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Effective, transition metal free and selective C–F activation under mild conditions

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A simple and effective aromatic nucleophilic monosubstitution reaction for the synthesis of aromatic amines *via* selective C–F bond cleavage of various fluoroarenes (mono-, di-, tri-, tetra-, penta- and perfluorobenzene) with primary and secondary aromatic amines under transition metal free conditions is demonstrated. The reaction conditions were investigated thoroughly for a wide range of fluoroarene substrates bearing different numbers of fluorine atoms, and the results showed that the solvent and reaction temperature are very crucial for the successful substitution reactions. The established methods enabled the formation of nonfluorinated and partially fluorinated aromatic amines in good to excellent yields. Several functional groups were tolerated under the optimized conditions.

Introduction

The activation of C–F bonds in organofluorines has been a long-standing challenge because the C–F bonds are among the most inert functionalities in chemistry.[1] Despite these difficulties, its selective activation and transformation has become an active subject of investigation due to the fact that fluorine-containing compounds have wide applications in material science and the pharmaceutical and agrochemical industries.[2] The majority of studies in C–F cleavage and transformation have focused on the transition-metal catalytic C–F activation, and the significant achievements have been obtained in the past few years. From the viewpoint of synthetic chemistry, functionalized aromatic compounds, such as nonfluorinated products by hydrodefluorination[3] and cross coupling of monofluoroarene,[4] partially fluorinated compounds by mono-functionalization of polyfluoroarenes[5] are synthesized. However, there are some obvious drawbacks in these methods. Most of reactions require harsh conditions, expensive transition metal complexes with ligands, addictives and the activated substrates with one or more strong electron withdrawing groups. In additions, selectivity and yield of the reactions are no reliable.[6] Therefore, the development of efficient transition metal-free methods under mild conditions for the direct C–F bond activation and transformation is highly desirable. Replacement of fluorine on an aromatic ring with nucleophile by nucleophilic substitution is one of the choices.

The aromatic amines are widely found in biologically active and industrially useful molecules. Syntheses of amine have perhaps received more attention than syntheses of other functional groups. The transition metal catalyzed amination reaction was developed and is today often recognized as a powerful tool for synthetic organic chemists.[7] Generally, expensive and often sensitive ligands are necessary, and the separation and recovery of homogeneous catalysts are difficult or even impossible. An alternative way to solve the problem is a transition-metal free *N*-nucleophilic substitution as this approach is much simple, economic and environmentally friendly.[8] Despite nucleophilic substitution reaction of fluoroarene with various nucleophiles has been reported, the report of C–N bond formation *via* the reactions of aryl fluoride with N–H containing compounds is relatively unexplored. In addition, the conventional methods to generate fluorinated aromatic amines using aniline as nucleophile have significant limitations, including requirement for strong base such as NaH, *n*-BuLi or LiN(Me_3Si)$_2$, special apparatus for reagent handling and harsh conditions, limited reaction selectivity,[9] elevated temperature and prolonged reaction time.[10] Furthermore, nucleophilic substitution mainly proceed with the activated fluoroarenes (very electron-deficient fluoroarenes), and very few examples of reactions of non-activated fluoroarenes catalyzed by transition metal complexes are reported.[11] Therefore, it would be valuable to find a methodology provide access to a variety of *N*-functionalized fluoroarenes in high yields with high selectivity under mild conditions.

One of our research goals is to develop a practical, efficient and transition-metal-free method for amination of both activated and non-activated monofluoroarenes, as well as selective amination of polyfluoroarenes. Herein, we report amination of various fluoroarenes (mono-, di-, tri-, tetra-, penta- and

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perfluorobenzene) without transition metal catalyst under mild conditions.

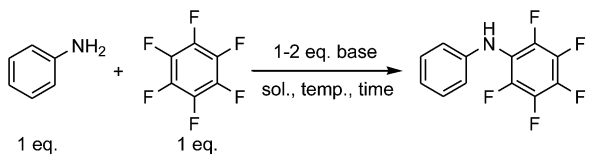
Results and discussion

Our investigation of the direct C–F bond activation and transformation began with the development of a methodology for the amination of the activated fluoroarenes, perfluorobenzene. Because of the strong electron-withdrawing nature of fluorine atom, perfluoro-substitution makes the aryl ring more susceptible to nucleophilic attack. Therefore, perfluorobenzene is remarkably reactive with various nucleophiles, causing that clean amination with aryl amine is more difficult. Only very strong, but non-nucleophilic base can lead to the successful amination.

In the first stage of our work, it was tested whether easily handling and weaker base *t*-BuOK could be an efficient base in the reaction of hexafluorobenzene to generate mono-substituted fluorobenzene selectively (Table 1). When the reaction of hexafluorobenzene (1 eq.) with aniline (1 eq.) was carried out in THF at 60 °C for 3 h with *t*-BuOK (1 eq.), only 14% of 2,3,4,5,6-pentafluoro-*N*-phenylbenzenamine with 100% selectivity was obtained (Table 1, entry 1). Even if the reaction time was prolonged to 5 h, the yield of desired product did not increase at all (Table 1, entry 2). There are probably two reasons for low yield of mono-amination product. Firstly, the basicity of *t*-BuOK is not strong enough to generate $C_6H_5NH^-$ anion effectively even at elevated temperature as pK_a of *t*-BuOH and $PhNH_2$ is 20 and 28, respectively. Secondly, potassium *t*-butoxide worked not only as a base, but also as a nucleophile in the reaction. It is proved by that a large amount of *t*-butoxy-2,3,4,5,6-penta-fluorobenzene was observed in the reaction mixtures. It is assumed that increasing amount of $C_6H_5NH^-$ anion or the related 'active species' in the reaction will be of benefit to form amination product, so aniline was allowed to react with *t*-BuOK at 60 °C for a while before hexafluorobenzene was added. The screening of reaction time was performed and the results were shown in Table 1 (entries 3–9). The pre-reaction time before adding hexafluorobenzene had a big effect on the yield; however, the reaction time after addition of hexafluorobenzene affected the yield insignificantly. The yield increased remarkably with increasing the pre-reaction time from 0 to 3 h, and then it increased slowly from 3 h to 5 h; whereas it is decreased after 5 h. The yield of pentafluoro-*N*-phenylbenzenamine was increased up to 85% under the conditions of entry 6. The effect of the solvents on the reactivity and selectivity was evaluated next (Table 1, entries 4 and 10–13). The low yield was observed in polar non-protic solvents such as DMSO or DMF, and also in the solvents with a low dielectric constant such as toluene. The ethereal solvents (THF or dioxane) provided better yield, whilst THF was the best solvent tested for the reaction. Different bases were screened as well (Table 1, entries 4 and 14–17). No product was observed when K_2CO_3, K_3PO_4 or NaOH was used as the base, whereas good yield was observed by using sodium *tert*-butoxide and potassium *tert*-butoxide. Reaction temperature has effect on the yields as well. Either lower or higher reaction temperature would lead to the lower yields and 60 °C is the optimum temperature under tested conditions (Table 1, entries 4 and 18–22). Increasing the amount of base used in the reaction would harm the yield of amination product (Table 1, entries 22–24) probably due to competing of *tert*-butoxide nucleophile. Therefore, the optimum reaction conditions for the mono-amination of perfluorobenzene were conducted in THF as the solvent and *tert*-BuOK (1 eq.) as base at 60 °C for (5 + 5) h.

To probe the substrate scope of this transformation, various anilines with different substituents were chosen to react with perfluorobenzene under the optimized conditions (Table 2). The results showed that anilines with either electron-donating substituent or electron-withdrawing substituent can be efficiently coupled in good yields and only the mono-aminated products of perfluorobenzene were detected. However, anilines with electron-withdrawing group gave higher yields due to their better reactivity and more acidity caused by electron-withdrawing substituent. In addition, some interesting functional group tolerances were noticed. Interestingly, the reaction only occurred on perfluorobenzene giving mono-

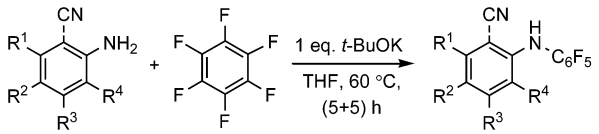
Table 1 Optimizing the reaction conditions of hexafluorobenzene reacting with aniline



Entry[a]	Base (eq.)	Solvent	Temp (°C)	Time (h)	GC Yield[b] (%)
1	*t*-BuOK (1)	THF	60	0 + 3	14
2	*t*-BuOK (1)	THF	60	0 + 5	14
3	*t*-BuOK (1)	THF	60	2 + 5	64
4	*t*-BuOK (1)	THF	60	3 + 5	80
5	*t*-BuOK (1)	THF	60	4 + 5	83
6	*t*-BuOK (1)	THF	60	5 + 5	85
7	*t*-BuOK (1)	THF	60	6 + 5	79
8	*t*-BuOK (1)	THF	60	3 + 4	77
9	*t*-BuOK (1)	THF	60	3 + 6	80
10	*t*-BuOK (1)	DMSO	60	3 + 5	12
11	*t*-BuOK (1)	DMF	60	3 + 5	5
12	*t*-BuOK (1)	Toluene	60	3 + 5	2
13	*t*-BuOK (1)	Dioxane	60	3 + 5	65
14	K_2CO_3 (1)	THF	60	3 + 5	0
15	K_3PO_4 (1)	THF	60	3 + 5	0
16	NaOH (1)	THF	60	3 + 5	0
17	*t*-BuONa (1)	THF	60	3 + 5	79
18	*t*-BuOK (1)	THF	0	3 + 5	12
19	*t*-BuOK (1)	THF	r.t.	3 + 5	40
20	*t*-BuOK (1)	THF	40	3 + 5	60
21	*t*-BuOK (1)	THF	50	3 + 5	74
22	*t*-BuOK (1)	THF	70	3 + 5	50
23	*t*-BuOK (1.5)	THF	60	3 + 5	75
24	*t*-BuOK (2)	THF	60	3 + 5	70

[a] Reaction conditions: the mixture of aniline (1 mmol), base (1–2 mmol) and solvent (1 mL) being stirred for 0–6 h, then adding hexafluorobenzene (1 mmol) and stirring for another 3–6 h. [b] Determined by GC-MS with tetraline as an internal standard.

