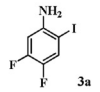
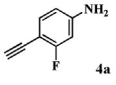
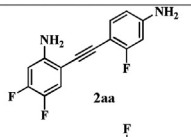
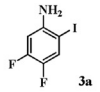
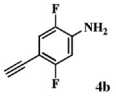
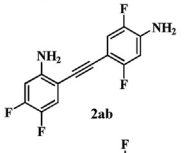
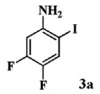
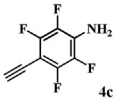
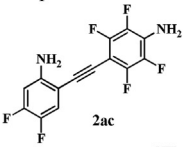
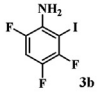
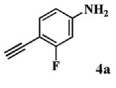
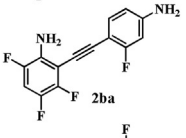
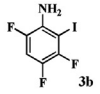
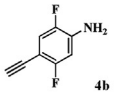
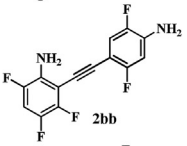
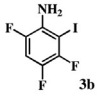
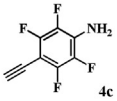
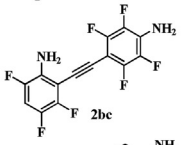
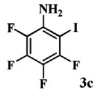
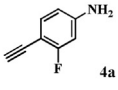
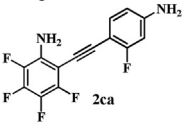
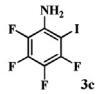
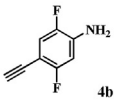
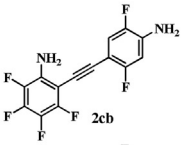
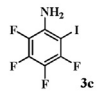
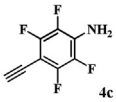
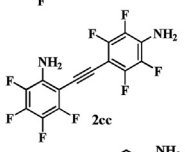
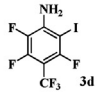
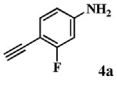
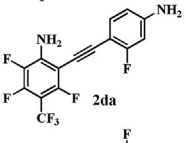
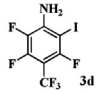
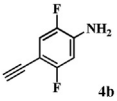
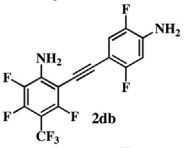
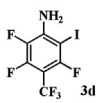
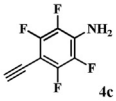
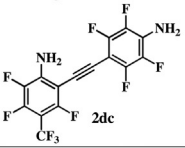
All the cross-coupling reactions were carried out in oven-dried glassware in an argon atmosphere. All solvents were purified using standard procedures and dried before use. Et_3N, MeCN were distilled and kept over CaH_2 before use, KOH (≥90%, flakes or heat-treated powder) were kept over P_2O_5. 2-Iodo-4,5-difluoroaniline (**3a**) [33], 2-iodo-3,4,6-trifluoroaniline (**3b**) [31], 2-iodo-3,5,6-trifluoro-4-(trifluoromethyl)aniline (**3d**) [31], 3-fluoro-4-iodoaniline (**6a**) [30], 2-ethynyl-3,5,6-trifluoro-4-(trifluoromethyl)aniline (**4d**) [26], $Pd(PPh_3)_2Cl_2$ [34] were prepared according to literature data. Other starting materials were obtained from commercial suppliers and used without purification.

Analytical thin-layer chromatography (TLC) was performed on Merck precoated silica gel 60 PF_{254} containing gypsum. Visualisation of the developed chromatograms was performed under UV light. To obtain analytically pure samples, the synthesised compounds were crystallized from hexane.

NMR spectra were recorded on a Bruker Avance-300 (300.13 MHz for ^1H and 282.37 MHz for ^{19}F), Avance-400 (400.13 MHz for ^1H, 376.44 MHz for ^{19}F and 100.62 MHz for ^{13}C) and DRX-500 (500.13 MHz for ^1H, 125.76 MHz for ^{13}C) spectrometers. Deuterochloroform ($CDCl_3$) and acetone-d_6 were used as solvents, with residual $CHCl_3$ (δ_H = 7.26 ppm) or $CDCl_3$ (δ_C = 77.0 ppm) and acetone (δ_H = 2.15 ppm) or acetone-d_6 (δ_C = 28.6 and 205.0 ppm) serving as internal standards. C_6F_6 (δ_F 163.0 ppm) was used as an external reference (^{19}F NMR). ^{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 infrared (IR) spectra were recorded on a Bruker Vector 22 spectrometer (KBr or thin layer). The Raman spectra were recorded on Ramanscope Senterra (25 mV, 785 nm). Elemental analyses were performed on a Euro EA-3000 CHNS analyser or a Carlo Erba 1106 CHN elemental analyser.

The structures of all the polyfluorinated 2-(arylethynyl)anilines and indoles prepared here were corroborated by their ^{19}F, ^1H and ^{13}C NMR, high-resolution mass spectrometry, and IR-spectroscopy data (see Supplementary data). Signals in the NMR spectra of anilines **2** and indoles **1** were assigned on the basis of spin coupling

Table 1
Synthesis of polyfluorinated 2-aminotolans **2**(**a–d**)(**a–c**).

Reaction #	2-Iodoaniline	4-Ethenylaniline	Product	Yield (%)
1	 **3a**	 **4a**	 **2aa**	96
2	 **3a**	 **4b**	 **2ab**	88
3	 **3a**	 **4c**	 **2ac**	98
4	 **3b**	 **4a**	 **2ba**	79
5	 **3b**	 **4b**	 **2bb**	85
6	 **3b**	 **4c**	 **2bc**	47
7	 **3c**	 **4a**	 **2ca**	81
8	 **3c**	 **4b**	 **2cb**	74
9	 **3c**	 **4c**	 **2cc**	48
10	 **3d**	 **4a**	 **2da**	80
11	 **3d**	 **4b**	 **2db**	64
12	 **3d**	 **4c**	 **2dc**	36

constants, which are typical for polyfluorinated benzenes [26,27,31].

4.2. Synthetic procedures

4.2.1. 2,3,5,6-Tetrafluoro-4-(trifluoromethyl)aniline (**7**)

1,2,3,4,5-Pentafluoro-6-(trifluoromethyl)benzene (50 g, 0.3 mol) and liquid ammonia were placed into the autoclave (volumetric capability 0.1 L). The reaction mixture was stirred at room temperature (r.t.) for 6 h. After completion of ammonia evaporation, H_2O (50 mL) was added to the residue. The reaction product was separated by steam distillation. The distillate was extracted with CH_2Cl_2 (2 × 100 mL) and dried ($MgSO_4$). After evaporation of the solvent *in vacuo*, the title product (47 g, 93%) was obtained as colorless liquid (the ^1H and ^{19}F NMR spectra agree well with the literature data [35].

4.2.2. 2,3,5,6-Tetrafluoroaniline (***8***)

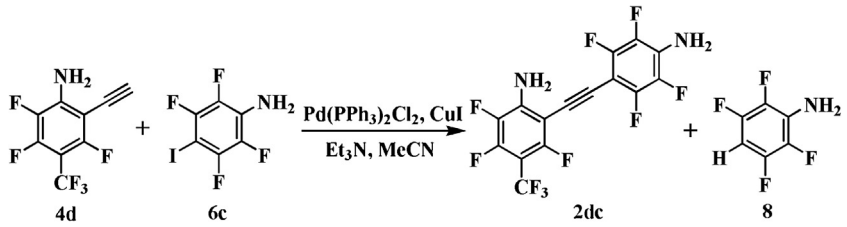
Aniline **7** (15 g, 64 mmol) in concentrated H_2SO_4 (50 mL) was stirred with a condenser at 150 °C for 2 h. Then, H_2O (100 mL) was added into the reaction flask, and the reaction product was separated by steam distillation. The distillate was extracted with CH_2Cl_2 (3 × 50 mL), washed with H_2O (50 mL) and dried ($MgSO_4$). After evaporation of the solvent *in vacuo*, the title product (7 g, 66%) was obtained as light yellow liquid (the ^1H and ^{19}F NMR spectra closely match the literature data [36]. ν_{max} (KBr): 3501, 3414 (NH_2), 1664, 1618, 1524, 1400, 1269, 1178, 1090, 887, 804, 716 cm^{-1}; ^1H NMR (300.13 MHz, $CDCl_3$): δ = 6.36 (tt, 1H, $J_{H,F}3$ = 10.5; $J_{H,F}2$ = 7.3 Hz, H_{ar}), 4.03 (br s, 2H, NH_2); ^{13}C NMR (100.62 MHz, $CDCl_3$): δ = 146.2 (dm, $^1J_{C3,F}$ = 243.4, $^2J_{C3,F}$ = 12.6 Hz, C^3), 136.3 (ddt, $^1J_{C2,F}$ = 238.1, $^2J_{C2,F}$ = 16.2 Hz, C^2), 126.7 (tt, $^2J_{C1,F}$ = 14.3, $^3J_{C1,F}$ = 4.3 Hz, C^1), 93.0 (t, $^2J_{C4,F}$ = 23.2 Hz, C^4); ^{19}F NMR (282.37 MHz, $CDCl_3$): δ = −142.9 (m, 2F, $J_{F3,F2}$ = 24, $J_{F3,H}$ = 10 Hz, F^3), −163.3 (m, 2F, $J_{F2,F3}$ = 24, $J_{F2,H}$ = 7 Hz, F^2); HRMS (EI): M^+, found 165.0205. $C_6H_3F_4N$ requires 165.0196.

4.2.3. 2,5-Difluoro-4-iodoaniline (***6b***)

A mixture of 2,5-difluoroaniline (0.5 g, 3.9 mmol), $NaHCO_3$ (0.8 g, 9.8 mmol), I_2 (2.5 g, 9.8 mmol) and H_2O (50 mL) was stirred at r.t. for 2 h. Than Na_2SO_3 (1 g, 8 mmol) was added, and the reaction mixture was extracted with CH_2Cl_2 (2 × 50 mL). The combined organic layers were washed with H_2O (50 mL), dried ($MgSO_4$) and purified by flash chromatography on Al_2O_3. Evaporation of the solvent was performed *in vacuo* to obtain **6b** (0.9 g, 91%) as brown solid (the ^1H and ^{13}C NMR spectra closely agree with the literature data [37]); ν_{max} (KBr): 3464, 3379, 3042, 2926, 2855, 1632, 1501, 1414, 1323, 1298, 1234, 1184, 1167, 864, 837, 795, 733, 596, 444 cm^{-1}; ^1H NMR (500.13 MHz, $CDCl_3$): δ = 7.27 (dd, 1H, $J_H3,_F2$ = 9.9, $J_H3,_F5$ = 5.6 Hz, H^3), 6.52 (d, 1H, $J_H6,_F5$ = 8.7, $J_H6,_F2$ = 7.7 Hz, H^6), 3.91 (br s, 2H, NH_2); ^{13}C NMR (125.76 MHz, $CDCl_3$): δ = 158.0 (d, $^1J_{C5,F5}$ = 239.1 Hz, C^5), 147.4 (d, $^1J_{C2,F2}$ = 239.6 Hz, C^2), 135.7 (dd, $^2J_{C1,F2}$ = 14.7, $^3J_{C1,F5}$ = 10.6 Hz, C^1), 123.8 (dd, $^2J_{C3,F2}$ = 22.8, $^3J_{C3,F5}$ = 3.5 Hz, C^3), 102.7 (dd, $^2J_{C6,F5}$ = 29.9, $^3J_{C6,F2}$ = 3.7 Hz, C^6), 62.8 (dd, $^2J_{C4,F5}$ = 29.1, $^3J_{C4,F2}$ = 8.1 Hz, C^4); ^{19}F NMR (282.37 MHz, $CDCl_3$): δ = −101.5 (ddd, 1F, $J_{F5,F2}$ = 13.4, $J_{F5,H}6$ = 8.7, $J_{F5,H}3$ = 5.6 Hz, F^5), −140.0 (ddd, 1F, $J_{F2,F5}$ = 13.4, $J_{F2,H}3$ = 9.9, $J_{F2,H}6$ = 7.7 Hz, F^2); HRMS (EI): M^+, found 254.9356. $C_6H_4F_2IN$ requires 254.9351.

4.2.4. 2,3,5,6-Tetrafluoro-4-iodoaniline (***6c***)

To a stirred solution of aniline **7** (3.0 g, 18 mmol) in dioxane (70 mL), we added fine-ground I_2 (2.3 g, 9 mmol) and a solution of HIO_3 (3.2 g, 18 mmol) in H_2O (12 mL). The reaction mixture was refluxed for 4 h, cooled to r.t., poured into H_2O (50 mL) and extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were washed with a saturated water solution of Na_2SO_3 (50 mL)



Scheme 5. Sonogashira cross-coupling of iodoaniline **6c** with ethynyl-3,5,6-trifluoro-4-(trifluoromethyl)aniline **4d**.

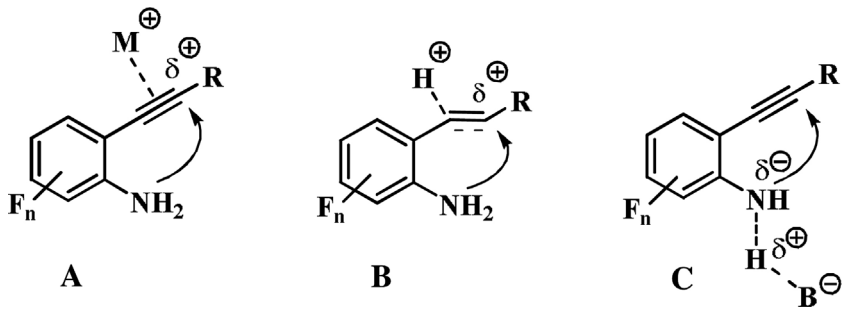


Fig. 1. Different ways of activation of the 2-aminotolan molecule.

solution several times, then with H_2O (100 mL) and dried ($MgSO_4$). After evaporation of the solvent *in vacuo*, the crude product was recrystallized from hexane to obtain the title product (5.0 g, 96%) as light brown solid; m.p. 73.4–74.0 °C (lit. data: 76.9–77.7 °C [36]); [Found: C, 24.38; H, 0.75; N, 4.44. $C_6H_2F_4IN$ requires C, 24.77; H, 0.69; N 4.81%]; ν_{max} (KBr): 3483, 3389, 1655, 1491, 1173, 1101, 920, 802 cm^{-1}; ^1H NMR (500.13 MHz, $CDCl_3$): δ = 4.12 (br s, 2H, NH_2); ^{13}C NMR (125.76 MHz, $CDCl_3$): δ = 146.8 (dm, $^1J_C3,_F$ = 240.9, $^2J_C3,_F$ = 11.8 Hz, C^3), 136.0 (ddt, $^1J_C2,_F$ = 242.0, $^2J_C2,_F$ = 17.3 Hz, C^2), 126.8 (tt, $^2J_C1,_F$ = 14.3, $^3J_C1,_F$ = 3.5 Hz, C^1), 55.1 (t, $^2J_C4,_F$ = 28.1 Hz, C^4); ^{19}F NMR (282.37 MHz, $CDCl_3$): δ = −122.4 (dm, 2F, $J_F3,_F2 \approx 16$ Hz, F^3), −157.6 (dm, 2F, $J_F2,_F3 \approx 16$ Hz, F^2); HRMS (EI): M^+, found 290.9166. $C_6H_2F_4IN$ requires 290.9168.

*4.2.5. General procedure for synthesis of alkynylanilines **5**(**a**,**b**)*

$Pd(PPh_3)_2Cl_2$ (28 mg, 0.04 mmol), CuI (17 mg, 0.09 mmol) and Et_3N (3 mL) were added to a stirred solution of iodoaniline **6** (1 mmol) and 2-methylbut-3-yn-2-ol (168 mg, 2 mmol) in dry MeCN (10 mL) at r.t. in an argon atmosphere. The mixture was heated at 60 °C for 1.5 h with stirring. The reaction mixture was allowed to cool down to r.t., 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 (20 mL) and dried ($MgSO_4$). After evaporation of the solvent *in vacuo*, the crude product was purified by preparative TLC to obtain **5**.

