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# Transition metal- and organophotocatalyst-free perfluoroalkylation reaction of amino(hetero) aromatics initiated by the complex [(TMEDA)I<sub>3</sub>] and visible light†

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Radical initiation for the perfluoroalkylation reaction of amino(hetero)aromatics has been accomplished employing the complex [(TMEDA)I<sub>3</sub>] and visible light. This methodology circumvents the use of metal(organo)catalysts and biologically-relevant substrates are easily substituted with R<sub>F</sub> moieties employing a mild and environmentally benign radical strategy starting from readily-available perfluoroalkyl iodides R<sub>F</sub>I.

## Introduction

Aminoaromatic compounds such as aniline derivatives can be perfluoroalkylated with ease<sup>1,2</sup> by radical reactions due to the electrophilic nature of the fluoroalkyl radical<sup>3,4</sup> and the high electron density of the aromatic ring. Even more so, fluoroalkylation can be attempted under visible light through the homolytic cleavage of the R<sub>F</sub>-I bond upon irradiation (*ca.* 201 kJ mol<sup>-1</sup>, 590 nm), albeit, in poor yields. Reports on visible-light photocatalytic perfluoroalkylations utilizing photoorganocatalysts<sup>4,6</sup> have provided alternative routes to better-yielding perfluoroalkyl-substituted compounds (Scheme 1).

Motivated by the results of Noel and collaborators<sup>5</sup> for the RS-H photosubstitution of cysteine derivatives employing TMEDA, R<sub>F</sub>-I and a transition metal photoorganocatalyst (POC) in MeCN, we replaced our reported strategy for the radical perfluoroalkylation reactions of anilines that employed Cs<sub>2</sub>CO<sub>3</sub>/POC<sup>5</sup> for TMEDA and used a commercial fluorescent light CFL in the absence of organophotocatalyst to attempt the visible-light perfluoroalkylation of amino aromatic compounds in the presence of TMEDA. In this work, we will show that radical initiation can take place from visible light-irradiation of TMEDA/I<sub>2</sub> complex and that organophotocatalysts are not necessary for improved substitution yields.

## Results and discussion

At start of our studies it was not clear the species responsible for the visible-light absorption, in the absence of photoorganocatalyst

POC Rose Bengal<sup>5</sup> (RB), since product formation seemed to improve substantially upon illumination (*cf.* entries 2 & 5, Table 1), and none of the reagents alone (*i.e.*: *n*-C<sub>4</sub>F<sub>9</sub>I, aniline, or TMEDA) showed enough optical density at the irradiation wavelengths.

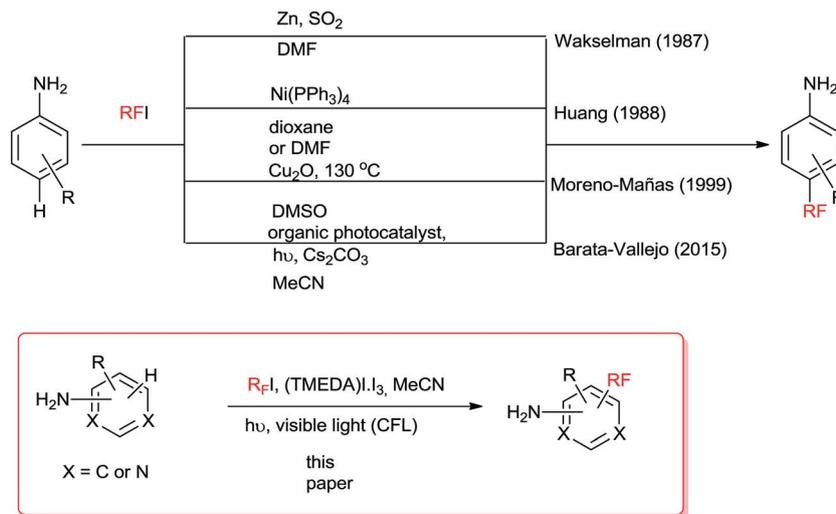
When aniline was subjected to the visible-light irradiation in the presence of *n*-C<sub>4</sub>F<sub>9</sub>I and TMEDA in MeCN as solvent, in the absence of photocatalyst, 62% yield of substitution product was obtained (entry 2, Table 1). By irradiating at 370 nm (with a black fluorescent light lamp), a 64% yield of substitution product was obtained (entry 4, Table 1). The dark reaction (entry 5, Table 1) afforded only 11% yield of product, whereas the absence of TMEDA reduced the yield significantly (entry 6, Table 1).

When we inspected the UV-vis spectrum of the solution mixture of aniline and *n*-C<sub>4</sub>F<sub>9</sub>I to be irradiated at the working concentrations, we noticed an absorption band at λ<sub>max</sub> = 458 nm, corresponding to the absorption of iodine in MeCN (Fig. S1, ESI†), with enough optical density to initiate the radical reaction through the production of iodine atoms.<sup>8,9</sup> Concerned about this absorption, we excluded iodine from the reagent *n*-C<sub>4</sub>F<sub>9</sub>I, passing the neat liquid through a neutral alumina column, and subjected the mixture of aniline, iodine-free *n*-C<sub>4</sub>F<sub>9</sub>I, and TMEDA to the photoreaction under visible-light (CFL) in MeCN as solvent. Under these latter reaction conditions, we obtained only 23% yield of substitution product, indicating that an iodine-containing species is intervening in the initiation process (entry 7, Table 1). However, when we purposely added tetra butyl ammonium iodide (TBAI) and iodine (entry 8, Table 1) to a solution of purified *n*-C<sub>4</sub>F<sub>9</sub>I (I<sub>2</sub>-free), a low yield of substitution product was again obtained (36%), indicating that I<sub>3</sub><sup>-</sup> (λ<sub>max</sub> = 291 nm and 364 nm in MeCN) was not responsible for the photoinitiation. Conducting the irradiation of aniline with a medium pressure Hg lamp (employing

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Scheme 1 Methods for radical perfluoroalkylation of aniline derivatives.