Table 2 Nucleophilic substitution of hexafluorobenzene with different anilines



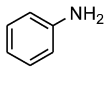
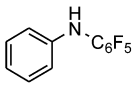
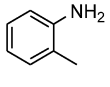
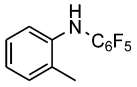
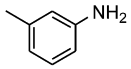
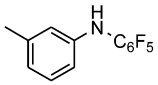
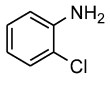
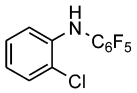
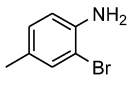
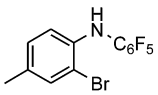
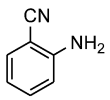
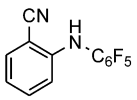
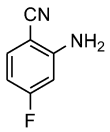
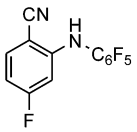
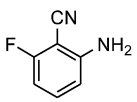
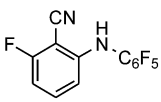
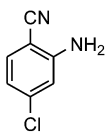
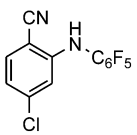
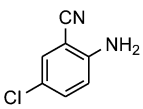
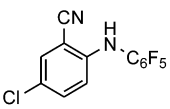
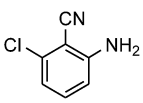
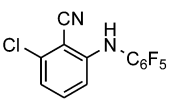
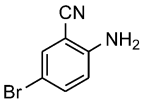
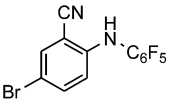
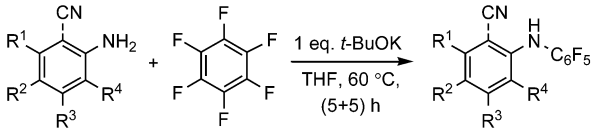
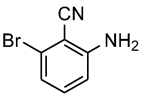
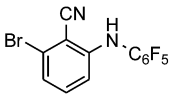
Entry[a]	Anline	Product	Yield[b] (%)
1			79
2			68
3			65
4			73
5			79
6			92
7			88
8			86
9			90
10			88
11			86
12			92

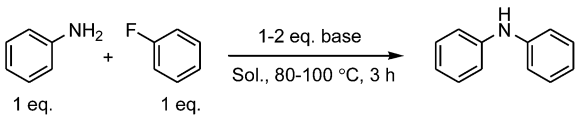
Table 2 (*Contd.*)



Entry[a]	Anline	Product	Yield[b] (%)
13			85

[a] Reaction conditions: the mixture of aniline (1 mmol), *t*-BuOK (1 mmol) and THF (1 mL) being stirred for 5 h at 60 °C, then adding hexafluorobenzene (1 mmol) and stirring for 5 h at the same temperature. [b] Isolated yield on average of two runs.

Table 3 Optimizing the reaction conditions of fluorobenzene with aniline



Entry[a]	Base (eq.)	Solvent	Temp (°C)	GC Yield[b] (%)
1	Cs_2CO_3 (1)	DMSO	90	0
2	K_2CO_3 (1)	DMSO	90	0
3	K_3PO_4 (1)	DMSO	90	0
4	*t*-BuONa (1)	DMSO	90	11
5	*t*-BuOK (1)	DMSO	90	92
6	*t*-BuOK (1)	DMF	90	0
7	*t*-BuOK (1)	THF	90	0
8	*t*-BuOK (1)	Toluene	90	0
9	*t*-BuOK (1)	Dioxane	90	0
10	*t*-BuOK (2)	DMSO	90	91
11	*t*-BuOK (1)	DMSO	80	79
12	*t*-BuOK (1)	DMSO	100	75

[a] Reaction conditions: the mixture of aniline (1 mmol), fluorobenzene (1 mmol) and base (1–2 mmol) in solvent (1 mL). [b] Determined by GC-MS with tetraline as an internal standard.

aminated pentafluorobenzene as single product in high yield. Substitution did not take place on monofluoro aniline and none of corresponding aminated aniline was detected in the reactions (Table 2, entries 7 and 8). This suggested the reaction conditions for substitution of hexafluorobenzene was not suitable for substitution of mono-fluoroarenes. To find out if the protocol works for *N*-substituted anilines, the reaction of fluorobenzene with *N*-methyl aniline was investigated. However, the reaction was too messy to isolate the desired product.

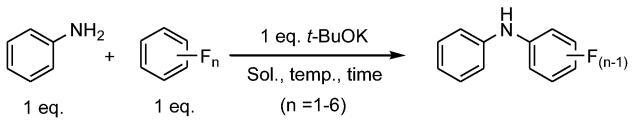
As the reaction conditions for activated hexafluorobenzene would be different from those for non-activated mono-fluoroarenes, we next investigated optimum conditions for the substitution reaction of less electron-poor mono-fluorobenzene. A survey of the effect of bases, solvents, temperatures was conducted in the reaction of fluorobenzene with aniline using 1–2 eq. of base at higher temperature (80–100 °C) for 3 h (Table 3). It was seen from the results that no product was observed when weaker base, such as cesium carbonate, potassium carbonate, or potassium phosphate (Table 3, entries 1–3) was used, whereas 11% of yield was observed with stronger base sodium *tert*-butoxide (Table 3, entry 4). However, when changing the base to potassium *tert*-butoxide, the reaction occurred smoothly with 92% high yield (Table 3, entry 5). It is worthy to mention that the pre-reaction of aniline with base was not necessary for this transformation. The possible reason is that the substitution reaction of unactivated fluorobenzene with amino anion (a better nucleophile) is more favorable than with alkoxide. In additions, product was only observed in high yield when DMSO was used, whereas, no product was detected in any of other tested solvents, such as DMF, THF, toluene or dioxane (Table 3, entries 5–9). Therefore, the choice of base and solvent is very crucial for the successful reaction of unactivated mono-fluorobenzene. Reaction temperature has big effect on the yield as well. It was found that either lower or higher reaction temperature would lead to the lower yield and 90 °C is the optimum temperature under tested conditions (Table 3, entries 5, 11 and 12). Double the amount of base used in the reaction has almost no effect on the yield of product. Therefore, the optimum reaction conditions for the amination of monofluorobenzene were conducted in DMSO as the solvent and with *t*-BuOK (1 eq.) as base at 90 °C for 3 h.

From the above investigation, it was found that *t*-BuOK are suitable base for the successful substitution reaction of both mono-fluorobenzene and hexafluorobenzene, however, the solvent, reaction temperature and time are very different. Therefore, we carried out a thorough investigation of the effect of reaction conditions on fluoroarene bearing different numbers of fluorine atoms, and the results were presented in Table 4. The result revealed that polar solvent, DMSO is good solvent for the reaction of mono-, di, tri-fluorobenzene, however, the reaction temperature for 1-fluorobenzene (90 °C) is much higher than that for 1,3-difluorobenzene and 1,3,5-trifluorobenzene (room temperature). The good solvent for tetra-fluorobenzene and penta-fluorobenzene is non-polar toluene. The reaction of 1,2,4,5-tetrafluorobenzene can be completed at room temperature for 3 h, whereas, the reaction of 1,2,3,4,5-pentafluorobenzene had been heated to 40 °C and pre-reaction of aniline with potassium *tert*-butoxide was required. Interestingly, the reaction conditions of monochloro-trifluorobenzene are the same as those of tetrafluorobenzene, which are different from those of trifluorobenzene.

To further probe the generality and scope of these conditions for the functionalization of specific fluoroarene, different anilines were chosen and studied. The results of the reaction of both mono- and difluorobenzenes with anilines were given in Table 5. It is worthy to note, that non-activated 4-fluorotoluene (fluorobenzene with electron donating group) can be functionalized successfully in good yield under this conditions (Table 5, entry 2). In addition, the amination only occurred on C–F bond over C–Cl (Table 5, entries 3, 5 and 8). Furthermore, *N*-substituted *N*-methyl aniline would react with mono-fluorobenzene or difluorobenzene smoothly, leading high yield of the product (Table 5, entries 4 and 9).

Trifluorobenzene can be aminated by a variety of anilines in DMSO at room temperature for only 3 h (Table 6). Reactions of both anilines with electron-donating groups (Table 6, entries 1 and 4–6) and electron withdrawing groups (Table 6, entries 2 and 7–8) gave the products in good yields. The amination would occur with secondary aromatic amine as well (Table 6, entries 11 and 13). However, sterically hindered *N*-substituted aniline lead to much lower 41% yield. C–F activation occurs exclusively, and only one C–F bond was functionalized to lead mono-aminated products under these conditions. The amination only occurred on C–F bond over C–Cl and C–Br, meanwhile, the

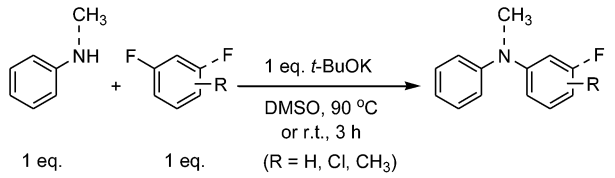
Table 4 The optimum conditions for amination of different fluoroarenes with aniline

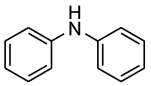
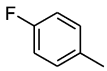
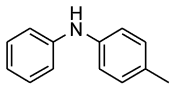
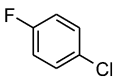
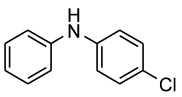
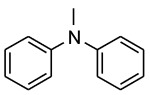
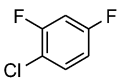
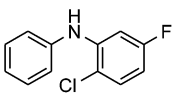
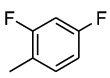
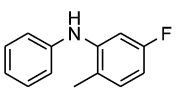
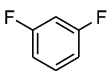
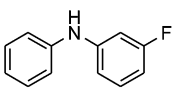
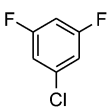
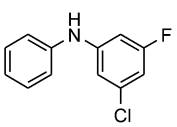
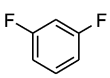
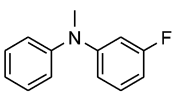


Entry[a]	*n*	Fluoroarene	Solvent	Time (h)	Temp. (°C)	Yield[b] (%)
1	1	1-Fluorobenzene	DMSO	3	90	87
2	2	1,3-Difluorobenzene	DMSO	3	r.t.	87
3	3	1,3,5-Trifluorobenzene	DMSO	3	r.t.	85
4	3	1-Chloro-2,4,6-trifluorobenzene	Toluene	3	r.t.	90
5	4	1,2,4,5-Tetrafluorobenzene	Toluene	3	r.t.	71
6	5	1,2,3,4,5-Pentafluorobenzene	Toluene	2 + 6	40	83
7	6	1,2,3,4,5,6-Hexafluorobenzene	THF	5 + 5	60	79

[a] Reaction conditions: the mixture of aniline (1 mmol), fluoroarene (1 mmol) and *t*-BuOK (1 mmol) in solvent (1 mL) was reacted at room temperature to 90 °C for 3–10 h. [b] Isolated yield on average of two runs.