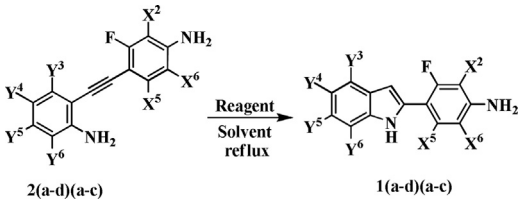
4.2.5.1. 4-(4-Amino-2-fluorophenyl)-2-methylbut-3-yn-2-ol (5a). Preparative TLC (Merck precoated plates, hexane/ethyl acetate, 5:1 three times) was used to obtain **5a** (114 mg, 54%) as brown oil material; R_f 0.29; ν_{max} (thin layer): 3362, 3235, 2982, 2932, 2870, 2225, 1628, 1564, 1512, 1452, 1364, 1331, 1283, 1234, 1169, 1121, 962, 903, 843, 816, 627, 604, 554, 459 cm^{-1}; ^1H NMR (300.13 MHz, $CDCl_3$): δ = 7.12 (t, 1H, $J_H5,_F \approx J_H5,_H6 \approx 9$ Hz, H^5), 6.35–6.29 (m, 2H, H^2, H^6), 3.92 (br s, 2H, NH_2), 2.38 (br s, 1H, $C(CH_3)_2\underline{OH}$), 1.57 (s, 6H, $C(\underline{CH_3})_2OH$); ^{13}C NMR (100.62 MHz, $CDCl_3$): δ = 163.6 (d, $^1J_C3,_F$ = 249.0 Hz, C^3), 148.3 (d, $^3J_C1,_F$ = 10.9 Hz, C^1), 134.0 (d, $^3J_C5,_F$ = 3.1 Hz, C^5), 110.3 (d, $^4J_C6,_F$ = 2.3 Hz, C^6), 101.5 (d, $^2J_C2,_F$ = 24.5 Hz, C^2), 100.0 (d, $^2J_C4,_F$ = 16.2 Hz, C^4), 96.3 (s, C|$\underline{C}$—C(CH_3)$_2$OH), 75.9 (s, $\underline{C}$|C—C(CH_3)$_2$OH), 65.5 (s, C|C—$\underline{C}$(CH_3)$_2$OH), 31.3 (s, C|C—C($\underline{C}H_3$)$_2$OH); ^{19}F NMR (282.37 MHz, $CDCl_3$): δ = −108.1 (dd, 1F, $J_F,_H2$ = 10.8, $J_F,_H5$ = 7.7 Hz, F); HRMS (EI): M^+, found 193.0898. $C_{11}H_{12}FNO$ requires 193.0897.

4.2.5.2. 4-(4-Amino-2,5-difluorophenyl)-2-methylbut-3-yn-2-ol (5b). Preparative TLC (Merck precoated plates, hexane/ethyl acetate, 5:1) was used to obtain **5b** (160 mg, 83%) as light brown oil material; R_f 0.12; ν_{max} (thin layer): 3364, 3225, 3080,2982, 2928, 2855, 2230, 1641, 1514, 1437, 1364, 1258, 1228, 1202, 1171, 1144, 1097, 962, 907, 876, 849, 733, 554, 438 cm^{-1}; ^1H NMR (300.13 MHz, $CDCl_3$): δ = 6.97 (dd, 1H, $J_H3,_F2$ = 11.0, $J_H3,_F5$ = 6.3 Hz, H^3), 6.42 (dd, 1H, $J_H6,_F5$ = 10.1, $J_H6,_F2$ = 7.5 Hz, H^6), 3.95 (br s, 2H, NH_2), 2.05 (br s, 1H, $C(CH_3)_2\underline{OH}$), 1.58 (s, 6H, $C(\underline{CH_3})_2OH$); ^{13}C NMR (100.62 MHz, $CDCl_3$): δ = 159.9 (d, $^1J_C5,_F5$ = 245.9 Hz, C^5), 146.6 (d, $^1J_C2,_F2$ = 235.7 Hz, C^2), 136.3 (dd, $^2J_C1,_F2$ = 15.0, $^3J_C1,_F5$ = 11.2 Hz, C^1), 118.7 (dd, $^2J_C3,_F2$ = 21.9, $^3J_C3,_F5$ = 3.4 Hz, C^3), 102.8 (dd, $^2J_C6,_F5$ = 27.1, $^3J_C6,_F2$ = 4.1 Hz, C^6), 99.4 (dd, $^2J_C4,_F5$ = 18.7, $^3J_C4,_F2$ = 8.8 Hz, C^4), 96.9 (d, $J_C,_F$ = 3.4 Hz, C|$\underline{C}$—C(CH_3)$_2$OH), 75.2 (d, $J_C,_F$ = 2.2 Hz, $\underline{C}$|C—C(CH_3)$_2$OH), 65.6 (s, C|C—$\underline{C}$(CH_3)$_2$OH), 31.3 (s, C|C—C($\underline{C}H_3$)$_2$OH); ^{19}F NMR (282.37 MHz, $CDCl_3$): δ = −116.4 (ddd, 1F, $J_F5,_F2$ = 14.2, $J_F5,_H6$ = 10.1, $J_F5,_H3$ = 6.3 Hz, F^5), −142.3 (ddd, 1F, $J_F2,_F5$ = 14.2, $J_F2,_H3$ = 11.0, $J_F2,_H6$ = 7.5 Hz, F^2); HRMS (EI): M^+, found 211.0805. $C_{11}H_{11}F_2NO$ requires 211.0803.

*4.2.6. 4-(4-Amino-2,3,5,6-tetrafluorophenyl)-2-methylbut-3-yn-2-ol (**5c**)*

$Pd(PPh_3)_2Cl_2$ (95 mg, 0.14 mmol) and CuI (58 mg, 0.31 mmol) were added to a stirred solution of **6c** (1 g, 3.4 mmol) and 2-methylbut-3-yn-2-ol (580 mg, 6.9 mmol) in dry Et_3N (15 mL) at r.t. in an argon atmosphere. The mixture was stirred at r.t. for 88 h. The reaction mixture was diluted with H_2O (20 mL) and extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were washed with H_2O (20 mL) and dried ($MgSO_4$). After evaporation of the solvent *in vacuo*, the crude product was purified by preparative TLC (Merck precoated plates, hexane/ethyl acetate, 5:1, twice) to obtain the title product (679 mg, 80%) as light brown solid; m.p. 91.9–92.5 °C; R_f 0.34; [Found: C, 53.46; H, 3.98; N, 5.79. $C_{11}H_9F_4NO$ requires C, 53.45; H, 3.67; N 5.67%]; ν_{max} (KBr): 3397, 3331, 3267, 2984, 2939, 1661, 1609, 1504, 1458, 1379, 1366, 1315, 1221, 1196, 1167, 1115, 1011, 953, 868, 789, 716, 569, 557 cm^{-1}; ν_{max} (Raman):

Table 2
Synthesis of polyfluorinated 2-arylindoles **1**(**a–d**)(**a–c**).



2(a-d)(a-c) 1(a-d)(a-c)

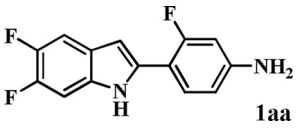
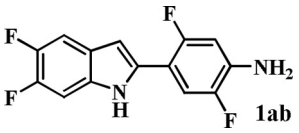
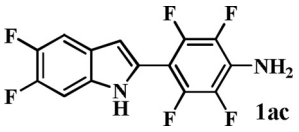
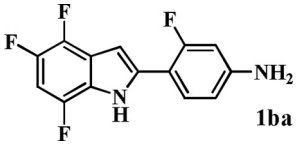
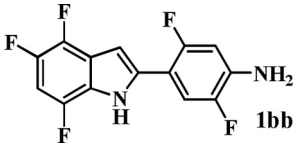
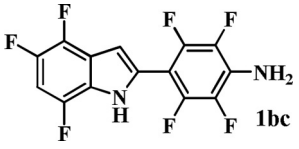
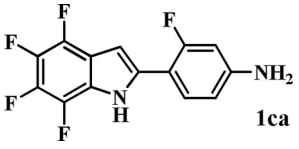
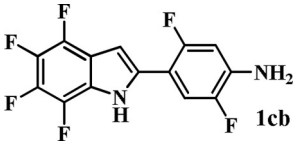
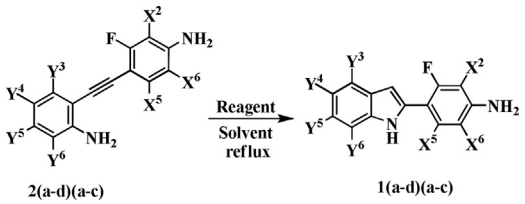
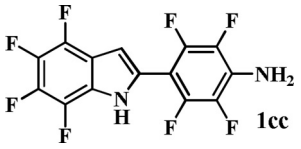
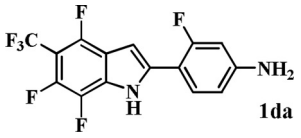
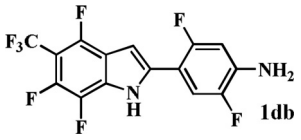
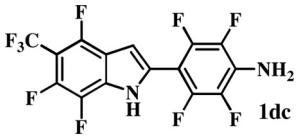
Reaction #	Substrate	Reagent	Solvent	Time (h)	Product	Yield (%)
1	**2aa**	*p*-TSA	EtOH	6	 **1aa**	45
2		$PdCl_2$	MeCN	6		12
3	**2ab**	*p*-TSA	EtOH	7	 **1ab**	63
4		$PdCl_2$	MeCN	5		21
5	**2ac**	*p*-TSA	EtOH	3	 **1ac**	53
6		$PdCl_2$	MeCN	4		67
7	**2ba**	*p*-TSA	EtOH	7.5	 **1ba**	78
8	**2bb**	*p*-TSA	EtOH	3 or 4	 **1bb**	60
9	**2bc**	*p*-TSA	EtOH	8	 **1bc**	45
10		$PdCl_2$	MeCN	6		57
11	**2ca**	*p*-TSA	EtOH	15	 **1ca**	72
12	**2cb**	*p*-TSA	EtOH	1.5	 **1cb**	73

Table 2 (*Continued*)



2(a-d)(a-c) 1(a-d)(a-c)

Reaction #	Substrate	Reagent	Solvent	Time (h)	Product	Yield (%)
13	**2cc**	*p*-TSA	EtOH	5	 **1cc**	n.r.
14		$PdCl_2$	MeCN	4.5		66
15		KOH	MeCN	6		71
16	**2da**	*p*-TSA	*n*-BuOH	20	 **1da**	73
17		*$PdCl_2$*	*MeCN*	5		15
18	**2db**	*p*-TSA	EtOH	9	 **1db**	81
19	**2dc**	*p*-TSA	EtOH	6	 **1dc**	n.r.
20		*p*-TSA	*n*-BuOH	22		9
21		$PdCl_2$	MeCN	6		22
22		KOH	MeCN	6		54

2237 (s), 1660, 1441, 1315, 866, 521 cm^{-1}; ^1H NMR (300.13 MHz, Acetone-d_6): 5.66 (br s, 2H, NH_2), 4.66 (br s, 1H, $C(CH_3)_2\underline{O}H$), 1.54 (s, 6H, $C(\underline{C}H_3)_2OH$); ^{13}C NMR (100.62 MHz, Acetone-d_6): δ = 147.1 (dm, $^1J_C3,_F3$ = 243.8 Hz, C^3), 135.9 (ddm, $^1J_C2,_F2$ = 237.1, $^2J_C2,_F3$ = 15.5 Hz, C^2), 129.0 (tt, $^2J_C1,_F2$ = 14.4, $^3J_C1,_F3$ = 4.0 Hz, C^1), 104.0 (t, $J_{C,F}$ = 3.4 Hz, C|$\underline{C}$—$C(CH_3)_2OH$), 88.9 (t, $^2J_C4,_F3$ = 18.6 Hz, C^4), 66.6 (t, $J_{C,F}$ = 4.0 Hz, $\underline{C}$|C—$C(CH_3)_2OH$), 64.6 (s, C|C—$\underline{C}(CH_3)_2OH$), 30.9 (s, C|C—C($\underline{C}H_3)_2OH$); ^{19}F NMR (282.37 MHz, Acetone-d_6): δ = −143.8 (dm, 2F, $J_F3,_F2 \approx 21$ Hz, F^3), −165.1 (dm, 2F, $J_F2,_F3 \approx 21$ Hz, F^2); HRMS (EI): M^+, found 247.0611. $C_{11}H_9F_4NO$ requires 247.0615.

*4.2.7. General procedure for synthesis of ethynylanilines **4**(**a**–**c**)*

Powdered KOH (336 mg, 6 mmol) was added to a stirred solution of **5** (3 mmol) in benzene (25 mL) at r.t. The mixture was heated under reflux with stirring for 4 h. The reaction mixture was allowed to cool down to r.t., diluted with CH_2Cl_2 (20 mL) and passed through Al_2O_3 (flash chromatography). Evaporation of the solvent and purification of the crude product by preparative TLC yielded **4**.

4.2.7.1. 4-Ethynyl-2-fluoroaniline (4a). Preparative TLC (Merck precoated plates, hexane/ethyl acetate, 6:1 twice) was used to obtain **4a** (271 mg, 67%) as brown oil material; R_f 0.35; ν_{max} (thin layer): 3480, 3391, 3292, 3225, 3067, 3046, 2926, 2853, 2106, 1632, 1605, 1559, 1510, 1491, 1450, 1420, 1369, 1331, 1298, 1250, 1171, 1121, 1101, 961, 839, 743, 664, 604, 432 cm^{-1}; ^1H NMR (400.13 MHz, $CDCl_3$): δ = 7.21 (t, 1H, $J_H5,_F \approx J_H5,_H6 \approx 8$ Hz, H^5), 6.36–6.32 (m, 2H, H^2, H^6), 3.91 (br s, 2H, NH_2), 3.15 (s, 1H, C|CH); ^{13}C NMR (100.62 MHz, $CDCl_3$): δ = 164.4 (d, $^1J_C3,_F$ = 249.9 Hz, C^3), 148.8 (d, $^3J_C1,_F$ = 11.0 Hz, C^1), 134.6 (d, $^3J_C5,_F$ = 3.3 Hz, C^5), 110.3 (d, $^4J_C6,_F$ = 2.6 Hz, C^6), 101.4 (d, $^2J_C2,_F$ = 24.4 Hz, C^2), 99.4 (d, $^2J_C4,_F$ = 16.1 Hz, C^4), 79.7 (d, $J_{C,F}$ = 3.0 Hz C|$\underline{C}$H), 77.7 (s, $\underline{C}$|CH); ^{19}F NMR (282.37 MHz, $CDCl_3$): δ = −111.0 (dd, 1F, $J_F,_H2$ = 10.7, $J_F,_H5$ = 7.6 Hz, F); HRMS (EI): M^+, found 135.0476. C_8H_6FN requires 135.0479.

4.2.7.2. 4-Ethynyl-2,5-difluoroaniline (4b). Preparative TLC (Merck precoated plates, hexane/ethyl acetate, 5:1) was used to obtain **4b** (399 mg, 87%) as brown oil material; R_f 0.28; ν_{max} (thin layer):

3493, 3379, 3314, 2953, 2922, 2853, 2112, 1742, 1641, 1524, 1462, 1377, 1302, 1240, 1213, 1177, 876, 839, 721, 590 cm^{-1}; ^1H NMR (400.13 MHz, $CDCl_3$): δ = 7.04 (dd, 1H, $J_H3,_F2$ = 11.0, $J_H3,_F5$ = 6.2 Hz, H^3), 6.44 (dd, 1H, $J_H6,_F5$ = 10.1, $J_H6,_F2$ = 7.5 Hz, H^6), 3.99 (br s, 2H, NH_2), 3.16 (d, 1H, $J_{H,F}$ = 0.5 Hz, C|C—H); ^{13}C NMR (125.77 MHz, $CDCl_3$): δ = 160.2 (dd, $^1J_C5,_F5$ = 246.6, $^4J_C5,_F2$ = 1.8 Hz, C^5), 146.5 (dd, $^1J_C2,_F2$ = 236.1, $^4J_C2,_F5$ = 2.3 Hz, C^2), 136.9 (dd, $^2J_C1,_F2$ = 14.8, $^3J_C1,_F5$ = 11.3 Hz, C^1), 119.1 (dd, $^2J_C3,_F2$ = 22.0, $^3J_C3,_F5$ = 3.4 Hz, C^3), 102.7 (dd, $^2J_C6,_F5$ = 27.0, $^3J_C6,_F2$ = 4.1 Hz, C^6), 98.6 (dd, $^2J_C4,_F5$ = 18.3, $^3J_C4,_F2$ = 8.6 Hz, C^4), 80.4 (d, $J_{C,F}$ = 3.3 Hz, C|C—H), 76.7 (d, $J_{C,F}$ = 3.5 Hz, C|C—H); ^{19}F NMR (282.37 MHz, $CDCl_3$): δ = −116.2 (ddd, 1F, $J_F5,_F2$ = 14.3, $J_F5,_H6$ = 10.1, $J_F5,_H3$ = 6.2 Hz, F^5), −142.1 (ddd, 1F, $J_F2,_F5$ = 14.3, $J_F2,_H3$ = 11.0, $J_F2,_H6$ = 7.5 Hz, F^2); HRMS (EI): M^+, found 153.0383. $C_8H_5F_2N$ requires 153.0385.