**Table 1** Substitution yields (%) of aniline (0.6 mmol) with  $n\text{-C}_4\text{F}_9\text{I}$  (3 equiv.),  $N,N,N',N'$ -tetramethylethylenediamine (TMEDA) (3 equiv.) under visible light irradiation (65 watt CFL or otherwise noted) in MeCN (3 mL) as solvent, under Ar atmosphere (20 h reaction)

Entry	Product yield (%)	Isomer ratio ( <i>o</i> : <i>p</i> )
1	76 <sup>a</sup>	1 : 1
2	62	0.9 : 1.1
3	— <sup>b</sup>	—
4	64 <sup>c</sup>	0.9 : 1.2
5	11 <sup>d</sup>	1 : 3
6	3 <sup>e</sup>	<sup>h</sup>
7	23 <sup>f</sup>	0.8 : 1.2
8	36 <sup>g,f</sup>	1 : 1.5
9	65 <sup>i</sup>	1 : 1
10	— <sup>e,f,k</sup>	—
11	— <sup>e,f</sup>	—

<sup>a</sup> In the presence of Rose bengal RB, 0.1 equiv. <sup>b</sup>  $\lambda_{\text{irradiation}} = 550\text{--}680\text{ nm}$  ( $\lambda_{\text{max}} = 585\text{ nm}$ ). BDE  $\text{C}_4\text{F}_9\text{I} = 201\text{ kJ mol}^{-1}$  corresponds to  $\lambda_{\text{max}} = 590\text{ nm}$ . <sup>c</sup>  $\lambda_{\text{irradiation}} = 370\text{ nm}$  (black fluorescent light bulb, 40 watt). <sup>d</sup> Dark reaction. <sup>e</sup> In the absence of TMEDA. <sup>f</sup>  $\text{I}_2$  was removed from the reagent  $n\text{-C}_4\text{F}_9\text{I}$  by neutral alumina column chromatography. <sup>g</sup> 0.5 equiv. TBAI + 0.5 equiv.  $\text{I}_2$ . <sup>h</sup> Only para-product observed. <sup>i</sup>  $\text{I}_2$  was thoroughly removed from the reagent  $\text{C}_4\text{F}_9\text{I}$  by neutral alumina column chromatography and then additional 0.5 mM of  $\text{I}_2$  to the reaction mixture was added. <sup>j</sup> 3 equiv of iodine added. <sup>k</sup>  $\lambda_{\text{irradiation}} = 410\text{--}490\text{ nm}$  ( $\lambda_{\text{max}} = 425\text{ nm}$ ).

a  $\text{NaNO}_2/\text{CuSO}_4$  filter for allowing a light band path range of 410–490 nm – where  $\text{I}_2$  absorbs), in the presence of  $\text{I}_2$ -free  $n\text{-C}_4\text{F}_9\text{I}$  and 3 additional equiv. of  $\text{I}_2$  in the absence of TMEDA, no product was obtained (entry 10, Table 1), indicating that iodine alone is not responsible for the initiation. When the same reaction was conducted with  $\text{I}_2$ -free  $n\text{-C}_4\text{F}_9\text{I}$ , 3 additional equiv. of  $\text{I}_2$ , but this time with TMEDA under visible light irradiation (CFL), a 65% yield of substitution product was obtained (entry 9, Table 1).

A complex between TMEDA and  $\text{I}_2$  (*i.e.*:  $[(\text{TMEDA})\text{I}\cdot\text{I}_3]$ ) has been informed by Adam and colleagues,<sup>10</sup> with  $\lambda_{\text{max}} = 360\text{ nm}$  in MeCN, ( $\epsilon = 4 \times 10^4\text{ M}^{-1}\text{ cm}^{-1}$ , a complex formation constant

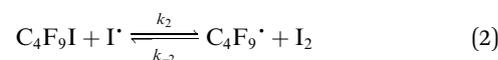
$\text{ca. } 4.7 \times 10^7\text{ M}^{-1}$  and  $E_{\text{CT}} = 4.35\text{ eV}$ ). Due to the traces of  $\text{I}_2$  present in the neat starting  $n\text{-C}_4\text{F}_9\text{I}$ , we deem proper to investigate whether complexation of these trace amounts of  $\text{I}_2$  present in  $n\text{-C}_4\text{F}_9\text{I}$  with TMEDA could trigger the radical initiation process. Fig. S2 and S3,<sup>†</sup> show the UV-vis spectra of mixtures of TMEDA and  $\text{I}_2$ , corroborating the remarkable increase in the absorptivity at 360 nm, responsible for the absorption of light. This charge transfer complex would be responsible, upon visible light absorption ( $\lambda_{\text{max}} = 360\text{ nm}$  from a commercial fluorescent light CFL or  $\lambda_{\text{max}} = 370\text{ nm}$  from a black fluorescent light bulb), of the initiation process, producing excited iodine atoms, as in eqn (1).<sup>9</sup>



$$\lambda_{\text{max}} = 360\text{ nm}$$

$$\epsilon = 46694\text{ M}^{-1}\text{ cm}^{-1}$$

The iodine atoms thus produced (eqn (1)) could then abstract I atoms from perfluoroalkyl (and alkyl) iodides such as  $n\text{-C}_4\text{F}_9\text{I}$ ,<sup>10</sup> thus initiating the chain reaction with the production of  $\text{C}_4\text{F}_9\cdot$  radicals (eqn (2)).



Rate constant  $k_2$  is a very exothermic process with very low activation energy<sup>10</sup> provided abstraction of iodine is carried out by excited iodine atoms,<sup>11–13</sup> which has been demonstrated to be the case when irradiation wavelengths lower than 500 nm (ref. 11) are employed.<sup>14</sup>

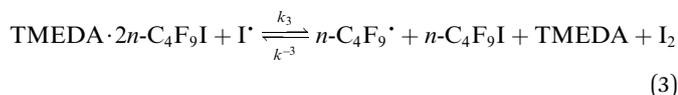
In order to corroborate that the complex  $[(\text{TMEDA})\text{I}\cdot\text{I}_3]$  does produce  $\text{I}^{\cdot}$  atoms upon 370 nm irradiation, we attempted the iodine atom-induced *cis/trans* radical isomerization of oleic fatty acid methyl ester.<sup>16</sup> However, elaidic acid methyl ester was not obtained, indicating that the complex  $[(\text{TMEDA})\text{I}\cdot\text{I}_3]$  does not produce iodine atoms upon irradiation at 370 nm, as in eqn (1), responsible for the *cis/trans* isomerization process.



The dark reaction (TMEDA,  $n\text{-C}_4\text{F}_9\text{I}$  and substrate) excluding iodine, does not yield any substitution product, purporting that also the dark component accounting for product formation (entry 11, Table 1) arises from a thermal ET initiation within the complex  $[(\text{TMEDA})\text{I}\cdot\text{I}_3]$  when present.