Table 5 Nucleophilic substitution in mono- or difluorobenzenes with aniline[a]



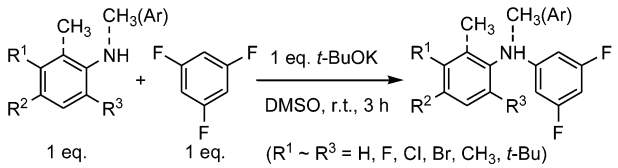
Entry	Fluorobenzene	Product	Yield[c] (%)
1[a]			87
2[a]			83
3[a]			81
4[a]			81
5[b]			81
6[b]			77
7[b]			87
8[b]			80
9[b]			83

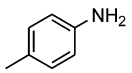
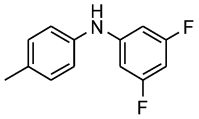
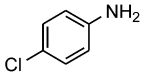
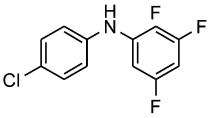
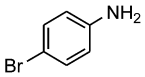
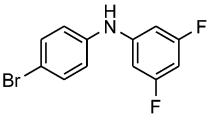
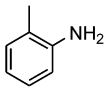
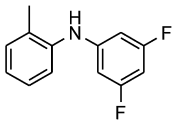
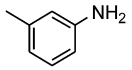
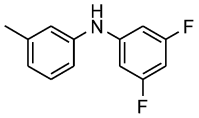
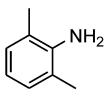
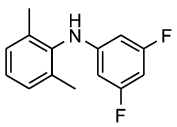
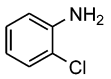
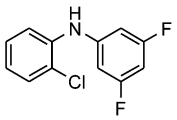
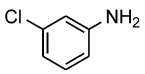
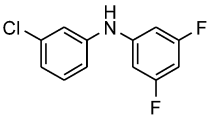
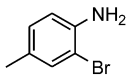
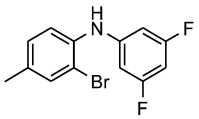
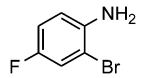
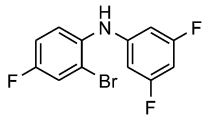
[a] Reaction conditions: the mixture of aniline (1 mmol), fluorobenzene (1 mmol), *t*-BuOK (1 mmol) and DMSO (1 mL) being stirred 3 h at 90 °C. [b] Reaction conditions: the mixture of aniline (1 mmol), fluorobenzene (1 mmol), *t*-BuOK (1 mmol) and DMSO (1 mL) being stirred 3 h at r.t. [c] Isolated yield on average of two runs.

substitution reactions selectively occurred on trifluorobenzene over monofluoroarene (Table 6, entry 10).

The results of reaction of monochloro-trifluorobenzene with anilines are summarized in Table 7. 1-Chloro-2,4,6-trifluorobenzene can be aminated by a variety of anilines in toluene at room temperature for 3 h. The nucleophilic substitution of 1-chloro-2,4,6-trifluorobenzene occurred regioselectively at C-2 instead of C-4 position in good yields under these conditions. Reactions of both anilines with electron donating groups and electron withdrawing groups gave the product in

Table 6 Nucleophilic substitution in tri-fluorobenzene with different anilines



Entry[a]	Anline	Product	Yield[b] (%)
1			81
2			80
3			86
4			81
5			80
6			61
7			74
8			81
9			87
10			80

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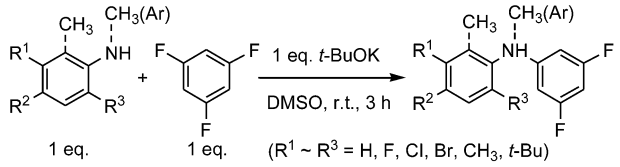
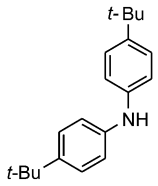
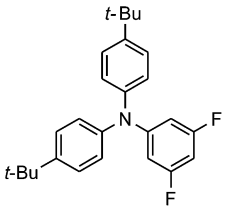
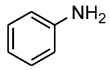
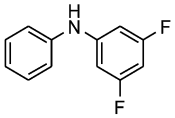
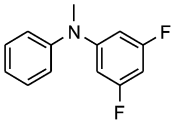


Entry[a]	Anline	Product	Yield[b] (%)
11			41
12			85
13			75

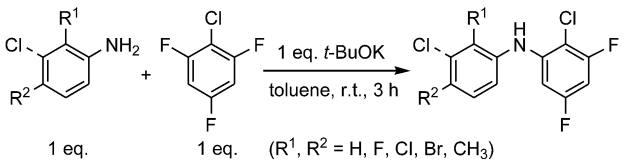
[a] Reaction conditions: the mixture of aniline (1 mmol), 1,3,5-trifluorobenzene (1 mmol), *t*-BuOK (1 mmol) and DMSO (1 mL) being stirred 3 h at r.t. [b] Isolated yield on average of two runs.

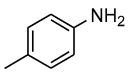
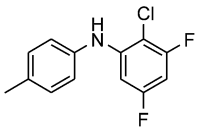
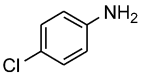
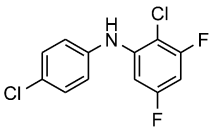
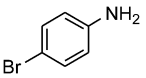
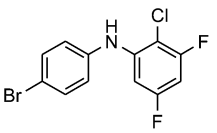
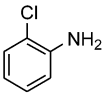
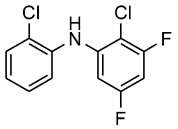
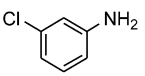
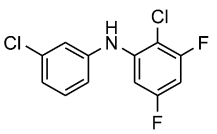
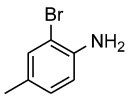
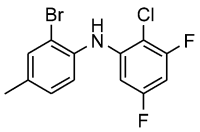
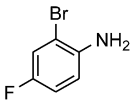
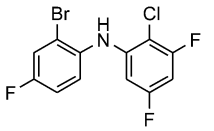
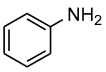
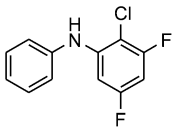
good yields. C–F activation occurs exclusively in the presence of C–Cl and C–Br bond, meanwhile, substitution selectively occurred on trifluoroarene over monofluoroarene. It was suggested that the electronic effect plays more important role than steric effect based on the results of *para*-chloroaniline, *ortho*-chloroaniline and *meta*-chloroaniline (Table 7, entries 2, 4 and 5).

The reactions of tetrafluorobenzene with aniline are summarized in Table 8. 1,2,4,5-Tetrafluorobenzene can be aminated by various anilines in toluene at room temperature for 3 h in good yield. Reactions of both anilines with electron-donating groups and electron withdrawing groups gave the product in good yields. Under these reaction conditions, C–F activation occurs exclusively on C–F bond in the presence of C–Cl and C–Br, and only one of four C–F bonds was functionalized. The amination would occur with secondary aromatic amine (*N*-methyl aniline) in moderate yield (Table 8, entry 9).

The results of reaction of pentafluorobenzene with anilines are summarized in Table 9. 1,2,3,4,5-Pentafluorobenzene can be aminated by a variety of anilines in toluene at 40 °C for (2 + 6) h. The nucleophilic substitution of pentafluorobenzene occurred selectively at C-3 over other C–F carbons in good yields under these conditions. It was noticed that several functional groups were tolerated under the conditions investigated. However, the reaction of pentafluorobenzene with *N*-methyl aniline was too messy to isolate the desired product.

Table 7 Nucleophilic substitution in 1-chloro-2,4,6-trifluorobenzene with different anilines



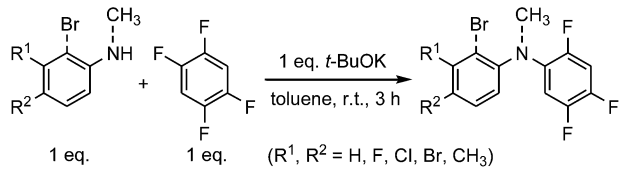
Entry[a]	Anline	Product	Yield[b] (%)
1			81
2			87
3			89
4			85
5			77
6			87
7			90
8			90

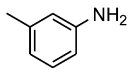
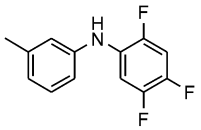
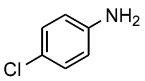
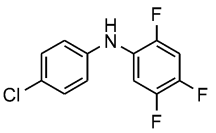
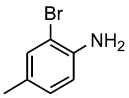
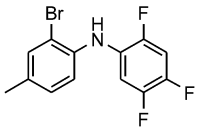
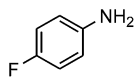
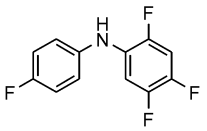
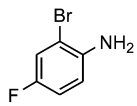
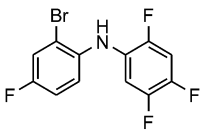
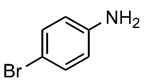
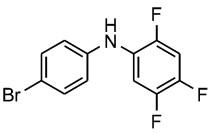
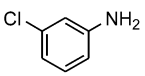
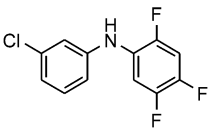
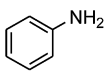
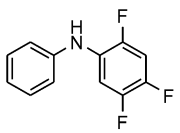
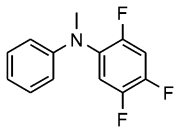
[a] Reaction conditions: the mixture of aniline (1 mmol), 1-chloro-2,4,6-trifluorobenzene (1 mmol), *t*-BuOK (1 mmol) and toluene (1 mL) being stirred 3 h at r.t. [b] Isolated yield on average of two runs.