4.2.7.3. 4-Ethynyl-2,3,5,6-tetrafluoroaniline (4c). Preparative TLC (Merck precoated plates, hexane/ethyl acetate, 7:1, twice) was used to isolate the title product (516 mg, 91%) as brown solid; m.p. 50.1 °C (decomp.); R_f 0.37; ν_{max} (KBr): 3483, 3385, 3302, 3198, 2932, 2120, 1665, 1622, 1504, 1433, 1364, 1310, 1250, 1173, 1146, 1113, 953, 935, 802, 689, 627 cm^{-1}; ^1H NMR (400.13 MHz, Acetone-d_6): 5.87 (br s, 2H, NH_2), 4.10 (s, 1H, C|C—H); ^{13}C NMR (100.62 MHz, Acetone-d_6): δ = 147.8 (dm, $^1J_C3,_F3$ = 244.5 Hz, C^3), 136.8 (ddm, $^1J_C2,_F2$ = 237.4, $^2J_C2,_F3$ = 15.3 Hz, C^2), 129.9 (tt, $^2J_C1,_F2$ = 14.2, $^3J_C1,_F3$ = 4.3 Hz, C^1), 87.6 (t, $^2J_C4,_F3$ = 18.5 Hz, C^4), 87.5 (t, $J_{C,F}$ = 3.2 Hz, C|C—H), 69.3 (t, $J_{C,F}$ = 3.8 Hz, C|C—H); ^{19}F NMR (282.37 MHz, Acetone-d_6): δ = −140.6 (dm, 2F, $J_F3,_F2 \approx 22$ Hz, F^3), −163.5 (dm, 2F, $J_F2,_F3 \approx 22$ Hz, F^2); HRMS (EI): M^+, found 189.0192. $C_8H_3F_4N$ requires 189.0196.

*4.2.8. General procedure for synthesis of 2-aminotolans **2**(**a**–**d**)(**a**–**c**)*

$Pd(PPh_3)_2Cl_2$ (28 mg, 0.04 mmol), CuI (17 mg, 0.09 mmol) and Et_3N (3 mL) were added to a stirred solution of 2-iodaniline **3** (1 mmol) and ethynylaniline **4** (1.3 mmol) in MeCN (12 mL) at r.t. in an argon atmosphere. The reaction mixture was stirred at 60 °C for 4 h and allowed to cool to r.t. Then, the mixture was diluted with CH_2Cl_2 (10 mL), poured into H_2O (40 mL) and extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were washed with H_2O (30 mL) and dried ($MgSO_4$). Evaporation of the solvent *in vacuo* yielded crude product **2** and a small amount of **9** that were separated and purified by preparative TLC.

4.2.8.1. 2-[(4-Amino-2-fluorophenyl)ethynyl]-4,5-difluoroaniline (2aa). Preparative TLC (Merck precoated plates, hexane/ethyl acetate, 5:1 twice) was used to isolate **2aa** (252 mg, 96%) as light brown solid; m.p. 92.4 °C (decomp.); R_f 0.35; [Found: C, 64.02; H, 3.25. $C_{14}H_9F_3N_2$ requires C, 64.12; H, 3.46%]; ν_{max} (KBr): 3485, 3400, 3377, 3219, 3053, 2974, 2927, 2854, 2200, 1699, 1626, 1562, 1518, 1471, 1441, 1362, 1327, 1302, 1281, 1236, 1203, 1165, 1122, 1066, 958, 887, 854, 820, 764, 741, 627, 488, 463 cm^{-1}; ^1H NMR (300.13 MHz, acetone-d_6): δ = 7.39–7.27 (m, 2H, H^7, H^3), 6.71 (dd, 1H, $J_H6,_F5$ = 12.8, $J_H6,_F4$ = 7.3 Hz, H^6), 6.55 (dd, 1H, $J_H10,_F11$ = 11.5, $J_H10,_H8$ = 2.6 Hz, H^{10}), 6.37 (td, 1H, $J_H8,_H7 \approx J_H8,_F11 \approx 9$, $J_H8,_H10$ = 2.6 Hz, H^8), 5.46 (br s, 2H, NH_2), 5.28 (br s, 2H, NH_2); ^{13}C NMR (100.62 MHz, acetone-d_6): δ = 164.0 (d, $^1J_C10,_F$ = 244.5 Hz, C^{10}), 151.2 (d, $^3J_C12,_F$ = 12.2 Hz, C^{12}), 150.9 (dd, $^1J_C5,_F5$ = 245.8, $^2J_C5,_F4$ = 13.8 Hz, C^5), 146.8 (d, $^3J_C1,_F5$ = 9.6 Hz, C^1), 141.6 (dd, $^1J_C4,_F4$ = 234.1, $^2J_C4,_F5$ = 13.6 Hz, C^4), 133.8 (d, $^3J_C14,_F10$ = 10.7 Hz, C^{14}), 119.5 (d, $^2J_C3,_F4$ = 18.9 Hz, C^3), 103.3 (d, $^2J_C6,_F5$ = 23.0 Hz C^6), 103.2 (d, $^2J_C9,_F10 \approx 14$ Hz C^9), 102.9 (dd, $^3J_C2,_F4$ = 7.5, $^4J_C2,_F5$ = 2.6 Hz C^2), 102.0 (d, $^4J_C13,_F10$ = 21.1 Hz, C^{13}), 100.2 (d, $^2J_C11,_F10$ = 25.6 Hz, C^{11}), 90.5 (d, $J_C7,_F10$ = 1.1 Hz $C^7|C^8$), 88.2 (d, $J_C8,_F10$ = 1.3 Hz, $C^7|C^8$); ^{19}F NMR (282.37 MHz, acetone-d_6): δ = −109.8 (dd, 1F, $J_F11,_H10$ = 11.5, $J_F11,_H7$ = 8.0 Hz, F^{11}), −135.5 (ddd, 1F, $J_F5,_F4$ = 22.5, $J_F5,_H6$ = 12.8, $J_F5,_H3$ = 8.8 Hz, F^5), −153.1 (ddd, 1F, $J_F4,_F5$ = 22.5, $J_F4,_H3$ = 11.1, $J_F4,_H6$ = 7.3 Hz, F^{11}); HRMS (EI): M^+, found 262.0707. $C_{14}H_9F_3N_2$ requires 262.0712.

4.2.8.2. 2-((4-Amino-2,5-difluorophenyl)ethynyl)-4,5-difluoroaniline (2ab). Preparative TLC (Merck precoated plates, hexane/ethyl acetate, 5:1 twice) was used to obtain **2ab** (262 mg, 88%) as light brown solid; m.p. 122.5 °C (decomp.); R_f 0.42; [Found: C, 60.23; H, 2.80; N, 10.08. $C_{14}H_8F_4N_2$ requires C, 60.01; H, 2.88; N, 10.00%]; ν_{max} (KBr): 3500, 3454, 3404, 3331, 3205, 3086, 3063, 1639, 1603, 1529, 1518, 1437, 1375, 1300, 1259, 1232, 1209, 1186, 1169, 1134, 874, 841, 820, 742, 717, 642, 511 cm^{-1}; ν_{max} (Raman): 2214 (s) cm^{-1}; ^1H NMR (300.13 MHz, acetone-d_6): δ = 7.20–7.11 (m, 2H, H^7, H^3), 6.71–6.62 (m, 2H, H^6, H^{10}), 5.39 (br s, 2H, NH_2), 5.21 (br s, 2H, NH_2); ^{13}C NMR (100.62 MHz, acetone-d_6): δ = 164.0 (d, $^1J_C10,_F$ = 244.5 Hz, C^{10}), 151.2 (d, $^3J_C12,_F$ = 12.2 Hz, C^{12}), 150.9 (dd, $^1J_C5,_F5$ = 245.8, $^2J_C5,_F4$ = 13.8 Hz, C^5), 146.8 (d, $^3J_C1,_F5$ = 9.6 Hz, C^1), 141.6 (dd, $^1J_C4,_F4$ = 234.1, $^2J_C4,_F5$ = 13.6 Hz, C^4), 133.8 (d, $^3J_C14,_F10$ = 10.7 Hz, C^{14}), 119.5 (d, $^2J_C3,_F4$ = 18.9 Hz, C^3), 103.3 (d, $^2J_C6,_F5$ = 23.0 Hz C^6), 103.2 (d, $^2J_C9,_F10 \approx 14$ Hz C^9), 102.9 (dd, $^3J_C2,_F4$ = 7.5, $^4J_C2,_F5$ = 2.6 Hz C^2), 102.0 (d, $^4J_C13,_F10$ = 21.1 Hz, C^{13}), 100.2 (d, $^2J_C11,_F10$ = 25.6 Hz, C^{11}), 90.5 (d, $J_C7,_F10$ = 1.1 Hz $C^7|C^8$), 88.2 (d, $J_C8,_F10$ = 1.3 Hz, $C^7|C^8$); ^{19}F NMR (282.37 MHz, acetone-d_6): δ = −114.8 (ddd, 1F, $J_F11,_F8$ = 13.8, $J_F11,_H10$ = 11.0, $J_F11,_H7$ = 6.4 Hz, F^{11}), −135.2 (ddd, 1F, $J_F5,_F4$ = 22.5, $J_F5,_H6$ = 12.6, $J_F5,_H3$ = 8.8 Hz, F^5), −140.3 (ddd, 1F, $J_F8,_F11$ = 13.8, $J_F8,_H7$ = 11.5, $J_F8,_H10$ = 7.7 Hz, F^8), −153.3 (ddd, 1F, $J_F4,_F5$ = 22.5, $J_F4,_H3$ = 11.1, $J_F4,_H6$ = 7.4 Hz, F^4); HRMS (EI): M^+, found 280.0617. $C_{14}H_8F_4N_2$ requires 280.0618.

4.2.8.3. 4-((2-Amino-4,5-difluorophenyl)ethynyl)-2,3,5,6-tetrafluoroaniline (2ac). Preparative TLC (Merck precoated plates, hexane/ethyl acetate, 5:1) was used to isolate **2ac** (310 mg, 98%) as light brown solid; m.p. 163.0 °C (decomp.); R_f 0.42; [Found: C, 53.29; H, 2.27. $C_{14}H_6F_6N_2$ requires C, 53.18; H, 1.91%]; ν_{max} (KBr): 3510, 3471, 3406, 3377, 3199, 3059, 2220 (ww), 1622, 1664, 1593, 1525, 1500, 1458, 1431, 1358, 1313, 1292, 1227, 1192, 1161, 1103, 958, 935, 883, 845, 833, 742, 685, 633, 542 cm^{-1}; ν_{max} (Raman): 2218 (s) cm^{-1}; ^1H NMR (300.13 MHz, acetone-d_6): δ = 7.20 (dd, 1H, $J_H3,_F4$ = 10.9, $J_H3,_F5$ = 8.8 Hz, H^3), 6.72 (dd, 1H, $J_H6,_F5$ = 12.7, $J_H6,_F4$ = 7.2 Hz, H^6), 5.81 (br s, 2H, NH_2), 5.23 (br s, 2H, NH_2); ^{13}C NMR (100.62 MHz, acetone-d_6): δ = 151.6 (d, $^1J_C5,_F$ = 247.5 Hz, C^5), 147.3 (d, $^3J_C1,_F$ = 10.1 Hz, C^1), 146.8 (dm, $^1J_C10,_F$ = 248.8 Hz, C^{10}), 141.7 (dd, $^1J_C4,_F$ = 234.9, $^2J_C4,_F$ = 13.8 Hz, C^4), 135.8 (dm, $^1J_C11,_F$ = 237.6, $^2J_C11,_F$ = 15.4 Hz, C^{11}), 129.5 (td, $^2J_C12,_F$ = 14.4, $^3J_C12,_F$ = 4.1 Hz, C^{12}), 119.1 (dd, $^2J_C3,_F$ = 19.1, $^3J_C3,_F$ = 2.0 Hz, C^3), 102.2 (d, $^2J_C6,_F$ = 21.1 Hz, C^6), 101.5 (dd, $^3J_C2,_F$ = 7.2, $^4J_C2,_F$ = 2.7 Hz C^2), 92.9 (t, $^4J_C7,_F$ = 2.3 Hz $C^7|C^8$), 88.7 (t, $^2J_C9,_F10$ = 18.7 Hz, C^9), 80.2 (s, $C^7|C^8$); ^{19}F NMR (282.37 MHz, acetone-d_6): δ = −133.9 (ddd, 1F, $J_F5,_F4$ = 22.5, $J_F5,_H6$ = 12.7, $J_F5,_H3$ = 8.8 Hz, F^5), −140.2 (dm, 2F, $J_F7,_F8 \approx 21$ Hz, F^7), −152.9 (ddd, 1F, $J_F4,_F5$ = 22.5, $J_F4,_H3$ = 10.9, $J_F4,_H6$ = 7.2 Hz, F^4), −161.9 (dm, 2F, $J_F8,_F7 \approx 21$ Hz, F^8); HRMS (EI): M^+, found 316.0431. $C_{14}H_6F_6N_2$ requires 316.0430.

4.2.8.4. 2-((4-Amino-2-fluorophenyl)ethynyl)-3,4,6-trifluoroaniline (2ba). Preparative TLC (Merck precoated plates, hexane/ethyl acetate, 10:1 twice) was used to obtain **2ba** (221 mg, 79%) as light brown solid; (decomp. befor melt.); R_f 0.22; ν_{max} (KBr): 3481, 3385, 3227, 3067, 2205, 1618, 1591, 1562, 1501, 1385, 1335, 1310, 1219, 1173, 1119, 984, 957, 910, 839, 814, 745, 708, 692, 606, 532 cm^{-1}; ^1H NMR (300.13 MHz, acetone-d_6): δ = 7.32 (t, 1H, $J_H7,_H8 \approx J_H7,_F = 8.2$ Hz, H^7), 7.10 (td, 1H, $J_H5,_F6 \approx J_H5,_F4 = 10.6$, $J_H5,_F3 = 7.3$ Hz, H^5), 6.57–6.50 (m, 2H, H^{10}, H^8), 5.47 (br s, 2H, NH_2), 5.08 (br s, 2H, NH_2); ^{13}C NMR (125.77 MHz, acetone-d_6): δ = 164.0 (d, $^1J_C10,_F$ = 246.9 Hz, C^{10}), 151.3 (d, $^3J_C12,_F$ = 11.8 Hz, C^{12}), 146.4 (ddd, $^1J_C3,_F$ = 243.0, $^2J_C3,_F$ = 13.6 Hz,

C^3), 145.3 (dd, $^1J_C6,_F = 237.0$, $^3J_C6,_F = 10.9$, $^4J_C6,_F = 3.2$ Hz, C^6), 140.4 (dt, $^1J_C4,_F = 235.8$, $^2J_C4,_F \approx {}^3J_C4,_F = 13.9$ Hz, C^4), 134.7 (d, $^2J_C1,_F = 15.0$ Hz, C^1), 134.0 (s, C^{14}), 110.4 (s, C^{13}), 104.8 (t, $^2J_C5,_F4 \approx {}^2J_C5,_F6 = 24.8$ Hz, C^5), 101.1 (d, $^2J_C2,_F = 24.1$ Hz, C^2), 99.3 (d, $^2J_C11,_F = 24.1$ Hz, C^{11}), 97.2 (d, $^2J_C9,_F = 16.2$ Hz, C^9), 96.2 (d, $J_C8,_F = 3.4$ Hz $C^7|\underline{C}^8$), 80.0 (m, $J_C7,_F = 2.6$ Hz, $\underline{C}^7|C^8$); ^{19}F NMR (282.37 MHz, acetone-d_6): δ = −109.7 (dd, 1F, $J_F11,_H10 = 11.8$, $J_F11,_H7 = 8.6$ Hz, F^{11}), −136.0 (ddd, 1F, $J_F6,_F3 = 13.5$, $J_F6,_H5 = 11.1$, $J_F6,_F4 = 3.1$ Hz, F^6), −141.2 (ddd, 1F, $J_F3,_F4 = 21.8$, $J_F3,_F6 = 13.5$, $J_F3,_H5 = 7.3$ Hz, F^3), −151.9 (ddd, 1F, $J_F4,_F3 = 21.8$, $J_F4,_H5 = 10.5$, $J_F4,_F6 = 3.1$ Hz, F^4); HRMS (EI): M^+, found 280.0613. $C_{14}H_8F_4N_2$ requires 280.0618.