UV-vis spectra of mixtures of  $n\text{-C}_4\text{F}_9\text{I}$  and TMEDA do not show a distinct change in absorption or extinction coefficients. The  $\text{TMEDA}\cdot 2\text{-CF}_3\text{I}$  complex has been postulated by Ritter<sup>15,17</sup> and colleagues, based on calculations, X-ray crystallographic analysis, and spectroscopic data ( $^1\text{H}$ ,  $^{19}\text{F}$ ,  $^{13}\text{C}$  NMR). A complex between a nitrogen base and  $\text{R}_\text{F}\text{-I}$  has very recently been postulated to generate  $\text{R}_\text{F}$  radicals upon visible light irradiation.<sup>18–20</sup> We have also observed the same trends for the formation of a complex  $\text{TMEDA}\cdot 2\text{C}_4\text{F}_9\text{I}$  based on NMR data ( $^{19}\text{F}$ ,  $^{13}\text{C}$  NMR), where spectral changes are observed when going from free reagents to the complexed mixture, as indicated in Table S1.†

The  $^{19}\text{F}$  NMR upfield shifts observed in the  $\text{I}\text{-CF}_2\text{-C}_3\text{F}_7$  are indicative of a debilitated  $\text{I}\text{-C}$  bond in  $n\text{-C}_4\text{F}_9\text{I}$  when TMEDA is present, being the largest shift when a stoichiometry of the complex  $\text{TMEDA} : 2\text{C}_4\text{F}_9\text{I}$  is reached (Table S1†). Also, from Table S1,† there seems to be the presence of complexes between perfluoroalkyl iodides and aminoaromatic compounds,<sup>16</sup> the existence of which result in chemical shift changes of the signal from  $\text{ICF}_2\text{-R}_\text{F}$  in the  $^{19}\text{F}$  NMR spectra when  $n\text{-C}_4\text{F}_9\text{I}$  is in the presence of the amino substrate as compared with the innate chemical shift value of  $\text{ICF}_2\text{-R}_\text{F}$  signal, interpreted as halogen bonding to the nitrogen atom of the substrate.<sup>17</sup> The  $\text{-CF}_2\text{I}$  signals in the  $^{19}\text{F}$  NMR spectra of  $n\text{-C}_4\text{F}_9\text{I}$  in mixtures with amino aromatics (2,4,6-triaminopyrimidine, 2,4-dihydroxy-6-methylpyrimidine, 2,4-diamino-6-hydroxypyrimidine, respectively) are reported in Table S1,† where the similar upfield chemical shifts of the  $\text{ICF}_2\text{-R}_\text{F}$  can be observed. Analysis of the data presented in Table S1,† also reveals that the substituent amino group in amino aromatic compounds exerts a more favored halogen-bonding interaction with  $\text{I}\text{-C}_4\text{F}_9$  than the ring-nitrogen does, based on the magnitude of the upfield shifts. Also, this effect is increased when TMEDA is present in the mixture. This is consistent with electron lone pair availability on the nitrogen atom. We therefore could postulate a more facile iodine atom abstraction from  $\text{TMEDA} : 2n\text{-C}_4\text{F}_9\text{I}$  complex, as depicted in eqn (3).



With these reaction conditions in hand, we undertook the perfluoroalkylation reactions of a series of aniline derivatives employing the  $[(\text{TMEDA})\text{I}\cdot\text{I}_3]$  complex (*ca.* 0.25 mM) as initiator. The reaction of 2-anisidine afforded 57% yield of substitution products **1** (4-perfluorobutyl-2-methoxy aniline and 2-perfluorobutyl-2-methoxy aniline, 1 : 5) (Table 2), leading predominantly to the *para* isomer. 2,5-Dimethoxy aniline afforded 63% yield of product **2** (*i.e.*: 4-perfluorobutyl-2,5-dimethoxyaniline). By using other perfluoroalkyl iodides, such as  $\text{I}\text{-(CF}_2)_4\text{-I}$ ,  $\text{I}\text{-(CF}_2)_6\text{-I}$ , and  $n\text{-C}_{10}\text{F}_{21}\text{I}$ , the corresponding

substituted products **3–5** were obtained in 18, 76, and 10% yields, respectively, as indicated in Table 2. 2,3-Dimethylaniline afforded 35% yield of substitution products **6** (*o* : *p* isomer ratio = 1 : 2); whereas the yields for the substituted products derived from 2,3-dimethylaniline with  $n\text{-C}_8\text{F}_{17}\text{I}$ ,  $\text{I}\text{-(CF}_2)_6\text{-I}$ , and  $\text{I}\text{-(CF}_2)_4\text{-I}$ , and  $n\text{-C}_{10}\text{F}_{21}\text{I}$  (*i.e.*: products **6–10**, respectively), are 79, 71, 53, and 6% respectively, as indicated in Table 2. The less activated anilines, *i.e.*: 2,5-difluoroaniline, 2,5-dibromoaniline, 2-chloro-6-methylaniline, and 2,5-dichloroaniline, afforded products **11–14** in 9%, 15%, 15% and 16% yields respectively, as shown in Table 2. The low yields isolated from these products, *i.e.*: **11–14**, are attributed to volatility during the work-up/purification process.

Benzocaine,<sup>4</sup> a local anesthetic, affords 12% yield of the  $\text{C}_4\text{F}_9$  substitution product **15** (Table 2). Starting from 2-mercaptoaniline, under the reaction conditions of Table 2, 2-((perfluorobutyl)thio)aniline **16** is obtained in almost quantitative yield (>95%) in 2 hour reaction.

We have attempted a large scale reaction of 2-anisidine (see Experimental) and obtained a 36% yield of purified **1** (1.474 g), indicating that a scale-up process is applicable with this methodology.

Taking into account the presence of dissolved iodine in commercial  $\text{R}_\text{F}\text{I}$ , the use of TMEDA can aid in the initiation process through the  $[(\text{TMEDA})\text{I}\cdot\text{I}_3]$  complex formation. This is likely the case in many studies<sup>7,21,22</sup> where a combination of  $\text{R}_\text{F}\text{I}$ , TMEDA, and visible light is employed.