Conclusions

In summary, a simple and efficient nucleophilic substitution approach for the amination of various fluoroarenes (mono-, di-, tri-, tetra-, penta- and perfluorobenzene) with different anilines (primary and secondary amine) was developed. Mono- and

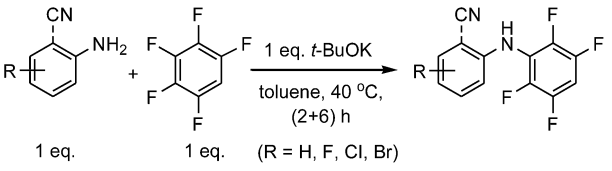
Table 8 Nucleophilic substitution in tetrafluorobenzene with different anilines

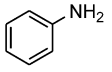
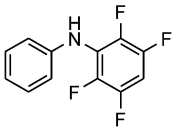
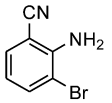
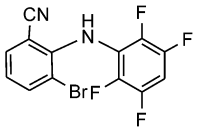
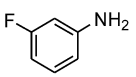
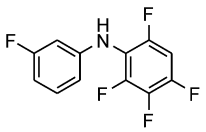
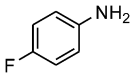
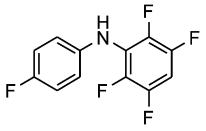
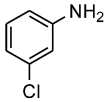
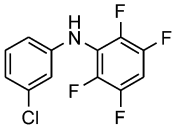
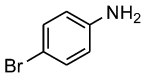
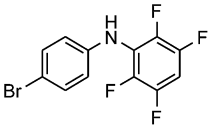
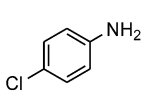
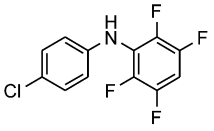


Entry[a]	Anline	Product	Yield[b] (%)
1			81
2			68
3			72
4			80
5			82
6			75
7			72
8			71
9			41

[a] Reaction conditions: the mixture of aniline (1 mmol), 1,2,4,5-tetrafluorobenzene (1 mmol), *t*-BuOK (1 mmol) and toluene (1 mL) being stirred 3 h at r.t. [b] Isolated yield on average of two runs.

Table 9 Nucleophilic substitution in pentafluorobenzene with different anilines



Entry[a]	Anline	Product	Yield[b] (%)
1			83
2			91
3			80
4			89
5			73
6			79
7			74

[a] Reaction conditions: the mixture of aniline (1 mmol), *t*-BuOK (1 mmol) and toluene (1 mL) being stirred for 2 h at 40 °C, then adding 1,2,3,4,5-pentafluorobenzene (1 mmol) and stirring for 6 h at the same temperature. [b] Isolated yield on average of two runs.

polyfluoroarenes can be converted to aromatic amines in good yields under very mild conditions without transition metal catalyst. Our system is preferentially active C–F bond over other C–X bonds (X = H, Cl, Br), and selectively mono-functionalization of polyfluorobenzene to form fluorosubstituted aromatic amine is of particular merit. The unique discovery of the amination of polyfluorobenzene will benefit the drug and agriculture chemistry. Our research will no doubt

expand the usefulness and applicability of C–F activation chemistry.

Experimental section

General information

DMSO was distilled from calcium hydride and dioxane was distilled from sodium benzophenone ketyl prior to use. DMF, toluene and THF were dried using VAC Solvent Purifier Instrument. All other reagents were commercially available and were used without further purification. ^{1}H, ^{13}C and ^{19}F spectra were recorded on a Bruker AV 400 MHz spectrometer at room temperature and referenced to the residual signals of the solvent (for ^{1}H and ^{13}C) or to CF_3COOH (^{19}F). GC-MS was performed on an Agilent 6890-5973 N system with electron ionization (EI) mass spectrometry. Melting points were detected by microscope melting point apparatus. HRMS was recorded on a Fisher LTQ-Orbitrap XL combined-type mass spectrometry.

General procedure of amination of perfluorobenzene

In a typical run, a 4 mL vial with a stir bar was charged with *t*-BuOK (1 mmol) in glove box, and the capped vial was move out of glove box. Aniline (1 mmol) and THF (1 mL) were injected into the vial respectively. After the mixture was stirred for 3 h at 60 °C, the vial was cooled to room temperature and perfluorobenzene (1 mmol) was injected. The new mixture was stirred for 5 h at 60 °C. Then the vial was cooled and the reaction mixture was poured into the saturated NaCl aqueous solution and was extracted with DCM (3 × 10 mL). The combined organic phase was dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (PE/EtOAc = 100 : 1).

2,3,4,5,6-Pentafluoro-*N*-phenylbenzenamine (Table 2, entry 1).[12,14] White solid (205 mg, 79%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36–7.26 (m, 2H), 7.04–6.94 (m, 1H), 6.85–6.79 (m, 2H), 5.43 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.1, 129.2, 121.9, 116.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ −163.6 (m), −162.8 (m), −149.3 (m); HRMS (ESI): *m*/*z* $[M + H]^+$ calc. for $C_{12}H_6F_5N$ 260.0499, found 260.0501.

2,3,4,5,6-Pentafluoro-*N*-*o*-tolylbenzenamine (Table 2, entry 2).[13] White solid (186 mg, 68%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20 (d, J = 7.4 Hz, 1H), 7.13 (t, J = 7.7 Hz, 1H), 6.96 (t, J = 7.4 Hz, 1H), 6.67 (d, J = 8.0 Hz, 1H), 5.11 (br, 1H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.3, 130.7, 126.8, 126.5, 122.3, 115.5, 17.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ −163.8 (m), −162.9 (m), −149.4 (m); HRMS (ESI): *m*/*z* $[M + H]^+$ calc. for $C_{13}H_9F_5N$ 274.0655, found 274.0652.

2,3,4,5,6-Pentafluoro-*N*-3-tolylbenzenamine (Table 2, entry 3).[14] White solid (177 mg, 65%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.15 (t, J = 7.6 Hz, 1H), 6.81 (d, J = 7.4 Hz, 1H), 6.62 (d, J = 8.9 Hz, 2H), 5.39 (br, 1H), 2.31 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.1, 139.3, 129.1, 122.8, 117.1, 113.5, 21.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ −163.7 (m), −162.8 (m), −149.5 (m); HRMS (ESI): *m*/*z* $[M + H]^+$ calc. for $C_{13}H_9F_5N$ 274.0655, found 274.0651.

***N*-(2-Chlorophenyl)-2,3,4,5,6-pentafluorobenzenamine (Table 2, entry 4).** White solid (214 mg, 73%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (d, J = 7.9 Hz, 1H), 7.16 (t, J = 7.8 Hz, 1H), 6.90 (dt, J = 11.2, 4.1 Hz, 1H), 6.63 (d, J = 8.1 Hz, 1H), 5.78 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.9, 129.6, 127.6, 121.7, 121.5, 114.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ −162.2 (m), −160.8 (m), −147.5 (m); HRMS (ESI): *m*/*z* $[M - H]^-$ calc. for $C_{12}H_4ClF_5N$ 291.9946, found 291.9939.

***N*-(2-Bromo-4-methylphenyl)-2,3,4,5,6-pentafluorobenzenamine (Table 2, entry 5).** White solid (278 mg, 79%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (s, 1H), 7.00 (d, J = 8.2 Hz, 1H), 6.54 (dt, J = 8.2, 2.5 Hz, 1H), 5.63 (br, 1H), 2.28 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.4, 133.1, 132.4, 128.8, 115.1, 112.0, 20.3; ^{19}F NMR (376 MHz, $CDCl_3$) δ −161.5 (m), −158.6 (m), −146.5 (m); HRMS (ESI): *m*/*z* $[M - H]^-$ calc. for $C_{13}H_6BrF_5N$ 349.9598, found 349.9572.

2-(Perfluorophenylamino)benzonitrile (Table 2, entry 6). White solid (261 mg, 92%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, J = 7.8 Hz, 1H), 7.45 (t, J = 7.9 Hz, 1H), 7.00 (t, J = 7.6 Hz, 1H), 6.65 (d, J = 8.4 Hz, 1H), 5.92 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.3, 134.1, 132.9, 121.1, 116.8, 114.1, 99.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ −161.5 (m), −158.6 (m), −146.5 (m); HRMS (ESI): *m*/*z* $[M - H]^-$ calc. for $C_{13}H_4F_5N_2$ 283.0289, found 283.0279.

4-Fluoro-2-(perfluorophenylamino)benzonitrile (Table 2, entry 7). White solid (302 mg, 88%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (dd, J = 8.6, 5.9 Hz, 1H), 6.70 (td, J = 8.2, 2.2 Hz, 1H), 6.30 (dd, J = 10.2, 2.0 Hz, 1H), 6.03 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.5 (d, J = 17.0 Hz), 135.1 (d, J = 11.0 Hz), 116.3 (d, J = 16.0 Hz), 108.8 (d, J = 23.0 Hz), 101.28–101.61 (m), 95.3 (d, J = 3.0 Hz), 86.7 (d, J = 3.0 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ −160.8 (m), −156.6 (t, J = 21.4 Hz), −145.7 (m), −100.3; HRMS (ESI): *m*/*z* $[M - H]^-$ calc. for $C_{13}H_3F_6N_2$ 301.0195, found 301.0184.

2-Fluoro-6-(perfluorophenylamino)benzonitrile (Table 2, entry 8). White solid (260 mg, 86%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (m, 1H), 6.74 (t, J = 8.4 Hz, 1H), 6.39 (d, J = 8.5 Hz, 1H), 5.97 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.7 (d, J = 311.0 Hz), 147.1–146.9 (m) 135.3 (d, J = 5.0 Hz), 112.3 (d, J = 11.0 Hz), 109.4–109.0 (m), 107.5 (d, J = 19.0 Hz), 89.8–89.6 (m); ^{19}F NMR (376 MHz, $CDCl_3$) δ −161.3 (m), −159.0 (t, J = 21.8 Hz), −145.2 (m), −120.7; HRMS (ESI): *m*/*z* $[M - H]^-$ calc. for $C_{13}H_3F_6N_2$ 301.0195, found 301.0190.

4-Chloro-2-(perfluorophenylamino)benzonitrile (Table 2, entry 9). White solid (287 mg, 90%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (d, J = 8.3 Hz, 1H), 6.97 (dd, J = 8.3, 1.6 Hz, 1H), 6.58 (d, J = 1.8 Hz, 1H), 5.95 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.6, 141.0, 133.8, 121.4, 116.1, 114.0, 97.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ −161.0 (m), −157.8 (t, J = 21.4 Hz), −146.3 (m); HRMS (ESI): *m*/*z* $[M - H]^-$ calc. for $C_{13}H_3ClF_5N_2$ 316.9899, found 316.9896.