4.2.8.5. 2-((4-Amino-2,5-difluorophenyl)ethynyl)-3,4,6-trifluoroaniline (2bb). Preparative TLC (Merck precoated plates, hexane/ethyl acetate, 5:1 twice) was used to obtain **2bb** (253 mg, 85%) as brown solid; m.p. 125.2 °C (decomp.); R_f 0.44; [Found: C, 56.44; H, 2.61; N, 9.05. $C_{14}H_7F_5N_2$ requires C, 56.39; H, 2.37; N, 9.39%]; ν_{max} (KBr): 3496, 3479, 3449, 3394, 3353, 3100, 3075, 2213, 1639, 1610, 1586, 1529, 1505, 1438, 395, 1366, 1311, 1289, 1242, 1219, 1174, 1112, 982, 912, 873, 838, 747, 689, 545 cm^{-1}; ^{1}H NMR (300.13 MHz, acetone-d_6): δ = 7.28 (dd, 1H, $J_H7,_F8 = 11.4$, $J_H7,_F11 = 6.4$ Hz, H^7), 7.15 (td, 1H, $J_H5,_F6 \approx J_H5,_F4 = 10.7$, $J_H5,_F3 = 7.3$ Hz, H^5), 6.70 (dd, 1H, $J_H10,_F11 = 11.0$, $J_H10,_F8 = 7.5$ Hz, H^{10}), 5.54 (br s, 2H, NH_2), 5.17 (br s, 2H, NH_2); ^{13}C NMR (100.62 MHz, acetone-d_6): δ = 160.5 (d, $^1J_C10,_F = 244.2$ Hz, C^{10}), 147.3 (d, $^1J_C13,_F = 235.0$ Hz, C^{13}), 147.2 (ddd, $^1J_C3,_F = 243.6$, $^2J_C3,_F = 13.7$, $^4J_C3,_F = 3.6$ Hz, C^3), 146.0 (ddd, $^1J_C6,_F = 237.2$, $^3J_C6,_F = 10.8$, $^4J_C6,_F = 3.3$ Hz, C^6), 140.9 (dt, $^1J_C4,_F = 235.8$, $^2J_C4,_F \approx {}^3J_C4,_F = 13.8$ Hz, C^4), 140.5 (dd, $^2J_C12,_F = 15.1$, $^3J_C12,_F = 12.0$ Hz, C^{12}), 135.5 (dm, $^2J_C1,_F = 15.4$, $^3J_C1,_F = 2.6$ Hz, C^1), 119.0 (dd, $^2J_C14,_F = 22.2$, $^3J_C14,_F = 3.4$ Hz, C^{14}), 105.9 (t, $^2J_C5,_F4 \approx {}^2J_C5,_F6 = 23.7$ Hz, C^5), 102.8 (dd, $^2J_C11,_F = 27.0$, $^3J_C11,_F = 5.0$ Hz, C^{11}), 100.0 (ddd, $^2J_C2,_F = 17.4$, $^3J_C2,_F = 7.1$, $^3J_C2,_F = 1.7$ Hz, C^2), 97.3 (dd, $^2J_C9,_F = 18.8$, $^3J_C9,_F = 9.0$ Hz, C^9), 95.5 (m, $J_C7,_F = 2.2$ Hz $\underline{C}^7|C^8$), 81.4 (m, $J_C8,_F = 2.2$ Hz, $C^7|\underline{C}^8$); ^{19}F NMR (282.37 MHz, acetone-d_6): δ = −114.2 (ddd, 1F, $J_F11,_F8 = 13.8$, $J_F11,_H10 = 11.0$, $J_F11,_H7 = 6.4$ Hz, F^{11}), −135.8 (ddd, 1F, $J_F6,_F3 = 13.7$, $J_F6,_H5 = 11.1$, $J_F6,_F4 = 2.9$ Hz, F^6), −140.2 (ddd, 1F, $J_F8,_F11 = 13.8$, $J_F8,_H7 = 11.4$, $J_F8,_H10 = 7.5$ Hz, F^8), −140.8 (ddd, 1F, $J_F3,_F4 = 21.8$, $J_F3,_F6 = 13.7$, $J_F3,_H5 = 7.3$ Hz, F^3), −151.7 (ddd, 1F, $J_F4,_F3 = 21.8$, $J_F4,_H5 = 10.5$, $J_F4,_F6 = 2.9$ Hz, F^4); HRMS (EI): M^+, found 298.0526. $C_{14}H_7F_5N_2$ requires 298.0524.

4.2.8.6. 4-((2-Amino-3,5,6-trifluorophenyl)ethynyl)-2,3,5,6-tetrafluoroaniline (2bc). Preparative TLC (Merck precoated plates, hexane/ethyl acetate, 5:1 twice) was used to isolate **2bc** (157 mg, 47%) as light brown solid; m.p. 135.1 °C (decomp.); R_f 0.53; [Found: C, 49.84; H, 1.76; N, 8.18. $C_{14}H_5F_7N_2$ requires C, 50.32; H, 1.51; N, 8.38%]; ν_{max} (KBr): 3491, 3452, 3385, 3203, 3064, 2968, 2931, 2220, 1664, 1608, 1504, 1433, 1387, 1329, 1306, 1279, 1173, 1130, 1115, 1038, 939, 920, 843, 725, 694, 642, 617, 579 cm^{-1}; ^{1}H NMR (300.13 MHz, acetone-d_6): δ = 7.23 (td, 1H, $J_H5,_F6 \approx J_H5,_F4 = 10.7$, $J_H5,_F3 = 7.3$ Hz, H^5), 6.02 (br s, 2H, NH_2), 5.22 (br s, 2H, NH_2); ^{13}C NMR (100.62 MHz, acetone-d_6): δ = 146.9 (dm, $^1J_C10,_F = 251.2$ Hz, C^{10}), 146.4 (ddd, $^1J_C3,_F = 244.7$, $^2J_C3,_F = 14.0$, $^4J_C3,_F = 3.6$ Hz, C^3), 145.2 (ddd, $^1J_C6,_F = 237.1$, $^3J_C6,_F = 11.1$, $^4J_C6,_F = 3.5$ Hz, C^6), 140.0 (dt, $^1J_C4,_F = 235.6$, $^2J_C4,_F \approx {}^3J_C4,_F = 13.0$ Hz, C^4), 135.9 (dm, $^1J_C11,_F = 237.2$, $^2J_C11,_F = 14.7$ Hz, C^{11}), 135.1 (dm, $^2J_C1,_F = 15.3$, $^3J_C1,_F = 2.4$ Hz, C^1), 130.4 (td, $^2J_C12,_F = 14.7$, $^3J_C12,_F = 4.7$ Hz, C^{12}), 106.0 (t, $^2J_C5,_F4 \approx {}^2J_C5,_F6 = 23.7$ Hz, C^5), 98.1 (ddd, $^2J_C2,_F = 17.7$, $^3J_C2,_F = 7.0$, $^3J_C2,_F = 1.6$ Hz, C^2), 87.9 (t, $^2J_C9,_F = 18.0$ Hz, C^9), 86.6 (m, $J_C7,_F = 4.0$ Hz $\underline{C}^7|C^8$), 86.1 (m, $J_C8,_F = 2.7$ Hz, $C^7|\underline{C}^8$); ^{19}F NMR (282.37 MHz, acetone-d_6): δ = −135.5 (ddd, 1F, $J_F6,_F3 = 13.6$, $J_F6,_H5 = 11.0$, $J_F6,_F4 = 2.8$ Hz, F^6), −139.8 (dm, 2F, $J_F7,_F8 \approx 19$ Hz, F^7), −140.5 (ddd, 1F, $J_F3,_F4 = 21.7$, $J_F3,_F6 = 13.4$, $J_F3,_H5 = 7.3$ Hz, F^3), −151.7 (ddd, 1F, $J_F4,_F3 = 21.7$, $J_F4,_H5 = 10.5$, $J_F4,_F6 = 2.8$ Hz, F^4), −161.9 (dm, 2F, $J_F8,_F7 \approx 19$ Hz, F^8); HRMS (EI): M^+, found 334.0337. $C_{14}H_5F_7N_2$ requires 334.0336.

4.2.8.7. 2-((4-Amino-2-fluorophenyl)ethynyl)-3,4,5,6-tetrafluoroaniline (2ca). Preparative TLC (Merck precoated plates, hexane/ethyl acetate, 10:1 twice) was used to obtain **2ca** (241 mg, 81%) as light brown solid; m.p. 112.5 °C (decomp.); R_f 0.25; ν_{max} (KBr): 3497, 3420, 3387, 3219, 3044, 3959, 2212, 1630, 1562, 1524, 1497, 1439, 1342, 1325, 1306, 1229, 1173, 1121, 984, 934, 839, 814, 745, 694, 625, 602, 532, 451 cm^{-1}; ^{1}H NMR (300.13 MHz, acetone-d_6): δ = 7.29 (t, 1H, $J_H7,_H8 \approx J_H7,_F = 8.2$ Hz, H^7), 6.54–6.47 (m, 2H, H^{10}, H^8), 5.49 (br s, 2H, NH_2), 5.41 (br s, 2H, NH_2); ^{13}C NMR (125.77 MHz, $CDCl_3$): δ = 164.0 (d, $^1J_C10,_F = 249.7$ Hz, C^{10}), 149.5 (d, $^3J_C12,_F = 11.1$ Hz, C^{12}), 147.5 (ddd, $^1J_C3,_F = 247.5$, $^2J_C3,_F = 11.2$ Hz, C^3), 141.4 (dtd, $^1J_C5,_F = 251.5$, $^2J_C5,_F = 14.0$, $^3J_C5,_F = 5.3$ Hz, C^5), 136.3 (ddm, $^1J_C6,_F = 239.0$, $^2J_C6,_F = 13.3$ Hz, C^6), 134.0 (s, C^{14}), 133.3 (dm, $^2J_C1,_F \approx 14$ Hz, C^1), 132.9 (dtm, $^1J_C4,_F = 244.2$, $^2J_C4,_F \approx {}^3J_C4,_F = 13.3$ Hz, C^4), 110.7 (d, $^4J_C13,_F = 2.2$ Hz, C^{13}), 101.6 (d, $^2J_C11,_F = 24.4$ Hz, C^{11}), 99.9 (d, $^2J_C9,_F = 16.1$ Hz, C^9), 95.4 (t, $J_C8,_F = 3.2$ Hz $C^7|\underline{C}^8$), 95.1 (dm, $^2J_C2,_F = 16.6$ Hz, C^2), 79.8 (m, $\underline{C}^7|C^8$); ^{19}F NMR (282.37 MHz, acetone-d_6): δ = −109.7 (dd, 1F, $J_F11,_H10 = 11.7$, $J_F11,_H7 = 8.2$ Hz, F^{11}), −139.2 (dd, 1F, $J_F3,_F4 = 22.2$, $J_F3,_F6 = 9.1$ Hz, F^3), −158.3 (t, 1F, $J_F5,_F6 \approx J_F5,_F4 \approx 21$ Hz, F^5), −162.3 (m, 1F, $J_F6,_F5 = 19.9$, $J_F6,_F3 = 9.1$, $J_F6,_F4 = 6.6$ Hz, F^6), −175.9 (tm, 1F, $J_F4,_F3 \approx J_F4,_F5 \approx 21$, $J_F4,_F6 = 6.6$ Hz, F^4); HRMS (EI): M^+, found 298.0525. $C_{14}H_7F_5N_2$ requires 298.0529.

4.2.8.8. 2-((4-Amino-2,5-difluorophenyl)ethynyl)-3,4,5,6-tetrafluoroaniline (2cb). Preparative TLC (Merck precoated plates, hexane/ethyl acetate, 7:1 twice) was used to isolate **2cb** (234 mg, 74%) as brown solid; m.p. 94.5 °C (decomp.); R_f 0.22; ν_{max} (KBr): 3483, 3412, 3310, 3196, 2955, 2928, 2868, 2216, 1641, 1530, 1499, 1452, 1429, 1366, 1312, 1246, 1221, 1184, 1119, 1086, 986, 937, 870, 841, 824, 691, 544, 482, 436 cm^{-1}; ^{1}H NMR (300.13 MHz, acetone-d_6): δ = 7.18 (dd, 1H, $J_H7,_F8 = 11.5$, $J_H7,_F11 = 6.4$ Hz, H^7), 6.63 (dd, 1H, $J_H10,_F11 = 11.0$, $J_H10,_F8 = 7.5$ Hz, H^{10}), 5.44 (br s, 2H, NH_2), 5.36 (br s, 2H, NH_2); ^{13}C NMR (100.62 MHz, acetone-d_6): δ = 159.8 (d, $^1J_C10,_F = 243.8$ Hz, C^{10}), 147.2 (dm, $^1J_C3,_F = 241.0$ Hz, C^3), 146.5 (dm, $^1J_C13,_F = 234.9$ Hz, C^{13}), 141.2 (dtd, $^1J_C5,_F = 248.5$, $^2J_C5,_F = 14.2$, $^3J_C5,_F = 5.7$ Hz, C^5), 139.8 (dd, $^2J_C12,_F = 15.4$, $^3J_C12,_F = 12.3$ Hz, C^{12}), 135.8 (ddm, $^1J_C6,_F = 238.5$, $^2J_C6,_F = 12.4$ Hz, C^6), 135.1 (dm, $^2J_C1,_F = 11.3$ Hz, C^1), 131.6 (dtm, $^1J_C4,_F = 239.6$, $^2J_C4,_F = 14.7$, $^3J_C4,_F = 3.4$ Hz, C^4), 118.2 (dd, $^2J_C14,_F = 22.2$, $^3J_C14,_F = 3.0$ Hz, C^{14}), 101.9 (dd, $^2J_C11,_F = 27.1$, $^3J_C11,_F = 5.3$ Hz, C^{11}), 96.3 (dd, $^2J_C9,_F = 18.6$, $^3J_C9,_F = 9.4$ Hz, C^9), 94.4 (m, $C^7|\underline{C}^8$), 93.8 (dm, $^2J_C2,_F = 16.9$ Hz, C^2), 79.2 (m, $J_C7,_F = 2.0$ Hz $\underline{C}^7|C^8$); ^{19}F NMR (282.37 MHz, acetone-d_6): δ = −114.2 (ddd, 1F, $J_F11,_F8 = 13.7$, $J_F11,_H10 = 11.0$, $J_F11,_H7 = 6.5$ Hz, F^{11}), −138.7 (ddd, 1F, $J_F3,_F4 = 22.1$, $J_F3,_F6 = 9.1$, $J_F3,_F5 = 1.5$ Hz, F^3), −140.2 (ddd, 1F, $J_F8,_F11 = 13.7$, $J_F8,_H7 = 11.5$, $J_F8,_H10 = 7.5$ Hz, F^8), −157.4 (td, 1F, $J_F5,_F6 \approx J_F5,_F4 \approx 21$, $J_F5,_F3 = 1.5$ Hz, F^5), −162.0 (m, 1F, $J_F6,_F5 = 19.8$, $J_F6,_F3 = 9.1$, $J_F6,_F4 = 6.6$ Hz, F^6), −175.4 (td, 1F, $J_F4,_F3 \approx J_F4,_F5 \approx 21$, $J_F4,_F6 = 6.6$ Hz, F^4); HRMS (EI): M^+, found 316.0429. $C_{14}H_6F_6N_2$ requires 316.0430.

4.2.8.9. 2-((4-Amino-2,3,5,6-tetrafluorophenyl)ethynyl)-3,4,5,6-tetrafluoroaniline (2cc). Preparative TLC (Merck precoated plates, hexane/ethyl acetate, 4:1 twice) was used to obtain **2cc** (169 mg, 48%) as white solid; m.p. 151.3 °C (decomp.); R_f 0.53; ν_{max} (KBr): 3510, 3416, 3397, 3202, 2926, 2230, 1665, 1609, 1530, 1504, 1460, 1337, 1321, 1306, 1169, 1115, 1013, 972, 939, 746, 692, 573, 523, 453 cm^{-1}; ^{1}H NMR (300.13 MHz, acetone-d_6): δ = 6.00 (br s, 2H, NH_2), 5.52 (br s, 2H, NH_2); ^{13}C NMR (100.62 MHz, acetone-d_6): δ = 148.2 (ddt, $^1J_C3,_F = 245.5$, $^2J_C3,_F = 11.1$, $^3J_C3,_F \approx {}^4J_C3,_F = 3.9$ Hz, C^3),

148.1 (dm, $^1J_C10,_F = 244.6$ Hz, C^{10}), 142.8 (dtd, $^1J_C5,_F = 249.6$, $^2J_C5,_F = 13.9$, $^3J_C5,_F = 5.3$ Hz, C^5), 136.8 (dm, $^1J_C11,_F \approx {}^1J_C6,_F \approx 235$ Hz, C^6, C^{11}), 136.3 (dm, $^2J_C1,_F = 11.6$ Hz, C^1), 132.5 (dtm, $^1J_C4,_F = 235.6$, $^2J_C4,_F = 13.6$ Hz, C^4), 131.2 (m, $^2J_C12,_F = 10.1$, $^3J_C12,_F = 4.3$ Hz, C^{12}), 93.8 (dm, $^2J_C2,_F = 14.8$ Hz, C^2), 88.8 (t, $^2J_C9,_F = 18.1$ Hz, C^9), 87.3 (m, $\underline{C}^7|C^8$), 85.8 (m, $C^7|\underline{C}^8$); ^{19}F NMR (282.37 MHz, acetone-d_6): δ = −138.4 (ddd, 1F, $J_F3,_F4 = 21.9$, $J_F3,_F6 = 9.2$, $J_F3,_F5 = 2.4$ Hz, F^3), −139.8 (dm, 2F, $J_F7,_F8 \approx 19$ Hz, F^7), −156.3 (td, 1F, $J_F5,_F6 \approx J_F5,_F4 \approx 20$, $J_F5,_F3 = 2.4$ Hz, F^5), −161.8 (m, 1F, $J_F6,_F5 = 19.7$, $J_F6,_F3 = 9.3$, $J_F6,_F4 = 6.5$ Hz, F^6), −161.9 (dm, 2F, $J_F8,_F7 \approx 19$ Hz, F^8) −175.4 (td, 1F, $J_F4,_F3 \approx J_F4,_F5 \approx 21$, $J_F4,_F6 = 6.5$ Hz, F^4); HRMS (EI): M^+, found 352.0245. $C_{14}H_4F_8N_2$ requires 352.0241.