The reactions of 2-anisidine in the presence of DBTN (di-*tert*-butylnitroxide, a well-known radical scavenger) as well as in the presence of 1,4-dinitrobenzene afford no substitution products, indicating the presence of radicals. The reaction of 2-anisidine in the presence of *p*-cresol (0.4 equiv.) affords only 20% yield of products **1**.

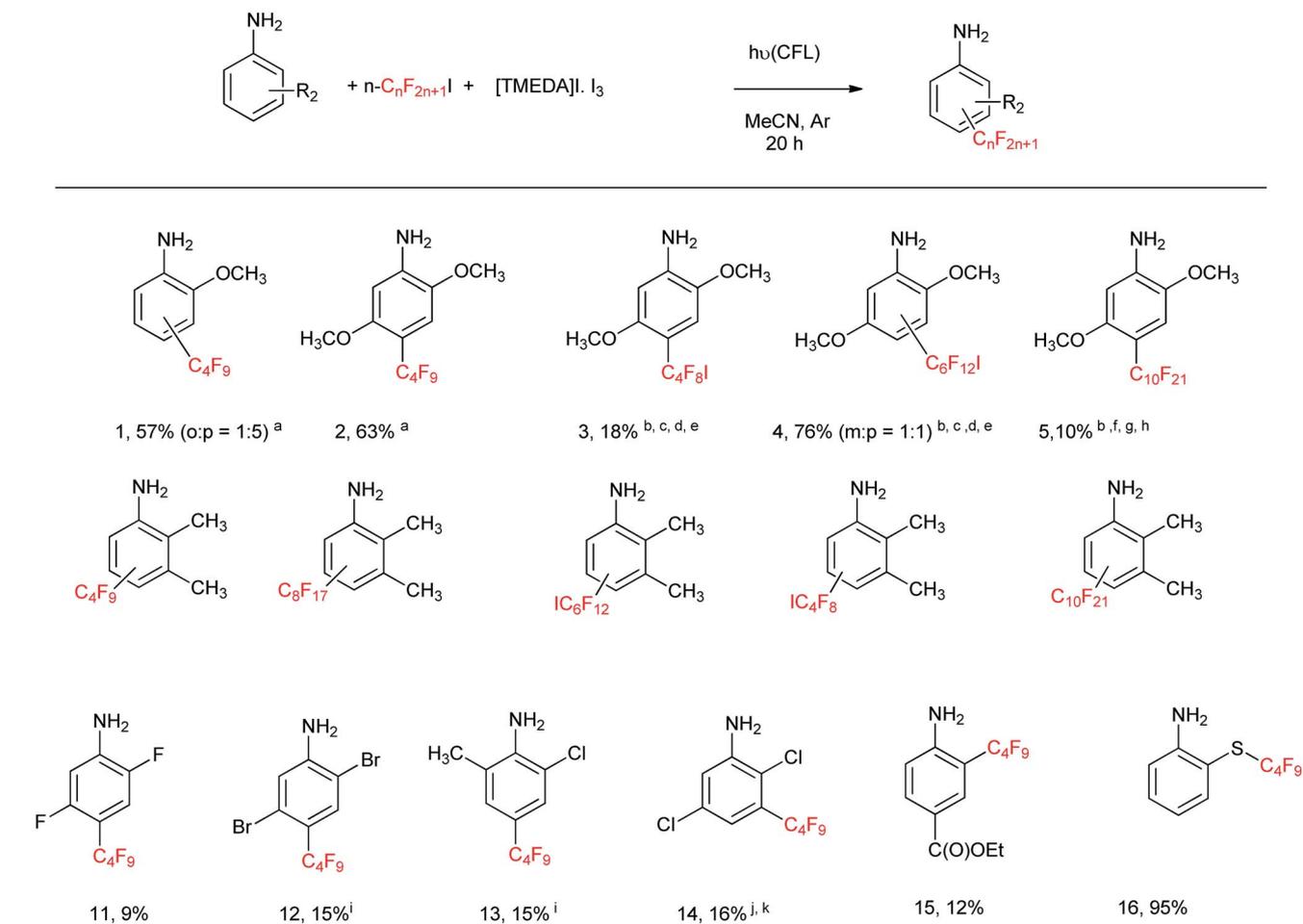
From Table 3, the  $\text{C}_4\text{F}_9$ -substitution yields of a series of aminopyrimidines and aminopyridines is illustrated. 2,4,6-Triaminopyrimidine affords 5-perfluorobutyl-2,4,6-triaminopyrimidine **17** in 48% yield. 2,5-Diamino-6-hydroxy-pyrimidine affords 5-perfluorobutyl-2,4-diamino-6-hydroxypyrimidine **18** in 64% yield. 2-Aminopyridine affords a mixture of 5-perfluorobutyl-2-aminopyridine **19** in 34% yield and 3-perfluorobutyl-2-aminopyridine **20** in 23% yield. 4-Aminopyridine affords 3-perfluorobutyl-4-aminopyridine **21** in 25% yield, whereas 2,3-diaminopyridine affords 4-perfluorobutyl-2,3-diaminopyridine **22** in 12% yield. 5-Methyl-2-aminopyridine and 5-bromo-2-aminopyridine afford 4-perfluorobutyl-5-methyl-2-aminopyridine **23** and 3-perfluorobutyl-5-bromo-2-aminopyridine **24** in 47 and 50% yields, respectively. The low substitution yields encountered for compounds **19–22** is due to volatility, as these products evaporate in the rotary evaporator during the extraction and purification processes.

A large-scale reaction of 5-bromo-2-aminopyridine with  $n\text{-C}_4\text{F}_9\text{I}$  was attempted under the protocol proposed (see Experimental), and a 45% yield of purified product **24** (2.111 g) was isolated.

A proposed reaction mechanism is illustrated in Scheme 2. The complex formed by  $\text{I}_2$  and TMEDA (*i.e.*:  $[(\text{TMEDA})\text{I}\cdot\text{I}_3]$ ), absorbs light from either a commercial fluorescent light bulb



**Table 2** Substitution product yields (%) of aniline derivatives (0.6 mmol) with  $n$ - $C_nF_{2n+1}I$  (3 equiv.), and TMEDA (1.8 mmol)  $[(\text{TMEDA})I \cdot I_3]$  complex ca. 0.25 mM) promoted by visible light irradiation (CFL, 65 watts) in MeCN (3 mL) as solvent, under Ar atmosphere (20 h) or otherwise noted



<sup>a</sup> In the presence of 0.1 equiv. RB. <sup>b</sup> In the presence of  $I_2$  0.55 mM. <sup>c</sup> Aniline derivative 1.8 mmol. <sup>d</sup>  $n$ - $C_nF_{2n+1}I$  0.17 equiv. <sup>e</sup> TMEDA 0.33 equiv. <sup>f</sup> Aniline derivative 0.3 mmol. <sup>g</sup>  $n$ - $C_nF_{2n+1}I$  2 equiv. <sup>h</sup> TMEDA 1 equiv. <sup>i</sup> 72 h-reaction. <sup>j</sup> 96 h-reaction.