5-Chloro-2-(perfluorophenylamino)benzonitrile (Table 2, entry 10). White solid (280 mg, 88%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, J = 2.4 Hz, 1H), 7.40 (dd, J = 8.8, 2.4 Hz, 1H), 6.59 (dt, J = 8.9, 2.0 Hz, 1H), 5.94 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.1, 134.4, 132.1, 125.9, 115.5 (d), 100.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ −161.0 (m), −157.8 (t, J = 21.8 Hz), −146.4 (m); HRMS (ESI): *m*/*z* $[M - H]^-$ calc. for $C_{13}H_3ClF_5N_2$ 316.9899, found 316.9891.

2-Chloro-6-(perfluorophenylamino)benzonitrile (Table 2, entry 11). White solid (274 mg, 86%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (t, J = 8.0 Hz, 1H), 7.03 (d, J = 8.0 Hz, 1H), 6.50 (dt, J = 8.4, 2.4 Hz, 1H), 6.03 (b, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.3, 137.4, 134.3, 121.4, 114.2, 111.7, 100.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ −161.1 (m), −157.2 (m), −145.8 (m); HRMS (ESI): m/z $[M - H]^-$ calc. for $C_{13}H_3ClF_5N_2$ 316.9899, found 316.9911.

5-Bromo-2-(perfluorophenylamino)benzonitrile (Table 2, entry 12). White solid (334 mg, 92%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, J = 2.0 Hz, 1H), 7.53 (dd, J = 9.2, 2.4 Hz, 1H), 6.53 (dt, J = 8.8, 2.0 Hz, 1H), 5.93 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.5, 137.2, 134.9, 115.7, 115.4, 112.5, 101.0; ^{19}F NMR (376 MHz, $CDCl_3$) δ −161.0 (m), −157.6 (t, J = 21.4 Hz), −146.2 (m); HRMS (ESI): m/z $[M - H]^-$ calc. for $C_{13}H_3BrF_5N_2$ 360.9394, found 360.9391.

2-Bromo-6-(perfluorophenylamino)benzonitrile (Table 2, entry 13). White solid (309 mg, 85%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30–7.18 (m, 2H), 6.55 (dt, J = 8.4, 2.0 Hz, 1H), 6.02 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.5, 134.4, 125.8, 124.6, 115.4, 112.1, 102.8; ^{19}F NMR (376 MHz, $CDCl_3$) δ −161.0 (m), −157.1 (t, J = 21.8 Hz), −145.8 (m); HRMS (ESI): m/z $[M - H]^-$ calc. for $C_{13}H_3BrF_5N_2$ 360.9394, found 360.9394.

General procedure of amination of mono- and di-fluorobenzene

In a typical run, a 4 mL vial was charged with *t*-BuOK (1 mmol) in glove box, and the capped vial was move out of glove box. Aniline (1 mmol), fluoroarene (1 mmol), and DMSO (1 mL) were injected into the vial respectively. The mixture was heated at 90 °C for 3 h for the reaction of monofluoroarenes, whereas the mixture was stirred at 25 °C for 3 h for the reaction of difluoroarenes. The reaction mixture was poured into water and was extracted with DCM (3 × 10 mL). The combined organic phase was dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (PE/EtOAc = 100 : 1).

Diphenylamine (Table 5, entry 1).[15] White solid (147 mg, 87%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28–7.24 (m, 4H), 7.08–7.06 (m, 4H), 6.92 (t, J = 7.2 Hz, 2H), 5.69 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.0, 129.3, 120.9, 117.7; HRMS (ESI): m/z $[M + H]^-$ calc. for $C_{12}H_{12}N$ 170.0970, found 170.0972.

4-Methyl-*N*-phenylbenzenamine (Table 5, entry 2).[15] White solid (152 mg, 83%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26–7.23 (m, 2H), 7.10–7.08 (m, 2H), 7.03–7.00 (m, 4H), 6.88 (t, J = 7.2 Hz, 1H), 5.61 (br, 1H), 2.31 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.9, 140.2, 130.9, 129.8, 129.3, 120.2, 118.8, 116.8, 20.7; HRMS (ESI): m/z $[M + H]^-$ calc. for $C_{13}H_{14}N$: 184.1126, found 184.1129.

4-Chloro-*N*-phenylbenzenamine (Table 5, entry 3).[16] White solid (165 mg, 81%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30–7.20 (m, 4H), 7.06–6.94 (m, 5H), 5.67 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.6, 141.8, 129.5, 129.3, 125.5, 121.5, 118.8, 118.1; HRMS (ESI): m/z $[M + H]^-$ calc. for $C_{12}H_{11}ClN$ 204.0580, found 204.0577.

***N*-Methyl-*N*-phenylaniline (Table 5, entry 4).**[17] Colourless liquid (150 mg, 81%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33–7.26 (m, 4H), 7.08–7.04 (m, 4H), 6.99 (tt, J = 7.2, 1.2 Hz, 2H), 3.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.0, 129.2, 121.2, 120.4, 112.4, 40.2.

2-Chloro-5-fluoro-*N*-phenylbenzenamine (Table 5, entry 5). White solid (180 mg, 81%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35 (m, 2H), 7.28–7.23 (m, 1H), 7.18 (m, 2H), 7.10 (t, J = 7.6 Hz, 1H), 6.91 (dd, J = 11.2, 2.8 Hz, 1H), 6.47 (dt, J = 8.4, 2.8 Hz, 1H), 6.16 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.1 (d, J = 242.0 Hz), 141.9 (d, J = 11.1 Hz), 140.3, 130.3 (d, J = 9.9 Hz), 129.6, 123.7, 121.3, 115.5 (d, J = 2.9 Hz), 106.4 (d, J = 23.4 Hz), 101.5 (d, J = 27.9 Hz); HRMS (ESI): m/z $[M - H]^-$ calc. for $C_{12}H_8ClFN$ 220.0329, found 220.0335.

5-Fluoro-2-methyl-*N*-phenylbenzenamine (Table 5, entry 6). White solid (155 mg, 77%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33–7.26 (m, 2H), 7.10–6.92 (m, 5H), 6.56 (dt, J = 8.2, 2.0 Hz, 1H), 5.43 (br, 1H), 2.22 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.0 (d, J = 240.1 Hz), 143.0 (d, J = 10.0 Hz), 142.3, 131.4 (d, J = 9.3 Hz), 129.4, 121.9, 119.1, 113.3 (d, J = 2.8 Hz), 107.1 (d, J = 21.1 Hz), 103.2 (d, J = 25.0 Hz), 17.2; HRMS (ESI): m/z $[M - H]^-$ calc. for $C_{13}H_{11}FN$ 200.0876, found 200.0871.

3-Fluoro-*N*-phenylbenzenamine (Table 5, entry 7). White solid (163 mg, 87%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33–7.10 (m, 5H), 7.00 (t, J = 7.6 Hz, 1H), 6.78 (d, J = 8.4 Hz, 2H), 6.59 (m, 1H), 5.77 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.7 (d, J = 242.5 Hz), 145.3 (d, J = 10.4 Hz), 141.9, 130.4 (d, J = 9.9 Hz), 129.4, 122.0, 119.0, 112.5 (d, J = 2.6 Hz), 107.0 (d, J = 21.3 Hz), 103.5 (d, J = 24.9 Hz); HRMS (ESI): m/z $[M - H]^-$ calc. for $C_{12}H_9FN$ 186.0719, found 186.0717.

3-Chloro-5-fluoro-*N*-phenylbenzenamine (Table 5, entry 8). White solid (177 mg, 80%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (m, 2H), 7.13–7.05 (m, 3H), 6.76 (s, 1H), 6.59 (m, 2H), 5.81 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.6 (d, J = 244.9 Hz), 146.3 (d, J = 11.8 Hz), 140.8, 135.6 (d, J = 13.4 Hz), 129.6, 123.1, 120.2, 111.8 (d, J = 2.8 Hz), 107.5 (d, J = 25.3 Hz), 101.2 (d, J = 25.2 Hz); HRMS (ESI): m/z $[M - H]^-$ calc. for $C_{12}H_8ClFN$ 220.0329, found 220.0327.

3-Fluoro-*N*-methyl-*N*-phenylaniline (Table 5, entry 9). Colorless liquid (166 mg, 83%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35–7.30 (m, 2H), 7.14–7.06 (m, 4H), 6.65–6.50 (m, 3H), 3.28 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.7 (d, J = 241.7 Hz), 150.8 (d, J = 10.2 Hz), 148.2, 129.9 (d, J = 9.90 Hz), 129.5, 123.7, 123.6, 112.7 (d, J = 2.4 Hz), 105.9 (d, J = 21.4 Hz), 104.1 (d, J = 24.9 Hz), 40.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ −112.4; HRMS (ESI): m/z $[M + H]^-$ calc. for $C_{13}H_{13}FN$ 202.1032, found 202.1033.

General procedure of amination of 1,3,5-trifluorobenzene

In a typical run, a 4 mL vial was charged with *t*-BuOK (1 mmol) in glove box, and the capped vial was move out of glove box. Aniline (1 mmol), 1,3,5-trifluorobenzene (1 mmol), and DMSO (1 mL) were injected into the vial respectively. The mixture was stirred at room temperature for 3 h. The reaction mixture was poured into water and was extracted with DCM (3 × 10 mL). The combined organic phase was dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (PE/EtOAc = 200 : 1).

3,5-Difluoro-*N*-*p*-tolylbenzenamine (Table 6, entry 1). White solid (178 mg, 81%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.15 (d, J = 8.4 Hz, 2H), 7.04 (d, J = 8.4 Hz, 2H), 6.43 (J = 9.2, 1.6 Hz, 2H), 6.26 (tt, J = 9.2, 2.0 Hz, 1H), 5.74 (br, 1H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.0 (d, J = 240.0, 15.6 Hz), 147.2 (t, J = 13.1 Hz), 138.1, 133.2, 130.1, 121.2, 98.1–97.8 (m), 94.5 (t, J = 25.9 Hz), 20.7; HRMS (ESI): m/z [M − H]$^-$ calc. for $C_{13}H_{10}F_2N$ 218.0776, found 218.0776.

***N*-(4-Chlorophenyl)-3,5-difluorobenzenamine (Table 6, entry 2).** White solid (192 mg, 80%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 (m, 2H), 7.04 (m, 2H), 6.46 (m, 2H), 6.33 (tt, J = 8.8, 2.0 Hz, 1H), 5.80 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.0 (dd, J = 245.0, 15.4 Hz), 145.9 (t, J = 13.1 Hz), 139.5, 129.6, 127.9, 121.4, 99.1–98.8 (m), 95.7 (t, J = 25.8 Hz); HRMS (ESI): m/z [M − H]$^-$ calc. for $C_{12}H_7ClF_2N$ 238.0230, found 238.0231.