4.2.8.10. 2-((4-Amino-2-fluorophenyl)ethynyl)-3,5,6-trifluoro-4-(trifluoromethyl)aniline (2da). Preparative TLC (Merck precoated plates, hexane/ethyl acetate, 10:1 twice) was used to obtain **2da** (278 mg, 80%) as light brown solid; m.p. 145.1 °C (decomp.); R_f 0.69; [Found: C, 51.94; H, 2.29; N, 7.63. $C_{15}H_7F_7N_2$ requires C, 51.74; H, 2.03; N, 8.04%]; ν_{max} (KBr): 3510, 3491, 3402, 3221, 2957, 2926, 2858, 2212, 1643, 1628, 1562, 1522, 1503, 1408, 1354, 1329, 1279, 1242, 1213, 1175, 1117, 930, 874, 845, 814, 743, 692, 667, 629, 606, 511, 494, 451 cm^{-1}; ^{1}H NMR (300.13 MHz, acetone-d_6): δ = 7.29 (t, 1H, $J_H7,_H8 \approx J_H7,_F = 8.2$ Hz, H^7), 6.53–6.48 (m, 2H, H^{10}, H^8), 6.23 (br s, 2H, NH_2), 5.46 (br s, 2H, NH_2); ^{13}C NMR (125.77 MHz, $CDCl_3$): δ = 163.6 (d, $^1J_C10,_F = 247.0$ Hz, C^{10}), 155.4 (dm, $^1J_C3,_F = 253.2$, $^3J_C3,_F = 6.8$ Hz, C^3), 151.9 (d, $^3J_C12,_F = 11.7$ Hz, C^{12}), 147.6 (dm, $^1J_C5,_F = 255.1$, $^2J_C5,_F = 15.2$ Hz, C^5), 142.4 (d, $^2J_C1,_F \approx 12$ Hz, C^1), 135.1 (ddd, $^1J_C6,_F = 237.5$, $^2J_C6,_F = 15.0$, $^4J_C6,_F = 3.5$ Hz, C^6), 133.7 (d, $^3J_C14,_F = 3.1$ Hz, C^{14}), 122.0 (q, $^1J_{CF3},_F = 271.3$ Hz, CF_3), 109.9 (d, $^4J_C13,_F = 2.0$ Hz, C^{13}), 99.8 (d, $^2J_C11,_F = 24.1$ Hz, C^{11}), 96.6 (d, $^2J_C9,_F = 16.2$ Hz, C^9), 95.6 (m, $C^7|\underline{C}^8$), 94.9 (dm, $^2J_C2,_F = 21.6$ Hz, C^2), 94.0 (m, $^2J_C4,_F = 34.2$, $^2J_C4,_F = 16.5$, $^2J_C4,_F = 12.7$ Hz, C^4), 77.9 (m, $\underline{C}^7|C^8$); ^{19}F NMR (282.37 MHz, $CDCl_3$): δ = −56.3 (t, 3F, $J_{CF3},_F3 \approx J_{CF3},_F5 = 21.5$ Hz, CF_3), −110.6 (dd, 1F, $J_F11,_H10 = 10.9$, $J_F11,_H7 = 7.8$ Hz, F^{11}), −114.7 (dq, 1F, $J_F3,_{CF3} = 21.6$, $J_F3,_F6 = 11.2$ Hz, F^3), −138.3 (dq, 1F, $J_F5,_{CF3} \approx J_F5,_F6 \approx 21$ Hz, F^5), −165.2 (dd, 1F, $J_F6,_F5 = 20.2$, $J_F6,_F3 = 11.2$ Hz, F^6); HRMS (EI): M^+, found 348.0492. $C_{15}H_7F_7N_2$ requires 348.0489.

4.2.8.11. 2-((4-Amino-2,5-difluorophenyl)ethynyl)-3,5,6-trifluoro-4-(trifluoromethyl)aniline (2db). By preparative TLC (Merck precoated plates, hexane/ethyl acetate, 5:1 three times), we isolated **2db** (234 mg, 64%) as light brown solid; m.p. 203.4 °C (decomp.); R_f 0.28; ν_{max} (KBr): 3514, 3485, 3402, 2928, 2857, 2216, 1641, 1612, 1530, 1503, 1489, 1443, 1408, 1371, 1331, 1308, 1259, 1215, 1180, 1132, 1080, 932, 881, 845, 816, 746, 660, 517, 438 cm^{-1}; ^{1}H NMR (300.13 MHz, acetone-d_6): δ = 7.26 (dd, 1H, $J_H7,_F8 = 11.5$, $J_H7,_F11 = 6.3$ Hz, H^7), 6.67 (dd, 1H, $J_H10,_F11 = 11.0$, $J_H10,_F8 = 7.5$ Hz, H^{10}), 6.37 (br s, 2H, NH_2), 5.55 (br s, 2H, NH_2); ^{13}C NMR (100.62 MHz, acetone-d_6): δ = 159.5 (d, $^1J_C10,_F = 244.4$ Hz, C^{10}), 155.5 (dm, $^1J_C3,_F = 253.8$ Hz, C^3), 147.4 (dm, $^1J_C5,_F = 255.2$, $^2J_C5,_F = 13.1$ Hz, C^5), 146.1 (dm, $^1J_C13,_F = 234.8$ Hz, C^{13}), 142.5 (m, $^2J_C1,_F \approx 12$ Hz, C^1), 139.4 (dd, $^2J_C12,_F = 15.6$, $^3J_C12,_F = 12.3$ Hz, C^{12}), 135.0 (ddm, $^1J_C6,_F = 237.8$, $^2J_C6,_F = 15.4$ Hz, C^6), 121.7 (q, $^1J_{CF3},_F = 271.2$ Hz, CF_3), 117.8 (dd, $^2J_C14,_F = 22.3$, $^3J_C14,_F = 3.3$ Hz, C^{14}), 103.4 (m, C^4), 101.5 (dd, $^2J_C11,_F = 26.9$, $^3J_C11,_F = 4.8$ Hz, C^{11}), 95.9 (dd, $^2J_C9,_F = 19.0$, $^3J_C9,_F = 9.0$ Hz, C^9), 94.2 (dm, $^2J_C2,_F \approx 20$ Hz, C^2), 94.0 (m, $C^7|\underline{C}^8$), 78.4 (m, $J_C7,_F = 2.0$ Hz $\underline{C}^7|C^8$); ^{19}F NMR (282.37 MHz, acetone-d_6): δ = −53.6 (t, 3F, $J_{CF3},_F3 \approx J_{CF3},_F5 = 21.4$ Hz, CF_3), −114.0 (dq, 1F, $J_F3,_{CF3} = 21.6$, $J_F3,_F6 = 10.4$ Hz, F^3), −114.3 (ddd, 1F, $J_F11,_F8 = 13.7$, $J_F11,_H10 = 11.0$, $J_F11,_H7 = 6.3$ Hz, F^{11}), −138.5 (dq, 1F, $J_F5,_{CF3} \approx J_F5,_F6 \approx 21$ Hz, F^5), −140.4 (ddd, 1F, $J_F8,_F11 = 13.7$, $J_F8,_H7 = 11.5$, $J_F8,_H10 = 7.5$ Hz, F^8), −163.3 (dd, 1F, $J_F6,_F5 = 19.6$, $J_F6,_F3 = 10.4$ Hz, F^6); HRMS (EI): M^+, found 366.0395. $C_{15}H_6F_8N_2$ requires 366.0400.

4.2.8.12. 2-((4-Amino-2,3,5,6-tetrafluorophenyl)ethynyl)-3,5,6-trifluoro-4-(trifluoromethyl)aniline (2dc). By preparative TLC (Merck precoated plates, hexane/ethyl acetate, 5:1 twice), we obtained **2dc** (145 mg, 36%) as light brown solid; m.p. 131.0 °C (decomp.); R_f 0.44; [Found: C, 44.56; H, 1.14; N, 6.90. $C_{15}H_4F_{10}N_2$ requires C, 44.79; H, 1.00; N, 6.97%]; ν_{max} (KBr): 3514, 3408, 3199, 2928, 2642, 2222, 1662, 1606, 1527, 1506, 1446, 1346, 1306, 1244, 1180, 1128, 993, 937, 903, 750, 708, 550, 451 cm^{-1}; ^{1}H NMR (300.13 MHz, acetone-d_6): δ = 6.36 (br s, 2H, NH_2), 5.98 (br s, 2H, NH_2); ^{13}C NMR (125.77 MHz, acetone-d_6): δ = 157.0 (dm, $^1J_C3,_F = 254.6$, $^3J_C3,_F = 7.2$ Hz, C^3), 149.1 (dm, $^1J_C5,_F = 256.5$, $^2J_C5,_F = 9.1$ Hz, C^5), 147.8 (dm, $^1J_C10,_F = 246.5$, $^2J_C10,_F = 10.6$ Hz, C^{10}), 144.1 (m, $^2J_C1,_F = 12.1$ Hz, C^1), 136.8 (dm, $^1J_C11,_F = 237.8$, $^2J_C11,_F = 15.1$ Hz, C^{11}), 136.3 (ddd, $^1J_C6,_F = 237.7$, $^2J_C6,_F = 15.0$ Hz, C^6), 130.3 (tt, $^2J_C12,_F = 14.2$, $^3J_C12,_F = 4.3$ Hz, C^{12}), 124.6 (q, $^1J_{CF3},_F = 271.9$ Hz, CF_3), 95.3 (m, $^2J_C4,_F = 34.6$, $^2J_C4,_F = 16.6$, $^2J_C4,_F = 12.9$ Hz, C^4), 94.6 (dm, $^2J_C2,_F = 21.9$ Hz, C^2), 88.7 (t, $^2J_C9,_F = 18.4$ Hz, C^9), 87.4 (m, $\underline{C}^7|C^8$), 85.3 (m, $C^7|\underline{C}^8$); ^{19}F NMR (282.37 MHz, acetone-d_6): δ = −53.7 (t, 3F, $J_{CF3},_F3 \approx J_{CF3},_F5 = 21.3$ Hz, CF_3), −113.3 (qd, 1F, $J_F3,_{CF3} = 21.8$, $J_F3,_F6 = 10.7$ Hz, F^3), −137.3 (m, 1F, $J_F5,_{CF3} \approx J_F5,_F6 \approx 20$ Hz, F^5), −139.6 (dm, 2F, $J_F7,_F8 \approx 19$ Hz, F^7), −161.9 (dm, 2F, $J_F8,_F7 \approx 20$ Hz, F^8), −162.9 (dd, 1F, $J_F6,_F5 = 19.4$, $J_F6,_F3 = 10.7$ Hz, F^6); HRMS (EI): M^+, found 402.0207. $C_{15}H_4F_{10}N_2$ requires 402.0209.

4.2.8.13. 4,4′-(Buta-1,3-diyne-1,4-diyl)bis(3-fluoroaniline) (9a). Preparative TLC (Merck precoated plates, hexane/ethyl acetate, 5:3) was used to isolate **9a** (10 mg, 7%) as light brown solid; (decomp. befor melt.); R_f 0.58; ν_{max} (KBr): 3444, 3329, 3209, 2956, 2926, 2854, 2145, 1616, 1566, 1502, 1452, 1323, 1246, 1209, 1163, 1128, 1093, 958, 839, 816, 741, 685, 600, 469, 428 cm^{-1}; ^{1}H NMR (400.13 MHz, acetone-d_6): δ = 7.23 (t, 2H, $J_H5,_F \approx J_H5,_H6 \approx 8$ Hz, H^5), 6.50–6.43 (m, 4H, H^2, H^6), 5.55 (br s, 4H, NH_2); ^{13}C NMR (125.77 MHz, acetone-d_6): δ = 165.9 (d, $^1J_C3,_F = 247.4$ Hz, C^3), 153.0 (d, $^3J_C1,_F = 11.7$ Hz, C^1), 135.6 (d, $^3J_C5,_F = 3.0$ Hz, C^5), 111.1 (d, $^4J_C6,_F = 1.9$ Hz, C^6), 101.0 (d, $^2J_C2,_F = 23.5$ Hz, C^2), 97.2 (d, $^2J_C4,_F = 16.2$ Hz, C^4), 77.3 (s, $C^7|\underline{C}^8$), 77.0 (d, $^3J_C7,_F = 2.2$ Hz, $\underline{C}^7|C^8$); ^{19}F NMR (282.37 MHz, acetone-d_6): δ = −109.2 (dd, 2F, $J_F,_H2 = 9.4$, $J_F,_H5 = 8.0$ Hz, F); HRMS (EI): M^+, found 268.0812. $C_{16}H_{10}F_2N_2$ requires 268.0807.

4.2.8.14. 4,4′-(Buta-1,3-diyne-1,4-diyl)bis(2,5-difluoroaniline) (9b). By preparative TLC (Merck precoated plates, hexane/ethyl acetate, 5:1, three times), we isolated **9b** (8 mg, 5%) as light brown solid; (decomp. befor melt.); R_f 0.14; ν_{max} (KBr):3507, 3406, 2143, 1639, 1574, 1526, 1441, 1362, 1310, 1242, 1215, 1169, 872, 839, 743, 671, cm^{-1}; ^{1}H NMR (400.13 MHz, acetone-d_6): δ = 7.16 (dd, 2H, $J_H3,_F2 = 11.4$, $J_H3,_F5 = 6.5$ Hz, H^3), 6.62 (dd, 2H, $J_H6,_F5 = 11.1$, $J_H6,_F2 = 7.5$ Hz, H^6), 5.63 (br s, 4H, NH_2); ^{13}C NMR (100.62 MHz, acetone-d_6): δ = 161.2 (d, $^1J_C5,_F5 = 244.7$ Hz, C^5), 146.4 (d, $^1J_C2,_F2 = 235.5$ Hz, C^2), 140.3 (t, $^2J_C1,_F2 \approx {}^3J_C1,_F5 \approx 14$ Hz, C^1), 118.8 (d, $^2J_C3,_F2 = 21.5$ Hz, C^3), 101.9 (d, $^2J_C6,_F5 = 26.8$ Hz, C^6), 95.4 (dd, $^2J_C4,_F5 = 19.3$, $^3J_C4,_F2 = 8.5$ Hz, C^4), 76.3 (s, $\underline{C}^7|C^8$), 75.7 (s, $C^7|\underline{C}^8$); ^{19}F NMR (282.37 MHz, acetone-d_6): δ = −113.8 (dm, 2F, $J_F5,_F2 = 13.4$, $J_F5,_H6 = 11.1$, $J_F5,_H3 = 6.5$ Hz, F^5), −139.9 (m, 2F, $J_F2,_F5 = 13.4$, $J_F2,_H3 = 11.4$, $J_F2,_H6 = 7.5$ Hz, F^2); HRMS (EI): M^+, found 304.0612. $C_{16}H_8F_4N_2$ requires 304.0618.

4.2.8.15. 4,4′-(Buta-1,3-diyne-1,4-diyl)bis(2,3,5,6-tetrafluoroaniline) (9c). Preparative TLC (Merck precoated plates, hexane/ethyl acetate, 4:1, twice) was used to obtain **9c** (13 mg, 7%) as light brown solid; m.p. 280.7 °C (decomp.); R_f 0.44; ν_{max} (KBr): 3518, 3470, 3416, 3192, 2924, 2648, 2559, 2153, 1661, 1626, 1603, 1508,

1423, 1306, 1163, 1113, 957, 937 cm^{-1}; ^1H NMR (300.13 MHz, Acetone-d_6): 5.95 (br s, 4H, NH_2); ^{13}C NMR (100.62 MHz, Acetone-d_6): δ = 147.0 (dm, $^1J_C3,_F3$ = 244.7 Hz, C^3), 136.8 (ddm, $^1J_C2,_F2$ = 237.7, $^2J_C2,_F3$ = 14.7 Hz, C^2), 130.1 (tt, $^2J_C1,_F2$ = 14.4, $^3J_C1,_F3$ = 4.2 Hz, C^1), 88.1 (t, $^2J_C4,_F3$ = 18.2 Hz, C^4), 83.4 (m, $J_C,_F$ = 3 Hz, C^7|C^8); ^{19}F NMR (282.37 MHz, Acetone-d_6): δ = −140.1 (dm, 4F, $J_F3,_F2 \approx 22$ Hz, F^3), −161.9 (dm, 4F, $J_F2,_F3 \approx 22$ Hz, F^2); HRMS (EI): M^+, found 376.0240. $C_{16}H_4F_8N_2$ requires 376.0241.