CFL, or black light fluorescent bulb,  $\lambda_{\text{max}} = 370$  nm) populating an excited state, which collapses into the excited iodine radicals (and ground state iodine radicals and  $I_2$ ).<sup>11,12</sup> Then, an iodine atom abstraction from  $n$ - $C_4F_9I$  takes place (as in eqn (3)), generating  $n$ - $C_4F_9\cdot$  radicals, which enter the electron-catalyzed cycle (Scheme 2) and substitute the amino-substrate, to generate a radical intermediate such as **B**, which by ET to  $n$ - $C_4F_9I$  produces more  $n$ - $C_4F_9\cdot$  radicals and the final product **C**. Interestingly,  $[(\text{TMEDA})I \cdot I_3]$  complex could be *in situ* regenerated through recombination of two molecules of iodine, one arising from the very decomposition of the complex, the other from  $n$ - $C_4F_9I$  by iodine atom abstraction. This photocatalytic initiation accounts for the increased yield of product upon visible light illumination.

Radical adduct **B** (Scheme 2) acts as a reductant to  $n$ - $C_4F_9I$ , generating  $n$ - $C_4F_9\cdot$  radicals and a cyclohexadienyl-type substituted cation (not shown) which gets deprotonated by TMEDA to afford **C**. To supply more evidence in favor of the mechanism proposed in Scheme 2, we monitored the

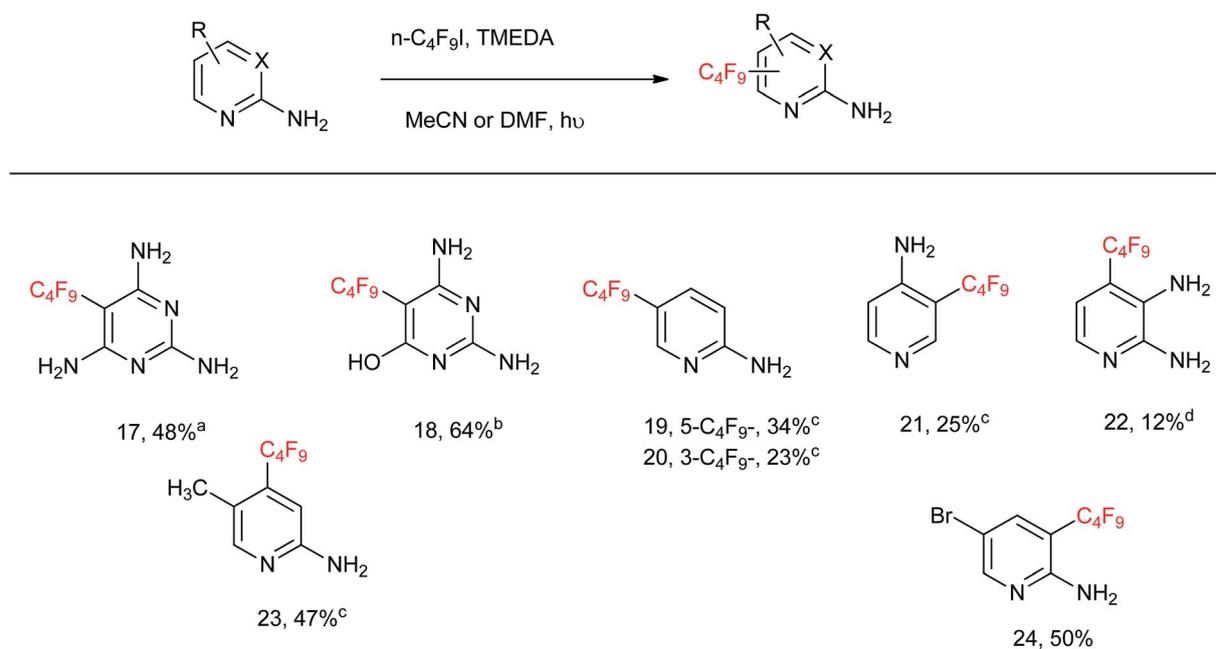
absorbance of the complex  $[(\text{TMEDA})I \cdot I_3]$  through irradiation time, and did not observe any decrease in absorbance, purporting that the complex concentration is not depleted with irradiation time in the presence of  $n$ - $C_4F_9I$  through regeneration of cycles **E** and **F** (Scheme 2).

Alternatively, we could also postulate that vertical excitation of the  $[(\text{TMEDA})I \cdot I_3]$  complex would produce an internal ET giving iodine atom radical  $I\cdot$ , triiodide  $I_3^-$ , and the radical cation of TMEDA, which would promptly deprotonate giving the radical of TMEDA, according to Scheme 3. TMEDA radical **G** could act as an electron reductant to  $n$ - $C_4F_9I$ , generating  $n$ - $C_4F_9\cdot$  radicals and the iminium ion **H** (Scheme 3). We did not observe any product derived from decomposition of TMEDA, through attempts of trapping any carbonyl intermediate with 2,4-dinitrophenylhydrazine/HPLC, indicating that ET from TMEDA radical **G** (Scheme 3) is not a major contributor to product formation.