***N*-(4-Bromophenyl)-3,5-difluorobenzenamine (Table 6, entry 3).** White solid (244 mg, 86%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (d, J = 8.4 Hz, 2H), 7.00 (d, J = 8.4 Hz, 2H), 6.48 (m, 2H), 6.33 (tt, J = 8.8, 2.0 Hz, 1H), 5.80 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.9 (dd, J = 244.0 Hz, J = 15.4 Hz), 145.7 (t, J = 13.1 Hz), 140.1, 132.5, 121.5, 115.2, 99.2–98.9 (m), 95.8 (t, J = 25.8 Hz); HRMS (ESI): m/z [M − H]$^-$ calc. for $C_{12}H_7BrF_2N$ 281.9730, found 281.9725.

3,5-Difluoro-*N*-*o*-tolylbenzenamine (Table 6, entry 4). White solid (178 mg, 81%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23–7.18 (m, 3H), 7.08 (m, 1H), 6.30 (m, 2H), 6.25 (m, 1H), 5.57 (br, 1H), 2.24 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.0 (dd, J = 244.0, 15.6 Hz), 147.6 (t, J = 13.1 Hz), 138.9, 131.5, 131.2, 126.9, 124.6, 122.8, 98.1–97.8 (m), 94.3 (J = 25.9 Hz), 17.8; HRMS (ESI): m/z [M − H]$^-$ calc. for $C_{13}H_{10}F_2N$ 218.0781, found 218.0783.

3,5-Difluoro-*N*-*m*-tolylbenzenamine (Table 6, entry 5). White solid (175 mg, 80%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22 (m, 1H), 6.94–6.88 (m, 3H), 6.48 (m, 2H), 6.28 (tt, J = 8.8, 2.0 Hz, 1H), 5.78 (br, 1H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.9 (dd, J = 243.0, 15.5 Hz), 146.5 (t, J = 13.1 Hz), 140.8, 139.5, 129.3, 124.0, 121.0, 117.3, 98.7–98.5 (m), 95.0 (J = 25.9 Hz), 21.5; HRMS (ESI): m/z [M − H]$^-$ calc. for $C_{13}H_{10}F_2N$ 218.0781, found 218.0777.

3,5-Difluoro-*N*-(2,6-dimethylphenyl)benzeneamine (Table 6, entry 6). White solid (142 mg, 61%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33–7.13 (m, 3H), 6.12 (m, 1H), 5.60 (d, J = 11.2 Hz, 2H), 5.33 (br, 1H), 2.10 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.9 (dd, J = 234.0, 15.8 Hz), 149.6 (t, J = 12.7 Hz), 142.9, 137.5, 129.8, 128.5, 95.4–95.1 (m), 93.2 (t, J = 26.1 Hz), 18.6; HRMS (ESI): m/z [M − H]$^-$ calc. for $C_{14}H_{12}F_2N$ 232.0938, found 232.0927.

***N*-(2-Chlorophenyl)-3,5-difluorobenzenamine (Table 6, entry 7).** White solid (177 mg, 74%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41–7.36 (m, 2H), 7.22 (m, 1H), 6.95 (m, 1H), 6.60 (m, 2H), 6.40 (tt, J = 8.8, 2.0 Hz, 1H), 6.13 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.9 (dd, J = 254.5, 15.1 Hz), 144.8 (t, J = 13.0 Hz), 138.1, 130.1, 127.6, 123.7, 122.7, 118.6, 100.7–100.4 (m), 96.7 (t, J = 25.7 Hz); HRMS (ESI): m/z [M − H]$^-$ calc. for $C_{12}H_7ClF_2N$ 238.0230, found 238.0228.

***N*-(3-Chlorophenyl)-3,5-difluorobenzenamine (Table 6, entry 8).** White solid (194 mg, 81%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 (m, 1H), 7.10 (m, 1H), 6.99 (m, 2H), 6.52 (m, 2H), 6.36 (tt, J = 8.8, 2.0 Hz, 1H), 5.84 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.9 (d, J = 244.0, 15.3 Hz), 145.3 (t, J = 12.8 Hz), 142.4, 135.1, 130.5, 122.6, 119.2, 117.4, 99.7–99.4 (m), 96.2 (t, J = 25.8 Hz). HRMS (ESI): m/z [M − H]$^-$ calc. for $C_{12}H_7ClF_2N$ 238.0230, found 238.0231.

***N*-(2-Bromo-4-methylphenyl)-3,5-difluorobenzenamine (Table 6, entry 9).** White solid (259 mg, 87%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (m, 1H), 7.24 (s, 1H), 7.08 (m, 1H), 6.50 (m, 2H), 6.34 (tt, J = 8.8, 2.0 Hz, 1H), 5.95 (br, 1H), 2.31 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.9 (dd, J = 237.0, 15.4 Hz), 145.8 (t, J = 12.9 Hz), 136.4, 134.0, 133.5, 128.9, 120.3, 115.3, 99.7–99.4 (m), 95.9 (t, J = 25.8 Hz), 20.4; HRMS (ESI): m/z [M − H]$^-$ calc. for $C_{13}H_9BrF_2N$ 295.9881, found 295.9876.

***N*-(2-Bromo-4-fluorophenyl)-3,5-difluorobenzenamine (Table 6, entry 10).** White solid (242 mg, 80%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37–7.30 (m, 2H), 7.02 (m, 1H), 6.46 (m, 2H), 6.37 (tt, J = 9.2, 2.4 Hz, 1H), 5.87 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.9 (dd, J = 244.0, 15.4 Hz), 158.0 (d, J = 245.3 Hz), 145.7 (t, J = 12.8 Hz), 135.6 (d, J = 3.1 Hz), 121.6 (d, J = 8.3 Hz), 120.3 (d, J = 25.2 Hz), 115.9 (d, J = 9.6 Hz), 115.3 (d, J = 22.0 Hz), 99.7–99.4 (m), 96.2 (t, J = 25.8 Hz); HRMS (ESI): m/z [M − H]$^-$ calc. for $C_{12}H_6BrF_3N$ 299.9630, found 299.9632.

***4-tert*-Butyl-*N*-(4-*tert*-butylphenyl)-*N*-(3,5-difluorophenyl)-benzeneamine (Table 6, entry 11).** White solid (161 mg, 41%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (d, J = 8.4 Hz, 4H), 7.07 (d, J = 8.4 Hz, 4H), 6.44 (d, J = 8.6 Hz, 2H), 6.29 (t, J = 8.8 Hz, 1H), 1.33 (s, 18H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.5 (dd, J = 243.0, 15.5 Hz), 150.7 (t, J = 12.8 Hz), 147.4, 143.6, 126.4, 125.4, 102.8–102.5 (m), 95.3 (t, J = 26.0 Hz), 34.4, 31.4; HRMS (ESI): m/z [M − H]$^-$ calc. for $C_{26}H_{28}F_2N$ 392.2190, found 392.2206.

3,5-Difluoro-*N*-phenylbenzenamine (Table 6, entry 12). White solid (174 mg, 85%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (m, 2H), 7.15–7.07 (m, 3H), 6.51 (d, J = 8.4 Hz, 2H), 6.32 (tt, J = 8.8, 2.0 Hz, 1H), 5.84 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.0 (dd, J = 244.0, 15.5 Hz), 140.9 (t, J = 13.0 Hz), 136.9, 129.5, 123.1, 120.3, 98.8–98.5 (m), 95.1 (J = 26.0 Hz); HRMS (ESI): m/z [M − H]$^-$ calc. for $C_{12}H_8F_2N$ 204.0625, found 204.0621.

3,5-Difluoro-*N*-phenylbenzenamine (Table 6, entry 13). White solid (164 mg, 75%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47 (m, 2H), 7.27 (m, 3H), 6.40–6.27 (m, 3H), 3.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.9 (dd, J = 242.1, 15.8 Hz), 151.3 (t, J = 12.9 Hz), 147.4, 129.8, 125.6, 125.3, 98.0–97.7 (m), 93.2 (t, J = 26.1 Hz), 40.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ −110.1; HRMS (ESI): m/z [M + H]$^-$ calc. for $C_{13}H_{12}F_2N$ 220.0938, found 220.0944.

General procedure of amination of 1-chloro-2,4,6-trifluorobenzene

In a typical run, a 4 mL vial was charged with *t*-BuOK (1 mmol) in glove box, and the capped vial was move out of glove box. Aniline (1 mmol), 1-chloro-2,4,6-trifluorobenzene (1 mmol), and toluene (1 mL) were injected into the vial respectively. The mixture was stirred at room temperature for 3 h. The reaction mixture was concentrated under reduced pressure, and the product was purified by flash column chromatography on silica gel (PE/EtOAc = 100 : 1).

***N*-(2-Chloro-3,5-difluorophenyl)-4-methylbenzenamine (Table 7, entry 1).** White solid (205 mg, 81%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 (d, J = 8.0 Hz, 2H), 7.10 (d, J = 7.6 Hz, 2H), 6.59 (dd, J = 10.0, 2.4 Hz, 1H), 6.36 (dt, J = 8.6, 2.4 Hz, 1H), 6.23 (br, 1H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.7 (dd, J = 242.0, 14.9 Hz), 158.9 (dd, J = 245.0, 15.7 Hz), 143.8 (dd, J = 12.5, 4.2 Hz), 136.9, 134.6, 130.2, 123.0, 102.3 (dd, J = 19.0, 6.0 Hz), 96.0 (dd, J = 27.0, 3.9 Hz), 94.3 (dd, J = 27.4, 25.5 Hz), 20.9; HRMS (ESI): m/z [M − H]$^-$ calc. for $C_{13}H_9ClF_2N$ 252.0392, found 252.0390.

4-Chloro-*N*-(2-chloro-3,5-difluorophenyl)benzeneamine (Table 7, entry 2). White solid (238 mg, 87%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (m, 2H), 7.13 (m, 2H), 6.61 (dt, J = 10.8, 2.4 Hz, 1H), 6.41 (tt, J = 8.8, 2.8 Hz, 1H), 6.23 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.7 (dd, J = 250.1, 17.6 Hz), 159.0 (dd, J = 246.3, 15.5 Hz), 142.8 (dd, J = 13.0, 4.2 Hz), 138.3, 129.8, 129.6, 123.4, 103.2 (dd, J = 20.0, 4.0 Hz), 96.7 (dd, J = 27.7, 3.0 Hz), 95.3 (dd, J = 27.0, 25.4 Hz); HRMS (ESI): m/z [M − H]$^-$ calc. for $C_{12}H_6Cl_2F_2N$ 271.9845, found 271.9841.