*4.2.9. General procedure for synthesis of 2-arylindoles **1**(**a**–**c**)(**a**–**d**)*

Method A. To a solution of **3** (0.5 mmol) in ethanol (25 mL), *p*-TSA (190 mg, 1 mmol) was added, and the mixture was heated at reflux with stirring. The mixture was allowed to cool to r.t., diluted with CH_2Cl_2 (10 mL), poured into H_2O (40 mL) and extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were washed with H_2O (40 mL) and dried ($MgSO_4$). The solvent was evaporated *in vacuo* to obtain compound **1**, which was then purified by preparative TLC.

Method B. To a solution of **3** (0.5 mmol) in MeCN (20 mL), $PdCl_2$ (24 mg, 0.1 mmol) was added, and the mixture was heated at reflux with stirring in an argon atmosphere. The mixture was allowed to cool to r.t., diluted with CH_2Cl_2 (10 mL), filtered, concentrated *in vacuo* and applied to Merck precoated plates to purify **1** by preparative TLC.

Method C. To a solution of **3** (0.5 mmol) in MeCN (25 mL), KOH (84 mg, 1.5 mmol) was added, and the mixture was heated at reflux with stirring for 6 h. The mixture was allowed to cool to r.t., diluted with CH_2Cl_2 (10 mL), poured into H_2O (40 mL) and extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were washed with H_2O (40 mL) and dried ($MgSO_4$). The solvent was evaporated *in vacuo* to obtain compound **1**, which was then purified by preparative TLC.

4.2.9.1. 4-(5,6-Difluoro-1H-indol-2-yl)-3-fluoroaniline (1aa). The above-mentioned general procedure (Method A) was followed, and the crude product was purified by preparative TLC (Merck precoated plates, hexane/ethyl acetate, 5:1, four times) to obtain **1aa** (59 mg, 45%) as light brown solid; m.p. 176.3 °C (decomp.); R_f 0.36; [Found: C, 64.11; H, 3.81. $C_{14}H_9F_3N_2$ requires C, 64.12; H, 3.46%]; ν_{max} (KBr): 3510, 3464, 3406, 3219, 3118, 3055, 1635, 1597, 1576, 1502, 1471, 1454, 1400, 1360, 1333, 1288, 1232, 1219, 1153, 1134, 1113, 1045, 962, 924, 862, 843, 820, 791, 750, 710, 634, 621, 577, 482 cm^{-1}; ^1H NMR (300.13 MHz, acetone-d_6): δ = 10.55 (br s, 1H, NH), 7.56 (t, 1H, $J_H12,_H11 \approx J_H12,_F8 \approx 9$ Hz, H^{12}), 7.39 (dd, 1H, $J_H4,_F5$ = 11.2, $J_H4,_F6$ = 8.0 Hz, H^4), 7.32 (dd, 1H, $J_H7,_F6$ = 11.2, $J_H7,_F5$ = 7.0 Hz, H^7), 7.32 (dd, 1H, $J_H7,_F6$ = 11.2, $J_H7,_F5$ = 7.0 Hz, H^7), 6.72 (m, 1H, $J_H3,_F \approx 1.4$ Hz, H^3), 6.63–6.53 (m, 2H, H^9, H^{11}), 5.24 (br s, 2H, NH_2); ^{13}C NMR (100.62 MHz, acetone-d_6): δ = 160.6 (d, $^1J_C9,_F$ = 244.9 Hz, C^9), 150.4 (d, $^2J_C11,_F$ = 12.0 Hz, C^{11}), 147.0 (dd, $^1J_C6,_F6$ = 237.1, $^2J_C6,_F5$ = 15.8 Hz, C^6), 146.1 (dd, $^1J_C5,_F5$ = 234.4, $^2J_C5,_F6$ = 14.8 Hz, C^5), 135.7 (m, $^3J_C2,_F \approx 2.5$ Hz, C^2), 131.8 (d, $^3J_C7a,_F6$ = 10.7 Hz, C^{7a}), 128.4 (d, $^3J_C13,_F9$ = 5.8 Hz, C^{13}), 124.5 (d, $^3J_C3a,_F5$ = 8.7 Hz, C^{3a}), 110.8 (d, $^4J_C12,_F$ = 1.7 Hz, C^{12}), 107.7 (d, $^2J_C8,_F$ = 12.6 Hz, C^8), 105.9 (d, $^2J_C4,_F5$ = 19.2 Hz, C^4), 101.0 (d, $^2J_C10,_F9$ = 25.7 Hz, C^{10}), 99.3 (m, $^4J_C3,_F$ = 4.7 Hz, C^3), 98.7 (d, $^2J_C7,_F6$ = 21.7 Hz, C^7); ^{19}F NMR (282.37 MHz, acetone-d_6): δ = −114.7 (dd, 1F, $J_F8,_H9$ = 13.9, $J_F8,_H12$ = 9.0 Hz, F^8), −145.6 (ddd, 1F, $J_F6,_F5$ = 20.5, $J_F6,_H7$ = 11.2, $J_F6,_H4$ = 8.0 Hz, F^6), −148.7 (ddd, 1F, $J_F5,_F6$ = 20.5, $J_F5,_H4$ = 11.2, $J_F5,_H7$ = 7.0 Hz, F^5); HRMS (EI): M^+, found 262.0711. $C_{14}H_9F_3N_2$ requires 262.0712.

4.2.9.2. 4-(5,6-Difluoro-1H-indol-2-yl)-2,5-difluoroaniline (1ab). The above-mentioned general procedure (Method A) was followed, and the crude product was purified by preparative TLC (Merck precoated plates, hexane/ethyl acetate, 5:1, three times) to obtain **1ab** (88 mg, 63%) as light brown solid; m.p. 156.3 °C (decomp.); R_f 0.58; [Found: C, 60.27; H, 3.08; N, 10.00. $C_{14}H_8F_4N_2$ requires C, 60.01; H, 2.88; N, 10.00%]; ν_{max} (KBr): 3475, 3414, 3217, 3072, 2956, 2928, 2856, 1703, 1647, 1601, 1560, 1516, 1473, 1439, 1398, 1369, 1335, 1308, 1279, 1219, 1178, 1113, 928, 872, 854, 802, 783, 744, 629, 602, 494, 465 cm^{-1}; ^1H NMR (300.13 MHz, acetone-d_6): δ = 10.61 (br s, 1H, NH), 7.49 (dd, 1H, $J_H12,_F11$ = 12.3, $J_H12,_F8$ = 7.1 Hz, H^{12}), 7.42 (dd, 1H, $J_H4,_F5$ = 11.2, $J_H4,_F6$ = 8.0 Hz, H^4), 7.32 (dd, 1H, $J_H7,_F6$ = 11.0, $J_H7,_F5$ = 7.0 Hz, H^7), 6.79 (m, 1H, $J_H3,_F \approx 2$ Hz, H^3), 6.74 (dd, 1H, $J_H9,_F8 \approx 13$, $J_H9,_F11$ = 7.6 Hz, H^9), 5.26 (br s, 2H, NH_2); ^{13}C NMR (100.62 MHz, acetone-d_6): δ = 156.2 (dd, $^1J_C9,_F9$ = 241.9, $^4J_C9,_F12$ = 1.3 Hz, C^9), 147.6 (dd, $^1J_C12,_F12$ = 233.8, $^4J_C12,_F9$ = 1.5 Hz, C^{12}), 147.4 (dd, $^1J_C6,_F6$ = 237.8, $^2J_C6,_F5$ = 15.9 Hz, C^6), 146.2 (dd, $^1J_C5,_F5$ = 234.9, $^2J_C5,_F6$ = 14.9 Hz, C^5), 137.5 (dd, $^2J_C11,_F12$ = 15.3, $^3J_C11,_F9$ = 12.6 Hz, C^{11}), 134.4 (s, C^2), 132.0 (d, $^3J_C7a,_F6$ = 10.7 Hz, C^{7a}), 124.4 (d, $^3J_C3a,_F5$ = 8.5 Hz, C^{3a}), 113.1 (dd, $^2J_C13,_F12$ = 22.6, $^3J_C13,_F9$ = 6.2 Hz, C^{13}), 107.3 (dd, $^2J_C8,_F9$ = 15.1, $^3J_C8,_F12$ = 7.2 Hz, C^8), 106.2 (d, $^2J_C4,_F5$ = 19.1 Hz, C^4), 103.1 (dd, $^2J_C10,_F9$ = 28.6, $^3J_C10,_F12$ = 4.8 Hz, C^{10}), 100.4 (m, $^4J_C3,_F$ = 4.3 Hz, C^3), 98.9 (d, $^2J_C7,_F6$ = 21.8 Hz, C^7); ^{19}F NMR (282.37 MHz, acetone-d_6): δ = −119.4 (m, 1F, $J_F8,_H9 \approx 14$, $J_F8,_H12$ = 7.1 Hz, F^8), −140.2 (ddd, 1F, $J_F11,_H12$ = 12.3, $J_F11,_H9$ = 7.6 Hz, F^{11}), −144.9 (ddd, 1F, $J_F6,_F5$ = 20.5, $J_F6,_H7$ = 11.0, $J_F6,_H4$ = 8.0 Hz, F^6), −148.4 (ddd, 1F, $J_F5,_F6$ = 20.5, $J_F5,_H4$ = 11.2, $J_F5,_H7$ = 7.0 Hz, F^5); HRMS (EI): M^+, found 280.0616. $C_{14}H_8F_4N_2$ requires 280.0618.

4.2.9.3. 4-(5,6-Difluoro-1H-indol-2-yl)-2,3,5,6-tetrafluoroaniline (1ac). The above-mentioned general procedure (Method B) was followed, and the crude product was purified by preparative TLC (Merck precoated plates, hexane/ethyl acetate, 5:1, three times) to obtain **1ac** (106 mg, 67%) as brown solid; m.p. 218.7 °C (decomp.); R_f 0.60; ν_{max} (KBr): 3485, 3385, 3205, 3070, 2962, 2926, 2854, 1666, 1639, 1614, 1549, 1502, 1473, 1396, 1344, 1302, 1263, 1207, 1174, 1119, 1078, 1034, 978, 935, 864, 843, 798, 741, 675, 631, 617, 525, 467, 446 cm^{-1}; ^1H NMR (300.13 MHz, acetone-d_6): δ = 10.67 (br s, 1H, NH), 7.49 (dd, 1H, $J_H4,_F5$ = 11.1, $J_H4,_F6$ = 8.0 Hz, H^4), 7.39 (dd, 1H, $J_H7,_F6$ = 11.0, $J_H7,_F5$ = 7.0 Hz, H^7), 6.85 (m, 1H, $J_H3,_F \approx 1$ Hz, H^3), 5.69 (br s, 2H, NH_2); ^{13}C NMR (125.77 MHz, acetone-d_6): δ = 147.7 (dd, $^1J_C6,_F6$ = 239.0, $^2J_C6,_F5$ = 16.1 Hz, C^6), 146.2 (dd, $^1J_C5,_F5$ = 235.7, $^2J_C5,_F6$ = 15.0 Hz, C^5), 144.1 (dm, $^1J_C9,_F9 \approx 243$ Hz, C^9), 136.5 (dm, $^1J_C10,_F10 \approx 237$ Hz, C^{10}), 131.8 (d, $^3J_C7a,_F6$ = 11.4 Hz, C^2), 127.6 (tm, $^2J_C11,_F10$ = 15.5 Hz, C^{11}), 126.7 (m, C^2), 123.4 (d, $^3J_C3a,_F5$ = 8.9 Hz, C^{3a}), 106.3 (d, $^2J_C4,_F5$ = 19.2 Hz, C^4), 103.7 (m, $^4J_C3,_F$ = 4.4 Hz, C^3), 99.0 (d, $^2J_C7,_F6$ = 21.9 Hz, C^7), 97.8 (t, $^2J_C8,_F9$ = 15.5 Hz, C^8); ^{19}F NMR (282.37 MHz, acetone-d_6): δ = −143.7 (ddd, 1F, $J_F6,_F5 \approx 20$, $J_F6,_H7$ = 11.0, $J_F6,_H4$ = 8.0 Hz, F^6), −144.9 (dm, 2F, $J_F8,_F9 \approx 20$ Hz, F^8), −147.8 (ddd, 1F, $J_F5,_F6$ = 20.2, $J_F5,_H4$ = 11.1, $J_F5,_H7$ = 7.0 Hz, F^5), −162.1 (dm, 2F, $J_F9,_F8 \approx 20$ Hz, F^9); HRMS (EI): M^+, found 316.0428. $C_{14}H_6F_6N_2$ requires 316.0430.

4.2.9.4. 3-Fluoro-4-(4,5,7-trifluoro-1H-indol-2-yl)aniline (1ba). The above-mentioned general procedure (Method A) was followed, and the crude product was purified by preparative TLC (Merck precoated plates, hexane/ethyl acetate, 6:1, three times) to obtain **1ba** (109 mg, 78%) as brown solid; m.p. 178.3–179.8 °C; R_f 0.26; [Found: C, 59.67; H, 3.21; N, 9.67. $C_{14}H_8F_4N_2$ requires C, 60.01; H, 2.88; N, 10.00%]; ν_{max} (KBr): 3481, 3447, 3418, 3344, 3229, 3080, 2957, 2926, 2857, 1630, 1535, 1491, 1454, 1406, 1385, 1335, 1304, 1217, 1119, 1076, 997, 957, 922, 843, 816, 773, 692, 606, 569, 496 cm^{-1}; ^1H NMR (500.13 MHz, acetone-d_6): δ = 10.92 (br s, 1H, NH), 7.65 (t, 1H, $J_H12,_H11 \approx J_H12,_F8 \approx 9$ Hz, H^{12}), 7.39 (ddd, 1H, $J_H6,_F5$ = 11.2, $J_H6,_F7$ = 10.4, $J_H6,_F4$ = 5.7 Hz, H^6), 6.84 (m, 1H, $J_H3,_F4$ = 5.4, $J_H3,_F7$ = 2.4 Hz, H^3), 6.60 (dd, 1H, $J_H11,_H12$ = 8.5, $J_H11,_H9$ = 2.2 Hz, H^{11}), 6.56 (dd, 1H, $J_H9,_F$ = 14.2, $J_H9,_H11$ = 2.2 Hz,

H^9), 5.35 (br s, 2H, NH_2); ^{13}C NMR (125.77 MHz, acetone-d_6): δ = 161.1 (d, $^1J_C9,_F$ = 246.3 Hz, C^9), 151.2 (d, $^3J_C11,_F$ = 12.1 Hz, C^{11}), 143.7 (dd, $^1J_C7,_F7$ = 242.3, $^3J_C7,_F5$ = 11.7 Hz, C^7), 142.4 (dt, $^1J_C5,_F5$ = 234.6, $^2J_C5,_F4 \approx {}^3J_C5,_F7 \approx$ 12 Hz, C^5), 138.8 (ddd, $^1J_C4,_F4$ = 240.7, $^2J_C4,_F5$ = 14.1, $^4J_C4,_F7$ = 4.0 Hz, C^4), 137.0 (s, C^2), 129.1 (d, $^3J_C13,_F9$ = 5.2 Hz, C^{13}), 122.1 (dd, $^2J_C7a,_F7$ = 15.2, $^3J_C7a,_F4$ = 9.7 Hz, C^{7a}), 121.2 (dd, $^2J_C3a,_F4$ = 20.2, $^3J_C3a,_F$ = 6.0 Hz, C^{3a}), 110.6 (d, $^4J_C12,_F$ = 1.6 Hz, C^{12}), 106.7 (d, $^2J_C8,_F$ = 12.8 Hz, C^8), 101.0 (d, $^2J_C10,_F9$ = 25.6 Hz, C^{10}), 96.6 (t, $^2J_C6,_F5 \approx {}^2J_C6,_F7 \approx$ 25 Hz, C^6), 96.6 (m, $^4J_C3,_F \approx$ 6 Hz, C^3); ^{19}F NMR (282.37 MHz, acetone-d_6): δ = −117.2 (m, 1F, $J_F8,_H9$ = 14.2, $J_F8,_H12$ = 8.6 Hz, F^8), −138.8 (ddd, 1F, $J_F7,_F4$ = 19.8, $J_F7,_H6$ = 10.4, $J_F7,_H3 \approx 3$, $J_F7,_F5 \approx$ 1 Hz, F^7), −150.0 (ddd, 1F, $J_F5,_F4 \approx 20$, $J_F5,_H6$ = 10.7, $J_F5,_F7 \approx$ 1 Hz, F^5), −155.2 (tdd, 1F, $J_F4,_F5 \approx J_F4,_F7 \approx 20$, $J_F4,_H6$ = 5.7, $J_F4,_H3 \approx$ 2 Hz, F^4); HRMS (EI): M^+, found 280.0616. $C_{14}H_8F_4N_2$ requires 280.