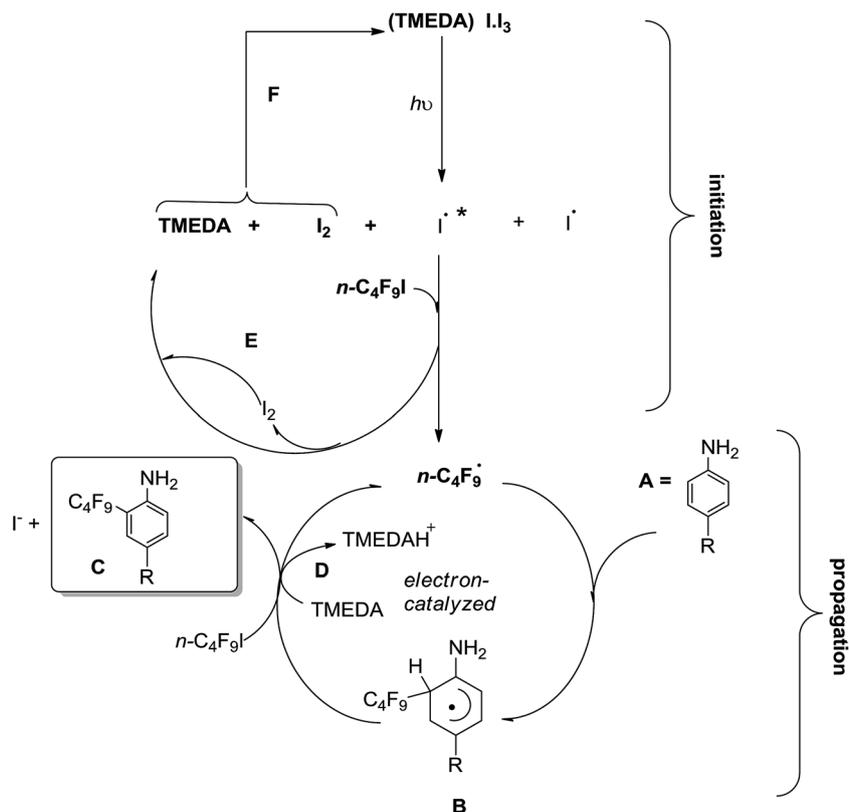
The role of TMEDA is relevant in the complexation with iodine, and the deprotonation (path **D**, Scheme 2). In the



**Table 3** Product yields (%) of amino-substituted heteroaromatics (0.6 mmol) with *n*-C<sub>4</sub>F<sub>9</sub>I (3 equiv.), and TMEDA (1.8 mmol) ((TMEDA)·I<sub>3</sub> complex ca. 0.25 mM) promoted by visible light irradiation (CFL, 65 watts) in MeCN (3 mL) as solvent or otherwise indicated, under Ar atmosphere (20 h)

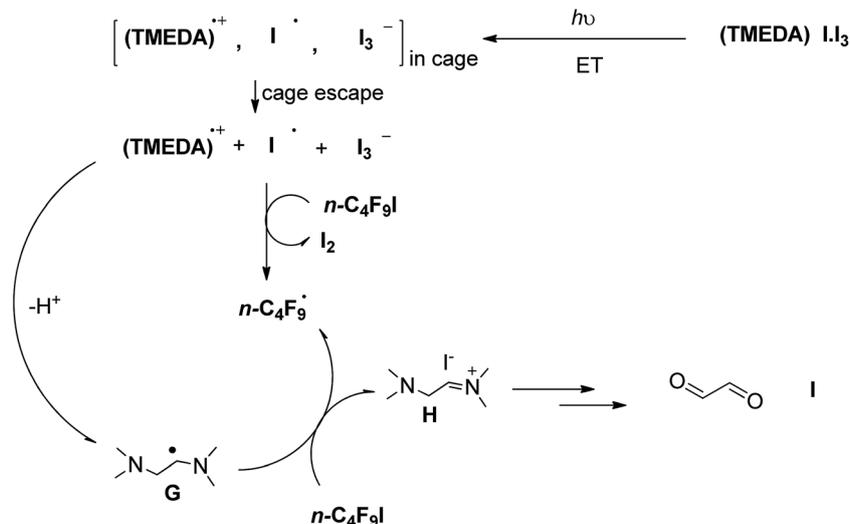


<sup>a</sup> MeOH. <sup>b</sup> Cs<sub>2</sub>CO<sub>3</sub> used instead of TMEDA, and Rose bengal as photocatalyst/DMF. <sup>c</sup> Rose bengal as photocatalyst. <sup>d</sup> MeCN : MeOH 5 : 1.



**Scheme 2** Proposed electron-catalyzed HAS of amino-substrates in the presence of TMEDA.





Scheme 3 Alternative proposed mechanism where the excited complex [(TMEDA)I·I<sub>3</sub>] undergoes inner-sphere ET.

presence of catalyst (POC), Noel and colleagues<sup>23</sup> found that TMEDA acts as an electron donor to the catalyst, involved in a reductive quenching pathway. Being the mechanism still under investigation, a third possibility should be considered: the outer-sphere ET from [(TMEDA)I·I<sub>3</sub>] to *n*-C<sub>4</sub>F<sub>9</sub>I, generating *n*-C<sub>4</sub>F<sub>9</sub> radicals (and iodide anion) in conjunction with the radical cation of TMEDA, which could act as an oxidant to intermediate **B** in Scheme 2 to re-generate thermoneutral TMEDA. Iodine could also intervene in the oxidation of intermediate **B**. These mechanistic alternatives are being studied at the moment.

## Conclusions

A simple and metal-/photoorganocatalyst-free strategy has been presented for the perfluoroalkylation of aminoaromatics employing a complex [(TMEDA)I·I<sub>3</sub>] that upon visible light illumination produces I atoms that generate R<sub>F</sub>· radicals from R<sub>F</sub>-I sources. These R<sub>F</sub>· radicals are capable of substituting biologically-relevant targets such as local anesthetic benzocaine, *etc.* This convenient, high-yielding and metal/photoorganocatalyst-free strategy outperforms traditional near-UV photocatalytic methods while operating under visible light and in the presence of only an additive (TMEDA).

Caution has to be exercised when employing R<sub>F</sub>I and TMEDA, since traces of iodine in the reagents (*i.e.*: R<sub>F</sub>I) can form a stable complex with TMEDA which could be responsible for the radical initiation process upon visible light irradiation. Moreover, given the high extinction coefficient of the complex [(TMEDA)I·I<sub>3</sub>] at the visible light wavelengths (>365 nm), iodine atom production is a key element in the radical process.