4-Bromo-*N*-(2-chloro-3,5-difluorophenyl)benzeneamine (Table 7, entry 3). White solid (284 g, 89%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 (m, 2H), 7.08 (m, 2H), 6.63 (dt, J = 10.8, 2.0 Hz, 1H), 6.41 (tt, J = 8.8, 2.8 Hz, 1H), 6.23 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.6 (dd, J = 242.6, 13.3 Hz), 159.0 (dd, J = 246.2, 15.7 Hz), 142.5 (dd, J = 13.0, 4.2 Hz), 138.8, 132.7, 123.5, 117.0, 103.3 (dd, J = 20.3, 4.4 Hz), 96.8 (dd, J = 27.7, 3.1 Hz), 95.4 (dd, J = 27.3, 25.4 Hz). HRMS (ESI): m/z [M − H]$^-$ calc. for $C_{12}H_6BrClF_2N$ 315.9340, found 315.9356.

2-Chloro-*N*-(2-chloro-3,5-difluorophenyl)benzeneamine (Table 7, entry 4). White solid (233 mg, 85%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47–7.39 (m, 2H), 7.30–7.28 (m, 1H), 7.06 (t, J = 7.6 Hz, 1H), 6.72 (d, J = 10.4 Hz, 1H), 6.55 (br, 1H), 6.47 (tt, J = 8.8, 2.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.6 (dd, J = 244.0, 14.3 Hz), 159.0 (dd, J = 246.0, 15.3 Hz), 141.9 (dd, J = 13.0, 2.0 Hz), 136.9, 130.3, 127.6, 125.9, 124.4, 121.1, 104.5 (dd, J = 21.0, 4.0 Hz), 97.7 (dd, J = 27.5, 3.2 Hz), 96.2 (dd, J = 27.1, 25.4 Hz); HRMS (ESI): m/z [M − H]$^-$ calc. for $C_{12}H_6Cl_2F_2N$ 271.9848, found 271.9840.

3-Chloro-*N*-(2-chloro-3,5-difluorophenyl)benzeneamine (Table 7, entry 5). White solid (211 mg, 77%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32–7.28 (m, 1H), 7.12–7.06 (m, 2H), 6.71 (d, J = 10.4 Hz, 1H), 6.44 (tt, J = 8.8, 2.0 Hz, 1H), 6.27 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.6 (dd, J = 258.0 Hz, 14.2 Hz), 159.2 (dd, J = 245.0 Hz, 15.2 Hz), 142.3 (dd, J = 13.0, 4.0 Hz), 141.2, 135.3, 130.7, 124.3, 121.5, 119.6, 103.9 (dd, J = 20.0, 5.0 Hz), 97.3 (dd, J = 27.0, 3.0 Hz), 95.9 (dd, J = 27.7, 25.4 Hz); HRMS (ESI): m/z [M − H]$^-$ calc. for $C_{12}H_6Cl_2F_2N$ 271.9848, found 271.9837.

2-Bromo-*N*-(2-chloro-3,5-difluorophenyl)-4-methylbenzenamine (Table 7, entry 6). White solid (289 mg, 87%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 (s, 1H), 7.27 (d, J = 8.0 Hz, 1H), 7.13 (d, J = 8.0 Hz, 1H), 6.55 (d, J = 10.8 Hz, 1H), 6.41 (m, 2H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.5 (dd, J = 243.0, 14.1 Hz), 159.0 (dd, J = 244.0, 16.1 Hz), 142.7 (dd, J = 13.0, 4.2 Hz), 135.7, 135.3, 133.8, 129.1, 122.7, 117.5, 103.6 (dd, J = 20.0, 5.0 Hz), 96.8 (dd, J = 27.8, 3.0 Hz), 95.4 (dd, J = 27.4, 25.4 Hz), 20.6; HRMS (ESI): m/z [M − H]$^-$ calc. for $C_{13}H_8BrClF_2N$ 329.9497, found 329.9487.

2-Bromo-*N*-(2-chloro-3,5-difluorophenyl)-4-fluorobenzenamine (Table 7, entry 7). White solid (303 mg, 90%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42–7.40 (m, 1H), 7.37–7.34 (m, 1H), 7.08 (dt, J = 7.6, 1.6 Hz, 1H), 6.44 (m, 2H), 6.33 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.6 (dd, J = 243.7, 14.1 Hz), 159.0 (d, J = 246.5 Hz), 159.0 (dd, J = 247.3, 15.7 Hz), 142.6 (dd, J = 13.1, 4.0 Hz), 134.4 (d, J = 3.4 Hz), 124.4 (d, J = 8.4 Hz), 120.6 (d, J = 25.2 Hz), 118.5 (d, J = 9.8 Hz), 115.5 (d, J = 22.2 Hz), 103.7 (dd, J = 18.5, 4.0 Hz), 96.8 (dd, J = 27.7, 3.1 Hz), 95.8 (dd, J = 27.2, 25.4 Hz); HRMS (ESI): m/z [M − H]$^-$ calc. for $C_{12}H_5BrClF_3N$ 333.9246, found 333.9241.

2-Chloro-3,5-difluoro-*N*-phenylbenzenamine (Table 7, entry 8). White solid (208 mg, 87%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (t, J = 7.6 Hz, 2H), 7.21–7.15 (m, 3H), 6.68 (d, J = 10.8 Hz, 1H), 6.39 (tt, J = 10.4, 2.4 Hz, 1H), 6.29 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.7 (dd, J = 244.3, 15.8 Hz), 159.1 (dd, J = 245.6, 15.6 Hz), 143.2 (dd, J = 13.1, 4.1 Hz), 139.7, 129.7, 124.5, 122.3, 102.9 (dd, J = 20.4, 3.8 Hz), 96.5 (dd, J = 27.8, 3.0 Hz), 94.9 (dd, J = 27.5, 25.5 Hz). HRMS (ESI): m/z [M − H]$^-$ calc. for $C_{12}H_7ClF_2N$ 238.0230, found 238.0239.

General procedure of amination of 1,2,4,5-tetrafluorobenzene

In a typical run, a 4 mL vial was charged with *t*-BuOK (1 mmol) in glove box, and the capped vial was move out of glove box. Aniline (1 mmol), 1,2,4,5-tetrafluorobenzene (1 mmol), and toluene (1 mL) were injected into the vial respectively. The mixture was stirred at room temperature for 3 h. The reaction mixture was concentrated under reduced pressure, and the product was purified by flash column chromatography on silica gel (PE/EtOAc = 100 : 1).

***m*-Tolyl-(2,4,5-trifluoro-phenyl)-amine (Table 8, entry 1).** Yellow solid (192 mg, 81%); mp: 50.2–52.4 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 (m, 1H), 7.09 (dt, J = 12.0, 8.0 Hz, 1H), 6.96 (td, J = 10.4, 7.2 Hz, 1H), 6.90–6.84 (m, 3H), 5.62 (s, 1H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.1, 139.6, 129.4, 123.6, 119.8, 116.2, 105.6–105.3 (m), 105.2–104.9 (m), 100.0, 21.5; ^{19}F NMR (376 MHz, $CDCl_3$) −145.9 (d, J = 22.2 Hz), −141.7 (dd, J = 22.2, 12.8 Hz), −134.9 (d, J = 12.8 Hz); HRMS (ESI): m/z [M − H]$^-$ calc. for $C_{13}H_9F_3N$ 236.0687, found: 236.0684.

(4-Chloro-phenyl)-(2,4,5-trifluoro-phenyl)-amine (Table 8, entry 2). Yellow solid (175 mg, 68%); mp: 63.5–65.2 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30–7.26 (m, 2H), 7.05 (dd, J = 9.8, 6.0 Hz, 1H), 7.04–6.99 (m, 2H), 6.97 (dd, J = 8.6, 5.6 Hz, 1H), 5.63 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.9, 129.6, 127.5, 120.1, 105.7 (m), 105.4 (m); ^{19}F NMR (376 MHz, $CDCl_3$) −144.6 (d, J = 22.2 Hz), −141.2 (dd, J = 22.2, 13.5 Hz), −133.9 (d, J = 13.5 Hz); HRMS (ESI): m/z [M − H]$^-$ calc. for $C_{12}H_6ClF_3N$ 256.0141, found: 256.0143.

(2-Bromo-4-methyl-phenyl)-(2,4,5-trifluoro-phenyl)-amine (Table 8, entry 3). Yellow solid (228 mg, 72%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (d, J = 1.0 Hz, 1H), 7.11–6.96 (m, 4H), 5.84 (br, 1H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.8, 133.6, 133.4, 129.0, 118.4, 114.6, 106.5–106.3 (m), 105.6–105.9 (m), 20.4; ^{19}F NMR (376 MHz, $CDCl_3$) −144.0 (m), −141.4 (m), −132.8 (m); HRMS (ESI): m/z [M − H]$^-$ calc. for $C_{13}H_8BrF_3N$ 313.9798, found 317.9792.

(4-Fluoro-phenyl)-(2,4,5-trifluoro-phenyl)-amine (Table 8, entry 4). Orange solid (193 mg, 80%); mp: 53.4–55.2 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.11–7.03 (m, 4H), 7.03–6.97 (m, 1H),

6.96–6.86 (m, 1H), 5.57 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.2, 157.8, 148.3–147.8 (m), 145.9–145.4 (m), 144.2–143.7, 141.5–141.3, 136.9 (d, J = 2.6 Hz), 129.6–129.4, 122.1 (d, J = 8.0 Hz), 116.3 (d, J = 22.5 Hz), 105.4 (m), 104.1 (dd, J = 23.1, 4.0 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) −146.3 (d, J = 22.2 Hz), −141.5 (dd, J = 22.2, 13.5 Hz), −135.6 (d, J = 13.5 Hz), −119.5; HRMS (ESI): m/z [M − H]$^-$ calc. for $C_{12}H_6F_4N$ 240.0442, found 240.0445.