4.2.9.5. 2,5-Difluoro-4-(4,5,7-trifluoro-1H-indol-2-yl)aniline (1bb). The above-mentioned general procedure (Method A) was followed and the crude product was purified by preparative TLC (Merck precoated plates, hexane/ethyl acetate, 5:1, twice) to afford **1bb** (89 mg, 60%) as light brown solid; m.p. 202.7 °C (decomp.); R_f 0.47; ν_{max} (KBr): 3475, 3454, 3369, 3219, 3138, 3088, 2928, 2852, 1645, 1593, 1568, 1537, 1495, 1456, 1441, 1408, 1335, 1300, 1257, 1225, 1257, 1171, 1117, 1076, 1036, 993, 962, 926, 868, 839, 812, 779, 746, 727, 692, 650, 611, 569, 503, 480, 432 cm^{-1}; ^1H NMR (300.13 MHz, acetone-d_6): δ = 10.92 (br s, 1H, NH), 7.60 (dd, 1H, $J_H12,_F11$ = 12.1, $J_H12,_F8$ = 6.9 Hz, H^{12}), 6.95–6.87 (m, 2H, $J_H6,_F4$ = 5.8 Hz, H^6, H^3), 6.75 (dd, 1H, $J_H9,_F8$ = 12.9, $J_H9,_F11$ = 7.6 Hz, H^9), 5.36 (br s, 2H, NH_2); ^{13}C NMR (100.62 MHz, acetone-d_6): δ = 157.5 (dd, $^1J_C9,_F9$ = 243.5, $^4J_C9,_F12$ = 1.5 Hz, C^9), 148.2 (dd, $^1J_C12,_F12$ = 233.9, $^4J_C12,_F9$ = 1.5 Hz, C^{12}), 144.6 (ddd, $^1J_C7,_F7$ = 242.6, $^3J_C7,_F5$ = 11.6, $^4J_C7,_F4$ = 2.7 Hz, C^7), 143.2 (dt, $^1J_C5,_F5$ = 235.0, $^2J_C5,_F4 \approx {}^3J_C5,_F7 \approx$ 12 Hz, C^5), 139.8 (ddd, $^1J_C4,_F4$ = 241.3, $^2J_C4,_F5$ = 14.2, $^4J_C4,_F7$ = 4.2 Hz, C^4), 139.2 (t, $^2J_C11,_F12 \approx {}^3J_C11,_F9 \approx$ 14 Hz, C^{11}), 136.4 (s, C^2), 123.0 (dd, $^2J_C7a,_F7$ = 15.2, $^3J_C7a,_F4$ = 9.5 Hz, C^{7a}), 121.9 (dd, $^2J_C3a,_F4$ = 19.9, $^3J_C3a,_F$ = 6.0 Hz, C^{3a}), 114.5 (dd, $^2J_C13,_F12$ = 22.7, $^3J_C13,_F9$ = 5.5 Hz, C^{13}), 107.0 (dd, $^2J_C8,_F9$ = 15.1, $^3J_C8,_F12$ = 7.2 Hz, C^8), 103.8 (dd, $^2J_C10,_F9$ = 28.4, $^3J_C10,_F12$ = 4.8 Hz, C^{10}), 98.4 (t, $^3J_C3,_F \approx {}^4J_C3,_F \approx$ 7 Hz, C^3), 97.9 (dd, $^2J_C6,_F5$, $^2J_C6,_F7$ = 23.3, 25.4 Hz, C^6); ^{19}F NMR (282.37 MHz, acetone-d_6): δ = −118.0 (m, 1F, $J_F8,_H9$ = 12,9, $J_F8,_H12$ = 7.1, $J_F8,_H3$ = 5.1 Hz, F^8), −135.0 (ddd, 1F, $J_F7,_F4$ = 19.8, $J_F7,_H6$ = 10.3, $J_F7,_H3 \approx 3$, $J_F7,_F5 \approx$ 1 Hz, F^7), −140.2 (m, 1F, $J_F11,_H12$ = 12.2, $J_F11,_H9$ = 7.6 Hz, F^{11}), −151.2 (ddd, 1F, $J_F5,_F4$ = 20.2, $J_F5,_H6$ = 11.2, $J_F5,_F7 \approx$ 1 Hz, F^5), −154.2 (td, 1F, $J_F4,_F5 \approx J_F4,_F7 \approx 20$, $J_F4,_H6$ = 5.8 Hz, F^4); HRMS (EI): M^+, found 298.0526. $C_{14}H_7F_5N_2$ requires 298.0524.

4.2.9.6. 2,3,5,6-Tetrafluoro-4-(4,5,7-trifluoro-1H-indol-2-yl)aniline (1bc). The above-mentioned general procedure (Method B) was followed, and the crude product was purified by preparative TLC (Merck precoated plates, hexane/ethyl acetate, 5:1, twice) to obtain **1bc** (95 mg, 57%) as light brown solid; m.p. 189.6 °C (decomp.); R_f 0.50; ν_{max} (KBr): 3485, 3410, 3203, 3088, 2929, 1664, 1605, 1539, 1514, 1495, 1444, 1400, 1336, 1313, 1300, 1207, 1176, 1124, 1086, 1005, 987, 964, 937, 818, 796, 719, 687, 615, 579, 467 cm^{-1}; ^1H NMR (300.13 MHz, acetone-d_6): δ = 11.11 (br s, 1H, NH), 7.03 (ddd, 1H, $J_H6,_F5$ = 11.0, $J_H6,_F7$ = 10.4, $J_H6,_F4$ = 5.8 Hz, H^6), 6.92 (m, 1H, $J_H3,_F$ = 1.5 Hz, H^3), 5.79 (br s, 2H, NH_2); ^{13}C NMR (125.77 MHz, acetone-d_6): δ = 146.0 (dm, $^1J_C9,_F9 \approx$ 245 Hz, C^9), 145.3 (ddd, $^1J_C7,_F7$ = 243.4, $^3J_C7,_F5$ = 11.7, $^4J_C7,_F4$ = 2.7 Hz, C^7), 143.8 (dt, $^1J_C5,_F5$ = 235.7, $^2J_C5,_F4 \approx {}^3J_C5,_F7 \approx$ 11 Hz, C^5), 140.3 (ddd, $^1J_C4,_F4$ = 242.7, $^2J_C4,_F5$ = 14.3, $^4J_C4,_F7$ = 4.5 Hz, C^4), 138.2 (dm, $^1J_C10,_F10$ = 237.8, $^2J_C10,_F9$ = 16.4 Hz, C^{10}), 130.2 (tt, $^2J_C11,_F10$ = 14.4, $^3J_C11,_F9$ = 4.1 Hz, C^{11}), 129.4 (s, C^2), 123.9 (dd, $^2J_C7a,_F7$ = 15.5, $^3J_C7a,_F4$ = 9.3 Hz, C^{7a}), 121.6 (dd, $^2J_C3a,_F4$ = 19.8, $^3J_C3a,_F$ = 6.4 Hz, C^{3a}), 102.1 (d, $^4J_C3,_F$ = 3.5 Hz, C^3), 99.3 (dd, $^2J_C6,_F5$, $^2J_C6,_F7$ = 23.5, 25.4 Hz, C^6), 98.2 (t, $^2J_C8,_F9$ = 16.4 Hz, C^8); ^{19}F NMR (282.37 MHz, acetone-d_6): δ = −134.6 (ddd, 1F, $J_F7,_F4$ = 20.1, $J_F7,_H6$ = 10.3, $J_F7,_H3$ = 2.4 1 Hz, F^7), −144.1 (dm, 2F, $J_F8,_F9 \approx$ 21 Hz, F^8), −148.8 (dd, 1F, $J_F5,_F4$ = 19.8, $J_F5,_H6$ = 11.3 Hz, F^5), −153.6 (td, 1F, $J_F4,_F5 \approx J_F4,_F7 \approx 20$, $J_F4,_H6$ = 5.8 Hz, F^4), −162.0 (dm, 2F, $J_F9,_F8 \approx$ 21 Hz, F^9); HRMS (EI): M^+, found 334.0332. $C_{14}H_5F_7N_2$ requires 334.0335.

4.2.9.7. 3-Fluoro-4-(4,5,6,7-tetrafluoro-1H-indol-2-yl)aniline (1ca). The above-mentioned general procedure (Method A) was followed, and the crude product was purified by preparative TLC (Merck precoated plates, hexane/ethyl acetate, 5:1, twice) to obtain **1ca** (107 mg, 72%) as light brown solid; (decomp. befor melt.); R_f 0.47; [Found: C, 56.41; H, 2.72; N, 8.97. $C_{14}H_7F_5N_2$ requires C, 56.39; H, 2.37; N, 9.39%]; ν_{max} (KBr): 3474, 3449, 3337, 3221, 2928, 1628, 1543, 1487, 1456, 1423, 1389, 1346, 1319, 1281, 1227, 1169, 1146, 1130, 1043, 1001, 966, 924, 841, 795, 779, 702, 617, 600, 534, 465 cm^{-1}; ^1H NMR (400.13 MHz, $CDCl_3$): δ = 8.89 (br s, 1H, NH), 7.49 (t, 1H, $J_H12,_H11 \approx J_H12,_F8$ = 9 Hz, H^{12}), 6.78 (t, 1H, $J_H3,_F \approx$ 3 Hz, H^3), 6.53 (dd, 1H, $J_H11,_H12$ = 8.4, $J_H11,_H9$ = 2.3 Hz, H^{11}), 6.47 (dd, 1H, $J_H9,_F$ = 13.9, $J_H9,_H11$ = 2.3 Hz, H^9), 3.97 (br s, 2H, NH_2); ^{13}C NMR (100.62 MHz, acetone-d_6): δ = 161.7 (d, $^1J_C9,_F$ = 246.3 Hz, C^9), 152.1 (d, $^3J_C11,_F$ = 12.1 Hz, C^{11}), 139.7 (ddt, $^1J_C4,_F4$ = 243.4, $^2J_C4,_F5$ = 11.5, $^3J_C4,_F6 \approx {}^4J_C4,_F7 \approx$ 3 Hz, C^4), 136.7 (dtd, $^1J_C6,_F6$ = 239.0, $^2J_C6,_F5 \approx {}^2J_C6,_F7 \approx$ 15, $^3J_C6,_F4$ = 3.0 Hz, C^6), 135.3 (dt, $^1J_C5,_F5$ = 237.9, $^2J_C5,_F4 \approx {}^2J_C5,_F6 \approx$ 16 Hz, C^5), 135.0 (ddm, $^1J_C7,_F7 \approx$ 240, $^2J_C7,_F6 \approx$ 14 Hz, C^7), 132.8 (d, $^3J_C2,_F9$ = 4.8 Hz, C^2), 129.7 (d, $^3J_C13,_F9$ = 5.2 Hz, C^{13}), 121.6 (td, $^2J_C7a,_F7 \approx {}^3J_C7a,_F4 \approx$ 12, $^3J_C7a,_F6 \approx$ 4 Hz, C^{7a}), 116.1 (dd, $^2J_C3a,_F4$ = 20.3, $^3J_C3a,_F5$ = 5.1 Hz, C^{3a}), 111.4 (d, $^4J_C12,_F$ = 2.0 Hz, C^{12}), 107.3 (d, $^2J_C8,_F9$ = 12.8 Hz, C^8), 101.7 (d, $^2J_C10,_F9$ = 25.5 Hz, C^{10}), 96.7 (t, $^3J_C3,_F \approx$ 6.5 Hz, C^3); ^{19}F NMR (282.37 MHz, $CDCl_3$): δ = −117.4 (m, 1F, $J_F8,_H9 \approx 14$, $J_F8,_H12$ = 8.5 Hz, F^8), −152.1 (tm, 1F, $J_F4,_F5 \approx J_F4,_F7 \approx$ 18 Hz, F^4), −163.3 (m, 1F, $J_F7,_F6$ = 19.7, $J_F7,_F4$ = 16.4, $J_F7,_F5 \approx J_F7,_H3 \approx$ 3.5 Hz, F^7), −163.3 (m, 1F, $J_F6,_F5 \approx J_F6,_F7 \approx 20$, $J_F6,_F4 \approx$ 2 Hz, F^6), −170.8 (td, 1F, $J_F5,_F6 \approx J_F5,_F4 \approx 20$, $J_F5,_F7 \approx$ 4 Hz, F^5); HRMS (EI): M^+, found 298.0522. $C_{14}H_7F_5N_2$ requires 298.0524.

4.2.9.8. 2,5-Difluoro-4-(4,5,6,7-tetrafluoro-1H-indol-2-yl)aniline (1cb). The above-mentioned general procedure (Method A) was followed, and the crude product was purified by preparative TLC (Merck precoated plates, hexane/ethyl acetate, 5:1, five times) to obtain **1cb** (115 mg, 73%) as white solid; (decomp. befor melt.); R_f 0.70; ν_{max} (KBr): 3537, 3510, 3477, 3415, 2928, 2854, 1645, 1614, 1545, 1491, 1454, 1423, 1340, 1227, 1178, 1140, 1115, 995, 928, 872, 796, 779, 669, 640, 604, 542, 507, 467 cm^{-1}; ^1H NMR (400.13 MHz, acetone-d_6): δ = 11.11 (br s, 1H, NH), 7.58 (dd, 1H, $J_H12,_F11$ = 12.2, $J_H12,_F8$ = 7.0 Hz, H^{12}), 6.88 (dd, 1H, $J_H3,_F4$ = 5.5, $J_H3,_F7 \approx$ 3 Hz, H^3), 6.74 (dd, 1H, $J_H9,_F8$ = 12.9, $J_H9,_F11$ = 7.6 Hz, H^9), 5.37 (br s, 2H, NH_2); ^{13}C NMR (100.62 MHz, acetone-d_6): δ = 157.4 (d, $^1J_C9,_F$ = 243.5 Hz, C^9), 148.2 (dd, $^1J_C12,_F12$ = 235.6, $^4J_C12,_F9$ = 1.6 Hz, C^{12}), 140.2 (ddt, $^1J_C4,_F4$ = 244.0, $^2J_C4,_F5$ = 11.5, $^3J_C4,_F6 \approx {}^4J_C4,_F7 \approx$ 4 Hz, C^4), 139.2 (t, $^2J_C11,_F12$ = 15.2, $^3J_C11,_F9$ = 12.7 Hz, C^{11}), 137.0 (dtm, $^1J_C6,_F6$ = 239.7, $^2J_C6,_F5 \approx {}^2J_C6,_F7 \approx$ 14, $^3J_C6,_F4$ = 3.0 Hz, C^6), 136.4 (m, C^2), 135.4 (dt, $^1J_C5,_F5$ = 238.4, $^2J_C5,_F4 \approx {}^2J_C5,_F6 \approx$ 16 Hz, C^5), 135.1 (ddm, $^1J_C7,_F7 \approx$ 245, $^2J_C7,_F6 \approx$ 16 Hz, C^7), 121.8 (td, $^2J_C7a,_F7 \approx {}^3J_C7a,_F4 \approx$ 11, $^3J_C7a,_F6 \approx$ 4 Hz, C^{7a}), 116.1 (dd, $^2J_C3a,_F4$ = 20.0, $^3J_C3a,_F5$ = 4.8 Hz, C^{3a}), 114.4 (dd, $^2J_C13,_F12$ = 22.8, $^3J_C13,_F9$ = 5.5 Hz, C^{13}), 106.8 (dd,

$^2J_C8,_F9 = 15.1$, $^3J_C8,_F12 = 7.2$ Hz, C^8), 103.8 (dd, $^2J_C10,_F9 = 28.4$, $^3J_C10,_F12 = 4.8$ Hz, C^{10}), 97.8 (t, $^3J_C3,_F \approx 8$ Hz, C^3); ^{19}F NMR (376.46 MHz, acetone-d_6): δ = −118.2 (m, 1F, $J_F8,_H9 = 13.3$, $J_F8,_H12 = 7.0$ Hz, F^8), −140.2 (m, 1F, $J_F11,_H12 = 12.2$, $J_F11,_H9 = 7.6$ Hz, F^{11}), −151.3 (tm, 1F, $J_F4,_F5 \approx 19$, $J_F4,_F7 = 16.5$, $J_F4,_F6$, $J_F4,_H3 \approx 2$ Hz, F^4), −160.4 (tm, 1F, $J_F7,_F6 = 19.8$, $J_F7,_F4 = 16.5$, $J_F7,_F5 \approx J_F7,_H3 \approx 4$ Hz, F^7), −167.9 (td, 1F, $J_F6,_F5 \approx J_F6,_F7 \approx 19$, $J_F6,_F4 \approx 2$ Hz, F^6), −170.9 (td, 1F, $J_F5,_F6 \approx J_F5,_F4 \approx 19$, $J_F5,_F7 \approx 4$ Hz, F^5); HRMS (EI): M^+, found 316.0428. $C_{14}H_6F_6N_2$ requires 316.0430.