## Experimental

### General procedure for the ((TMEDA·I)·I<sub>3</sub>)-initiated reactions

In a 4 mL screw-cap vial provided with a micro stir bar, TMEDA (1.8 mmol, (TMEDA)I·I<sub>3</sub> complex, *ca.* 0.25 mM), substrate

(0.6 mmol, aniline derivative or aminoheteroaromatic compound), or photocatalyst (PC) Rose bengal where needed (0.05 equiv.) and 3 mL of acetonitrile were introduced. The mixture was de-oxygenated with a stream of Ar for 15 min and *n*-C<sub>4</sub>F<sub>9</sub>I or other R<sub>F</sub>I (3 equiv.) was introduced by microliter syringe, and the vial sealed. The closed reaction vessel was placed in front of a 60 watt household fluorescent light bulb (or 20 watt fluorescent black light, λ<sub>max</sub> = 370 nm) and illuminated, under constant vigorous stirring, for 24 h or otherwise noted. After the reaction time was completed, the mixture was extracted thrice with CH<sub>2</sub>Cl<sub>2</sub>/water/brine. The organic layers were gathered and dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, filtered and evaporated under *vacuo*. The crude reaction mixture was purified by silica-gel (60 mesh) column chromatography, with the eluants indicated in the TLC conditions (*vide infra*, spectral data). When a PC was used, the polarity of the dye did not introduce any particular difficulty in the separation and purification protocol, as the several CH<sub>2</sub>Cl<sub>2</sub> extractions eliminated the PC. The eluants employed are referred to in the TLC conditions of each compound.

### Large scale reactions

In a 60 mL Schlenk-type tube 2-anisidine (12 mmol), TMEDA (36 mmol), and a stir bar were placed and a volume of 60 mL of MeCN was introduced by syringe through a septum. The mixture was de-oxygenated with a stream of dry Ar for 30 min, and 36 mmol of *n*-C<sub>4</sub>F<sub>9</sub>I were added to the mixture. The set-up was placed on a stir plate, and vigorously stirred throughout the reaction time. The vessel was placed in front (1 cm) of a 60 watt CFL, and irradiated for 40 hours. The crude reaction mixture was purified by silica-gel (60 mesh) column chromatography, with the eluants indicated in the TLC conditions (*vide infra*, spectral data). The large-scale reaction afforded 36% yield (1.474 g) of combined purified products **1**.

In a 60 mL Schlenk-type tube 5-bromo-2-aminopyridine (12 mmol), TMEDA (36 mmol), and a stir bar were placed. A



volume of 60 mL of MeCN was introduced by 50 mL syringe. The mixture was de-oxygenated with a stream of dry Ar for 30 min, and 36 mmol of *n*-C<sub>4</sub>F<sub>9</sub>I were added to the mixture by syringe through a septum. The set-up was placed on a stir plate, and vigorously stirred throughout the reaction time. The vessel was placed in front (1 cm) of a 60 watt CFL, and irradiated for 40 hours. The crude reaction mixture was purified by silica-gel (60 mesh) column chromatography, with the eluants indicated in the TLC conditions (*vide infra*, spectral data). The large-scale reaction afforded 45% yield (2.111 g) of purified product 24.

### Characterization of compounds

All compounds are unknown chemicals, unless otherwise noted, and are reported as % yields obtained by NMR integration (from <sup>1</sup>H and <sup>19</sup>F NMR integration) of the crude reaction mixtures. Isolated purified masses of compounds are expressed in gram units. Characterizations employ <sup>1</sup>H, <sup>13</sup>C, <sup>19</sup>F 1D-NMR techniques, and 2D NMR spectroscopic techniques (HSQC, HMBC, COSY experiments, and DEPT-135), and HRMS measurements (see ESI<sup>†</sup>).

**2-Methoxy-4-(perfluorobutyl)aniline (1) (ref. 4).** Yellow oil, 95%. Isolated and purified mass obtained: 67 mg. TLC (CH<sub>2</sub>Cl<sub>2</sub>/iso-octane 1 : 1 v/v): *R*<sub>f</sub> = 0.5; <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ: 7.01 (d, *J* = 10 Hz, 1H), 6.92 (s, 1H), 6.73 (d, *J* = 10 Hz, 1H), 4.15 (b s, 2H), 3.90 (s, 3H). <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>) δ: 146.5, 139.7, 120.4 (t, CF<sub>2</sub>), 118.7 (m, CF<sub>2</sub>), 118.1 (t, CF<sub>3</sub>), 116.7 (m), 113.5, 112.5, 109.7, 108.4, 55.6. <sup>19</sup>F NMR (564.603 MHz, CDCl<sub>3</sub>) δ: -81.11 (t, 3F), -109.32 (t, 2F), -122.78 (m, 2F), -125.68 (m, 2F). HRMS-EI+ (*M* + 1): calcd. For C<sub>11</sub>H<sub>9</sub>F<sub>9</sub>NO: 342.05349; found, 342.05388.

**2,5-Dimethoxy-4-(perfluorobutyl)aniline (2).** Yellow oil. Yield = 63%. Isolated and purified mass obtained: 27 mg. TLC (CH<sub>2</sub>Cl<sub>2</sub> : iso-octane 7 : 3 v/v): *R*<sub>f</sub> = 0.69; <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ: 6.82 (s, 1H), 6.35 (s, 1H), 4.15 (b s, 2H), 3.83 (s, 3H), 3.76 (s, 3H). <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>) δ: 154.1, 141.2, 140.6, 116.8 (CF<sub>2</sub>), 110.9, 104.9, 99.8, 56.7, 56.3. <sup>19</sup>F NMR (564.63 MHz, CDCl<sub>3</sub>) δ: -81.00 (t, 3F), -106.20 (t, 2F), -122.25 (m, 2F), -126.06 (m, 2F). HRMS-EI+ (*M* + 1): calcd. For C<sub>12</sub>H<sub>10</sub>F<sub>9</sub>NO<sub>2</sub>: 372.05678; found, 372.05670.

**2,5-Dimethoxy-4-(1,1,2,2,3,3,4,4-octafluoro-4-iodobutyl)aniline (3).** Pale yellow oil. Yield = 18%. Isolated and purified mass obtained: 21 mg. TLC (CH<sub>2</sub>Cl<sub>2</sub> : *n*-hexane 8 : 2 v/v): *R*<sub>f</sub> = 0.62; <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ: 6.82 (s, 1H), 6.35 (s, 1H), 4.13 (b s, 2H), 3.83 (s, 3H), 3.76 (s, 3H). <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>) δ: 154.1, 141.0, 140.6, 111.0, 100.1, 99.9, 56.8, 56.3. <sup>19</sup>F NMR (564.63 MHz, CDCl<sub>3</sub>) δ: -57.55 (t, 2F), -106.07 (t, 2F), -112.78 (m, 2F), -120.43 (m, 2F). HRMS-EI+ (*M* + 1): calcd. For C<sub>12</sub>H<sub>10</sub>F<sub>8</sub>INO<sub>2</sub>: 479.96285; found, 479.96280.