(2-Bromo-4-fluoro-phenyl)-(2,4,5-trifluoro-phenyl)-amine-(Table 8, entry 5). Orange solid (262 mg, 82%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (dd, J = 8.0, 2.9 Hz, 1H), 7.15 (dd, J = 8.80, 5.2 Hz, 1H), 7.05–6.91 (m, 3H), 5.76 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.9 (m), 120.4 (d, J = 25.0 Hz), 119.4 (d, J = 8.0 Hz), 114.9–115.5 (m), 106.1–106.8 (m); ^{19}F NMR (376 MHz, $CDCl_3$) −140.4 (dd, J = 22.2, 13.9 Hz), −139.7 (d, J = 22.2 Hz), −128.7 (d, J = 13.9 Hz), −112.0; HRMS (ESI): m/z [M − H]$^-$ calc. for $C_{12}H_5BrF_4N$ 317.9547, found: 317.9548.

(4-Bromo-phenyl)-(2,4,5-trifluoro-phenyl)-amine (Table 8, entry 6). Orange solid (227 mg, 75%); mp: 65.7–67.2 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43–7.39 (m, 2H), 7.09–6.93 (m, 4H), 5.63 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.5, 132.5, 120.2, 114.7, 105.9 (m), 105.7 (m); ^{19}F NMR (376 MHz, $CDCl_3$) −144.2 (d, J = 22.2 Hz), −141.1 (dd, J = 22.2, 13.2 Hz), −133.6 (d, J = 13.2 Hz); HRMS (ESI): m/z [M − H]$^-$ calc. for $C_{12}H_6BrF_3N$ 299.9636, found 299.9633.

(3-Chloro-phenyl)-(2,4,5-trifluoro-phenyl)-amine (Table 8, entry 7). Orange solid (186 mg, 72%); mp: 57.3–58.9 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 (t, J = 8.0 Hz, 1H), 7.12 (dt, J = 11.6, 7.9 Hz, 1H), 7.05–6.96 (m, 3H), 6.94–6.90 (m, 1H), 5.66 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.9, 135.3, 130.6, 122.2, 118.0, 116.2, 106.6–106.8 (m), 105.7 (m); ^{19}F NMR (376 MHz, $CDCl_3$) −142.4 (d, J = 22.2 Hz), −141.1 (dd, J = 22.2, 13.5 Hz), −131.2 (d, J = 13.5 Hz); HRMS (ESI): m/z [M − H]$^-$ calc. for $C_{12}H_6ClF_3N$ 256.0141, found: 256.0144.

2,4,5-Trifluoro-*N*-phenylbenzenamine (Table 8, entry 8). White solid (158 mg, 71%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 (m, 2H), 7.14–7.07 (m, 3H), 7.05–7.01 (m, 1H), 6.99–6.94 (m, 1H), 5.67 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.7–148.6 (m), 147.9–147.7 (m), 146.4–146.2 (m), 145.5–145.3 (m), 144.2–144.0 (m), 141.8–141.5 (m), 141.1, 129.6, 122.7, 119.1, 105.6–105.4 (m), 105.2–104.9 (m); ^{19}F NMR (376 MHz, $CDCl_3$) −142.6 (d, J = 22.2 Hz), −141.2 (dd, J = 22.2, 13.5 Hz), −132.2 (d, J = 13.5 Hz); HRMS (ESI): m/z [M − H]$^-$ calc. for $C_{12}H_7F_3N$ 222.0531, found: 222.0521.

2,4,5-Trifluoro-*N*-methyl-*N*-phenylbenzenamine (Table 8, entry 9). White solid (98 mg, 41%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 (m, 2H), 7.15–7.01 (m, 2H), 6.90 (m, 1H), 6.78 (d, J = 8.0 Hz, 2H), 3.29 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.0 (m), 152.5 (m), 148.5 (m), 148.1, 148.0 (m), 146.0 (m), 145.5 (m), 132.2 (m), 129.1, 119.4, 116.3 (m), 114.9, 106.5 (m), 39.6 (d, J = 2.2 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) −140.7 (dd, J = 22.2, 13.9 Hz), −137.5 (dd, J = 22.2, 2.6 Hz), −121.4 (dd, J = 13.9, 2.6 Hz); HRMS (ESI): m/z [M + H]$^-$ calc. for $C_{13}H_{11}F_3N$ 238.0844, found: 238.0837.

General procedure of amination of pentafluorobenzene

In a typical run, a 4 mL vial with a stir bar was charged with *t*-BuOK (1 mmol) in glove box, and the capped vial was move out of glove box. Aniline (1 mmol) and toluene (1 mL) were injected into the vial respectively. After the mixture was stirred at 40 °C for 2 h, the vial was cooled to room temperature and then pentafluorobenzene (1 mmol) was injected into the reaction. The resulting mixture was stirred for another 6 h at 40 °C. Then the vial was cooled and the reaction mixture was concentrated under reduced pressure and the residue was purified by flash column chromatography on silica gel (PE/EtOAc = 100 : 1).

Phenyl-(2,3,5,6-tetrafluoro-phenyl)-amine (Table 9, entry 1). Yellow solid (200 mg, 83%); mp: 69.3–71.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (dd, J = 8.4, 7.5 Hz, 2H), 7.02 (t, J = 7.4 Hz, 1H), 6.90 (d, J = 7.5 Hz, 2H), 6.75 (tt, J = 9.9, 7.1 Hz, 1H), 5.67 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.6, 129.1, 122.3, 117.4, 98.4, 98.1; ^{19}F NMR (376 MHz, $CDCl_3$) −150.2 (q, J = 10.1 Hz), −139.8 (q, J = 10.1 Hz); HRMS (ESI): m/z [M − H]$^-$ calc. for $C_{12}H_6F_4N$ 240.0442, found: 240.0437.

3-Bromo-2-(2,3,5,6-tetrafluoro-phenylamino)-benzonitrile (Table 9, entry 2). White solid (314 mg, 91%); mp: 152.3–154.1 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (t, J = 8.2 Hz, 1H), 7.21 (dd, J = 8.0, 0.9 Hz, 1H), 7.00 (tt, J = 9.7, 7.2 Hz, 1H), 6.65 (dt, J = 8.4, 2.2 Hz, 1H), 6.19 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.0, 134.3, 125.6, 124.5, 115.4, 113.1, 102.7–102.3 (m); ^{19}F NMR (376 MHz, $CDCl_3$) δ −146.7 (m), −138.0 (m); HRMS (ESI): m/z [M − H]$^-$ calc. for $C_{13}H_4BrF_4N_2$ 342.9499, found: 42.9489.

(3-Fluoro-phenyl)-(2,3,5,6-tetrafluoro-phenyl)-amine (Table 9, entry 3). White solid (207 mg, 80%); mp: 74.1–76.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 (td, J = 8.2, 6.5 Hz, 1H), 6.82 (ddd, J = 9.9, 7.2, 2.7 Hz, 1H), 6.74–6.63 (m, 2H), 6.56 (d, J = 10.6 Hz, 1H), 5.69 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.5 (d, J = 244.0 Hz), 130.3 (d, J = 10.0 Hz), 112.6 (d, J = 3.0 Hz), 108.8 (d, J = 21.0 Hz), 104.2 (dd, J = 2.0, 1.0 Hz), 99.8–99.3 (m); ^{19}F NMR (376 MHz, $CDCl_3$) δ −149.4 (q, J = 11.3 Hz), −139.2 (q, J = 11.3 Hz), −112.2; HRMS (ESI): m/z [M − H]$^-$ calc. for $C_{12}H_5F_5N$ 258.0348, found: 258.0345.

(4-Fluoro-phenyl)-(2,3,5,6-tetrafluoro-phenyl)-amine (Table 9, entry 4). White solid (231 mg, 89%); mp 75.2–76.1 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.04–6.95 (m, 2H), 6.89 (dd, J = 8.8, 4.5 Hz, 2H), 6.71 (tt, J = 9.9, 7.1 Hz, 1H), 5.61 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.9, 119.8 (d, J = 8.0 Hz), 115.8 (d, J = 23.0 Hz), 98.1–97.6 (m). ^{19}F NMR (376 MHz, $CDCl_3$) δ −151.4 (q, J = 11.7 Hz), −139.7 (q, J = 11.7 Hz), −120.8; HRMS (ESI): m/z [M − H]$^-$ calc. for $C_{12}H_5F_5N$ 258.0348, found: 258.0341.

(3-Chloro-phenyl)-(2,3,5,6-tetrafluoro-phenyl)-amine (Table 9, entry 5). White solid (201 mg, 73%); mp 79.2–80.4 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20 (t, J = 8.1 Hz, 1H), 6.98 (ddd, J = 8.0, 1.9, 0.8 Hz, 1H), 6.87–6.77 (m, 2H), 6.75 (dd, J = 8.1, 1.0 Hz, 1H), 5.66 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.0, 134.9, 130.1, 122.1, 117.0, 115.1, 99.8–99.3; ^{19}F NMR (376 MHz, $CDCl_3$) δ −149.4 (q, J = 11.7 Hz), −139.2 (q, J = 11.7 Hz); HRMS (ESI): m/z [M − H]$^-$ calc. for $C_{12}H_5ClF_4N$ 274.0052, found: 274.0051.

(4-Bromo-phenyl)-(2,3,5,6-tetrafluoro-phenyl)-amine (Table 9, entry 6). White solid (253 mg, 79%); mp 83.6–85.2 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44–7.36 (m, 2H), 6.84–6.72 (m, 3H), 5.64 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.7, 132.0, 114.6, 99.2–98.7 (m); ^{19}F NMR (376 MHz, $CDCl_3$) δ −149.9 (q, J = 11.3

Hz), −139.3 (q, $J = 11.3$ Hz); HRMS (ESI): m/z $[M - H]^-$ calc. for $C_{12}H_5BrF_4N$ 317.9547, found: 317.9556.

(4-Chloro-phenyl)-(2,3,5,6-tetrafluoro-phenyl)-amine (Table 9, entry 7). White solid (204 mg, 74%); 78.3–79.6 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26–7.22 (m, 2H), 6.85–6.80 (m, 2H), 6.77 (ddd, $J = 14.3$, 8.5, 4.9 Hz, 1H), 5.65 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.2, 129.1, 127.3118.6, 99.4–98.6 (m); δ −150.1 (q, $J =$ 11.3 Hz), −139.4 (q, $J = 11.3$ Hz); HRMS (ESI): m/z $[M - H]^-$ calc. for $C_{12}H_5ClF_4N$ 274.0052, found: 274.0053.

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