4.2.9.9. 2,3,5,6-Tetrafluoro-4-(4,5,6,7-tetrafluoro-1H-indol-2-yl) aniline (1cc). The above-mentioned general procedure (Method C) was followed, and the crude product was purified by preparative TLC (Merck precoated plates, hexane/ethyl acetate, 5:1, three times) to obtain **1cc** (125 mg, 71%) as white solid; m.p. 216.4 °C (decomp.); R_f 0.67; ν_{max} (KBr): 3520, 3487, 3419, 3190, 2926, 2854, 1664, 1608, 1545, 1522, 1491, 1419, 1342, 1317, 1242, 1176, 1101, 1082, 1005, 980, 935, 795, 721, 677, 633, 604, 565, 447 cm^{-1}; ^{1}H NMR (400.13 MHz, acetone-d_6): δ = 11.31 (br s, 1H, NH), 6.91 (m, 1H, $J_H3,_F \approx 3$ Hz, H^3), 5.80 (br s, 2H, NH_2); ^{13}C NMR (100.62 MHz, acetone-d_6): δ = 145.3 (dm, $^1J_C9,_F9 \approx 244$ Hz, C^9), 139.2 (ddt, $^1J_C4,_F4 \approx 248$, $^2J_C4,_F5 = 11.4$, $^3J_C4,_F6 \approx {}^4J_C4,_F7 \approx 4$ Hz, C^4), 137.4 (dm, $^1J_C10,_F10 \approx 238$ Hz, C^{10}), 137.3 (dm, $^1J_C6,_F6 = 240.6$ Hz, C^6), 135.5 (dt, $^1J_C5,_F5 = 239.1$, $^2J_C5,_F4 \approx {}^2J_C5,_F6 \approx 15$ Hz, C^5), 135.1 (ddm, $^1J_C7,_F7 = 245.5$, $^2J_C7,_F6 = 13.5$ Hz, C^7), 129.7 (tt, $^2J_C11,_F10 = 14.5$, $^3J_C11,_F9 = 4.3$ Hz, C^{11}), 128.8 (s, C^2), 122.1 (td, $^2J_C7a,_F7 \approx {}^3J_C7a,_F4 \approx 11$, $^3J_C7a,_F6 \approx 4$ Hz, C^{7a}), 115.3 (dd, $^2J_C3a,_F4 = 20.2$, $^3J_C3a,_F5 = 4.6$ Hz, C^{3a}), 101.1 (t, $^3J_C3,_F \approx 2$ Hz, C^3), 97.5 (t, $^2J_C8,_F9 = 16.0$ Hz, C^8); ^{19}F NMR (376.46 MHz, acetone-d_6): δ = −144.2 (dm, 2F, $J_F8,_F9 \approx 21$ Hz, F^8), −150.6 (tm, 1F, $J_F4,_F5 \approx 19$, $J_F4,_F7 = 16.4$, $J_F4,_F6$, $J_F4,_H3 \approx 2$ Hz, F^4), −159.9 (tm, 1F, $J_F7,_F6 = 19.4$, $J_F7,_F4 = 16.6$, $J_F7,_F5 \approx J_F7,_H3 \approx 4$ Hz, F^7), −162.9 (dm, 2F, $J_F9,_F8 \approx 21$ Hz, F^9), −166.6 (t, 1F, $J_F6,_F5 \approx J_F6,_F7 \approx 19$ Hz, F^6), −170.4 (td, 1F, $J_F5,_F6 \approx J_F5,_F4 \approx 19$, $J_F5,_F7 \approx 4$ Hz, F^5); HRMS (EI): M^+, found 352.0246. $C_{14}H_4F_8N_2$ requires 352.0241.

4.2.9.10. 3-Fluoro-4-(4,6,7-trifluoro-5-(trifluoromethyl)-1H-indol-2-yl)aniline (1da). The above-mentioned general procedure (Method A) was followed, and the crude product was purified by preparative TLC (Merck precoated plates, hexane/ethyl acetate, 10:1, twice) to obtain **1da** (127 mg, 73%) as brown solid; 141.6 °C (decomp.); R_f 0.20; [Found: C, 51.80; H, 2.34; N, 8.03. $C_{15}H_7F_7N_2$ requires C, 51.74; H, 2.03; N, 8.04%]; ν_{max} (KBr): 3478, 3426, 3362, 3235, 3146, 2959, 2920, 2853, 1659, 1636, 1585, 1526, 1493, 1466, 1454, 1354, 1325, 1288, 1246, 1211, 1177, 1124, 1097, 997, 961, 926, 872, 851, 822, 793, 743, 719, 631, 611, 507, 447 cm^{-1}; ^{1}H NMR (400.13 MHz, $CDCl_3$): δ = 9.10 (br s, 1H, NH), 7.49 (t, 1H, $J_H12,_H11 \approx J_H12,_F8 = 9$ Hz, H^{12}), 6.82 (t, 1H, $J_H3,_F \approx 3$ Hz, H^3), 6.54 (dd, 1H, $J_H11,_H12 = 8.5$, $J_H11,_H9 = 2.2$ Hz, H^{11}), 6.47 (dd, 1H, $J_H9,_F8 = 14.0$, $J_H9,_H11 = 2.2$ Hz, H^9), 4.00 (br s, 2H, NH_2); ^{13}C NMR (125.77 MHz, acetone-d_6): δ = 160.8 (d, $^1J_C9,_F = 246.7$ Hz, C^9), 151.2 (d, $^3J_C11,_F = 12.2$ Hz, C^{11}), 147.6 (dm, $^1J_C4,_F4 = 256.0$ Hz, C^4), 141.6 (ddd, $^1J_C6,_F6 = 245.7$, $^2J_C6,_F7 = 13.6$, $^3J_C6,_F4 = 4.4$ Hz, C^6), 134.2 (ddm, $^1J_C7,_F7 = 243.7$, $^2J_C7,_F6 = 16.2$, $^4J_C7,_F4 = 4.0$ Hz, C^7), 137.0 (s, C^2), 128.6 (d, $^3J_C13,_F9 = 5.0$ Hz, C^{13}), 127.4 (tm, $^2J_C7a,_F7 \approx {}^3J_C7a,_F4 \approx 12$, $^3J_C7a,_F6 \approx 5$ Hz, C^{7a}), 122.4 (q, $^1J_{CF3},_F = 272.0$ Hz, CF_3), 116.5 (dd, $^2J_C3a,_F4 = 23.6$, $^3J_C3a,_F7 = 4.6$ Hz, C^{3a}), 110.3 (d, $^4J_C12,_F \approx 2$ Hz, C^{12}), 105.8 (d, $^2J_C8,_F9 = 12.8$ Hz, C^8), 101.6 (d, $^2J_C10,_F9 = 25.5$ Hz, C^{10}), 97.8 (m, $^2J_C5,_{CF3} = 33.0$, $^2J_C5,_F4$, $^2J_C5,_F6 = 14.0$ Hz, C^5), 96.3 (d, $^3J_C3,_F = 8.7$ Hz, C^3); ^{19}F NMR (282.37 MHz, $CDCl_3$): δ = −53.0 (dd, 3F, $J_{CF3},_F4 = 24.4$, $J_{CF3},_F6 = 20.6$ Hz, CF_3), −114.2 (m, 1F, $J_F8,_H9 \approx 14$, $J_F8,_H12 = 8.5$ Hz, F^8), −122.8 (m, 1F, $J_F4,_{CF3} = 24.4$, $J_F4,_F7 = 17.7$, $J_F4,_F6 = 5.3$, $J_F4,_H3 = 2.4$ Hz, F^4), −147.1 (m, 1F, $J_F6,_{CF3} \approx J_F6,_F7 \approx 20$, $J_F6,_F4 = 5.3$ Hz, F^6), −161.2 (m, 1F, $J_F7,_F6 = 20.2$, $J_F7,_F4 = 17.7$ Hz, F^7); HRMS (EI): M^+, found 348.0487. $C_{15}H_7F_7N_2$ requires 348.0492.

4.2.9.11. 2,5-Difluoro-4-(4,6,7-trifluoro-5-(trifluoromethyl)-1H-indol-2-yl)aniline (1db). The above-mentioned general procedure (Method A) was followed, and the crude product was purified by preparative TLC (Merck precoated plates, hexane/ethyl acetate, 5:1, twice) to obtain **1db** (148 mg, 81%) as light brown solid; 188.3–189.8 °C; R_f 0.64; [Found: C, 49.53; H, 1.66; N, 7.46. $C_{15}H_6F_8N_2$ requires C, 49.20; H, 1.65; N, 7.65%]; ν_{max} (KBr): 3523, 3473, 3427, 3211, 3141, 2926, 2856, 1645, 1614, 1525, 1498, 1456, 1406, 1352, 1311, 1277, 1252, 1207, 1165, 1120, 1024, 999, 928, 874, 837, 793, 742, 717, 646, 519 cm^{-1}; ^{1}H NMR (400.13 MHz, acetone-d_6): δ = 11.27 (br s, 1H, NH), 7.50 (dd, 1H, $J_H12,_F11 = 12.1$, $J_H12,_F8 = 7.1$ Hz, H^{12}), 6.80 (t, 1H, $J_H3,_F \approx 3$ Hz, H^3), 6.68 (dd, 1H, $J_H9,_F8 = 13.0$, $J_H9,_F11 = 7.6$ Hz, H^9), 5.32 (br s, 2H, NH_2); ^{13}C NMR (125.77 MHz, acetone-d_6): δ = 157.5 (d, $^1J_C9,_F = 243.9$ Hz, C^9), 148.6 (dm, $^1J_C4,_F4 = 258.4$ Hz, C^4), 148.2 (dd, $^1J_C12,_F12 = 234.1$, $^4J_C12,_F9 = 1.3$ Hz, C^{12}), 142.9 (ddd, $^1J_C6,_F6 = 246.0$, $^2J_C6,_F7 = 13.7$, $^3J_C6,_F4 = 1.4$ Hz, C^6), 139.3 (dd, $^2J_C11,_F12 = 15.3$, $^3J_C11,_F9 = 12.8$ Hz, C^{11}), 136.7 (s, C^2), 135.3 (ddd, $^1J_C7,_F7 = 243.9$, $^2J_C7,_F6 = 16.3$, $^4J_C7,_F4 = 4.0$ Hz, C^7), 128.5 (tm, $^2J_C7a,_F7 \approx {}^3J_C7a,_F4 \approx 12$, $^3J_C7a,_F6 \approx 5$ Hz, C^{7a}), 123.5 (q, $^1J_{CF3},_F = 272.0$ Hz, CF_3), 117.4 (dd, $^2J_C3a,_F4 = 23.6$, $^3J_C3a,_F7 = 4.4$ Hz, C^{3a}), 114.1 (dd, $^2J_C13,_F12 = 22.9$, $^3J_C13,_F9 = 5.4$ Hz, C^{13}), 106.3 (dd, $^2J_C8,_F9 = 15.0$, $^3J_C8,_F12 = 7.3$ Hz, C^8), 103.7 (dd, $^2J_C10,_F9 = 28.4$, $^3J_C10,_F12 = 4.8$ Hz, C^{10}), 99.0 (m, $^2J_C5,_{CF3} = 33.1$, $^2J_C5,_F4$, $^2J_C5,_F6 = 13.8$ Hz, C^5), 98.4 (d, $^3J_C3,_F = 10.2$ Hz, C^3); ^{19}F NMR (376.46 MHz, acetone-d_6): δ = −53.5 (dd, 3F, $J_{CF3},_F4 = 24.3$, $J_{CF3},_F6 = 20.6$ Hz, CF_3), −117.7 (m, 1F, $J_F8,_H9 = 13.0$, $J_F8,_H12 = 7.1$ Hz, F^8), −124.9 (m, 1F, $J_F4,_{CF3} = 24.3$, $J_F4,_F7 = 18.0$, $J_F4,_F6 = 5.6$ Hz, F^4), −140.2 (m, 1F, $J_F11,_H12 = 12.1$, $J_F11,_H9 = 7.6$ Hz, F^{11}), −150.2 (m, 1F, $J_F6,_{CF3} \approx J_F6,_F7 \approx 20$, $J_F6,_F4 = 5.6$ Hz, F^6), −161.2 (m, 1F, $J_F7,_F6 = 19.1$, $J_F7,_F4 = 18.0$ Hz, F^7); HRMS (EI): M^+, found 366.0396. $C_{15}H_6F_8N_2$ requires 366.0398.

4.2.9.12. 2,3,5,6-Tetrafluoro-4-(4,6,7-trifluoro-5-(trifluoromethyl)-1H-indol-2-yl)aniline (1dc). The above-mentioned general procedure (Method C) was followed, and the crude product was purified by preparative TLC (Merck precoated plates, hexane/ethyl acetate, 5:1) to obtain **1dc** (109 mg, 54%) as white solid; 137.2 °C (decomp.); R_f 0.55; ν_{max} (KBr): 3522, 3479, 3423, 3199, 3167, 2966, 2937, 2877, 1664, 1610, 1522, 1495, 1462, 1396, 1358, 1323, 1267, 1215, 1174, 1126, 1078, 1003, 937, 883, 802, 748, 712, 679, 644, 611, 532, 515, 490 cm^{-1}; ^{1}H NMR (300.13 MHz, acetone-d_6): δ = 11.68 (br s, 1H, NH), 7.01 (m, 1H, $J_H3,_F \approx 3$ Hz, H^3), 5.87 (br s, 2H, NH_2); ^{13}C NMR (125.77 MHz, acetone-d_6): δ = 149.0 (dm, $^1J_C4,_F4 = 257.0$ Hz, C^4), 145.3 (dm, $^1J_C9,_F9 \approx 244$ Hz, C^9), 143.3 (ddd, $^1J_C6,_F6 = 246.9$, $^2J_C6,_F7 = 13.9$, $^3J_C6,_F4 = 4.7$ Hz, C^6), 137.3 (dm, $^1J_C10,_F10 = 237$ 1 Hz, C^{10}), 135.5 (ddd, $^1J_C7,_F7 = 244.4$, $^2J_C7,_F6 = 16.6$, $^4J_C7,_F4 = 4.2$ Hz, C^7), 130.0 (tt, $^2J_C11,_F10 = 14.6$, $^3J_C11,_F9 = 4.2$ Hz, C^{11}), 129.5 (m, C^2), 128.9 (tm, $^2J_C7a,_F7 \approx {}^3J_C7a,_F4 \approx 14$ Hz, C^{7a}), 123.5 (q, $^1J_{CF3},_F = 272.0$ Hz, CF_3), 116.8 (dd, $^2J_C3a,_F4 = 24.5$, $^3J_C3a,_F7 = 4.3$ Hz, C^{3a}), 102.0 (m, C^3), 99.4 (m, $^2J_C5,_{CF3} = 33.4$, $^2J_C5,_F4$, $^2J_C5,_F6 \approx 13$ Hz, C^5), 97.0 (t, $^2J_C8,_F9 = 16.7$ Hz, C^8); ^{19}F NMR (282.37 MHz, acetone-d_6): δ = −53.6 (dd, 3F, $J_{CF3},_F4 = 24.7$, $J_{CF3},_F6 = 20.6$ Hz, CF_3), −123.8 (m, 1F, $J_F4,_{CF3} = 24.7$, $J_F4,_F7 = 18.1$, $J_F4,_F6 = 5.3$ Hz, F^4), −144.1 (dm, 2F, $J_F8,_F9 \approx 20$ Hz, F^8), −149.2 (m, 1F, $J_F6,_{CF3} \approx J_F6,_F7 \approx 20$, $J_F6,_F4 = 5.3$ Hz, F^6), −160.7 (td, 1F, $J_F7,_F6 \approx J_F7,_F4 = 18.4$, $J_F7,_H3 = 2.6$ Hz, F^7), −161.9 (dm, 2F, $J_F9,_F8 \approx 21$ Hz, F^9); HRMS (EI): M^+, found 402.0212. $C_{15}H_4F_{10}N_2$ requires 402.0209.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.jfluchem.2016.06.010.

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