**2,5-Dimethoxy-4-(1,1,2,2,3,3,4,4,5,5,6,6-dodecafluoro-6-iodo-hexyl)aniline (4a).** Pale yellow oil. Yield = 39%. TLC (CH<sub>2</sub>Cl<sub>2</sub> : *n*-hexane 8 : 2 v/v): *R*<sub>f</sub> = 0.52; <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ: 6.85 (s, 1H), 6.14 (s, 1H), 3.99 (b s, 2H), 3.70 (s, 3H), 3.63 (s, 3H). <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>) δ: 152.3, 142.7, 139.9, 112.7, 108.5, 98.1, 56.7, 56.6. <sup>19</sup>F NMR (564.63 MHz, CDCl<sub>3</sub>) δ: -58.70 (t, 2F), -107.16 (t, 2F), -113.07 (m, 2F), -119.97 (m, 2F), -120.88 (m,

2F), -121.74 (m, 2F). HRMS-EI+ (*M* + 1): calcd. For C<sub>14</sub>H<sub>10</sub>F<sub>12</sub>INO<sub>2</sub>: 579.95646; found, 579.95635.

**2,5-Dimethoxy-3-(1,1,2,2,3,3,4,4,5,5,6,6-dodecafluoro-6-iodo-hexyl)aniline (4b).** Pale yellow oil. Yield = 37%. TLC (CH<sub>2</sub>Cl<sub>2</sub> : *n*-hexane 8 : 2 v/v): *R*<sub>f</sub> = 0.55; <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ: 6.45 (s, 1H), 6.31 (s, 1H), 3.99 (b s, 2H), 3.66 (s, 3H), 3.57 (s, 3H). <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>) δ: 153.1, 142.6, 140.6, 112.8, 111.2, 105.3, 56.2, 55.7. <sup>19</sup>F NMR (564.63 MHz, CDCl<sub>3</sub>) δ: -58.39 (t, 2F), -107.16 (t, 2F), -113.07 (m, 2F), -120.13 (m, 2F), -120.88 (m, 2F), -121.48 (m, 2F). HRMS-EI+ (*M* + 1): calcd. For C<sub>14</sub>H<sub>10</sub>F<sub>12</sub>INO<sub>2</sub>: 579.95646; found, 579.95640.

**2,5-Dimethoxy-4-(perfluorodecyl)aniline (5).** Pink solid. Yield = 10%. Isolated and purified mass obtained: 6 mg. TLC (ethyl acetate : *n*-hexane 4 : 6 v/v): *R*<sub>f</sub> = 0.70; <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ: 6.82 (s, 1H), 6.35 (s, 1H), 4.13 (b s, 2H), 3.83 (s, 3H), 3.77 (s, 3H). <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>) δ: 154.1, 141.1, 140.6, 110.9, 102.1, 99.8, 56.8, 56.3. <sup>19</sup>F NMR (564.63 MHz, CDCl<sub>3</sub>) δ: -80.74 (t, 3F), -105.98 (m, 2F), -121.33 (m, 2F), -121.78 (m, 10F), -122.67 (m, 2F), -126.08 (m, 2F). HRMS-EI+ (*M* + 1): calcd. For C<sub>18</sub>H<sub>10</sub>F<sub>21</sub>NO<sub>2</sub>: 672.03762; found, 672.03741.

**2,3-Dimethyl-4-(perfluorobutyl)aniline (6).** Dark amber oil. Yield = 24%. Isolated and purified mass obtained: 30 mg. TLC (CH<sub>2</sub>Cl<sub>2</sub> : iso-octane 7 : 3 v/v): *R*<sub>f</sub> = 0.57; <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ: 7.21 (d, *J* = 8.6 Hz, 1H), 6.61 (d, *J* = 8.6 Hz, 1H), 3.88 (b s, 2H), 2.33 (s, 3H), 2.10 (s, 3H). <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>) δ: 147.6, 137.6, 127.0, 121.9, 117.0, 112.3, 17.0, 13.1. <sup>19</sup>F NMR (564.63 MHz, CDCl<sub>3</sub>) δ: -80.98 (t, 3F), -102.89 (t, 2F), -121.33 (m, 2F), -125.79 (m, 2F). HRMS-EI+ (*M* + 1): calcd. For C<sub>12</sub>H<sub>10</sub>F<sub>9</sub>N 340.06695; found, 340.06690.

**2,3-Dimethyl-4-(perfluorooctyl)aniline (7).** Pale yellow solid. Yield = 58%. Isolated and purified mass obtained: 26 mg. TLC (CH<sub>2</sub>Cl<sub>2</sub> : *n*-hexane 1 : 1 v/v): *R*<sub>f</sub> = 0.67; <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ: 7.21 (d, *J* = 8.6 Hz, 1H), 6.61 (d, *J* = 8.6 Hz, 1H), 3.88 (b s, 2H), 2.33 (s, 3H), 2.10 (s, 3H). <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>) δ: 147.6, 137.7, 127.0, 121.9, 117.2, 112.3, 17.0, 13.1. <sup>19</sup>F NMR (564.63 MHz, CDCl<sub>3</sub>) δ: -80.81 (t, 3F), -102.72 (t, 2F), -120.40 (m, 2F), -121.49 (m, 2F), -121.87 (m, 4F), -122.73 (m, 2F), -126.13 (m, 2F). HRMS-EI+ (*M* + 1): calcd. For C<sub>16</sub>H<sub>10</sub>F<sub>17</sub>N: 540.05418; found, 540.05420.

**2,3-Dimethyl-4-(1,1,2,2,3,3,4,4,5,5,6,6-dodecafluoro-6-iodo-hexyl)aniline (8).** Pale yellow oil. Yield = 54%. Isolated and purified mass obtained: 13 mg. TLC (CH<sub>2</sub>Cl<sub>2</sub> : *n*-hexane 6 : 4 v/v): *R*<sub>f</sub> = 0.66; <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ: 7.21 (d, *J* = 8.6 Hz, 1H), 6.60 (d, *J* = 8.6 Hz, 1H), 3.87 (b s, 2H), 2.33 (s, 3H), 2.10 (s, 3H). <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>) δ: 147.6, 137.7, 127.1, 121.9, 117.3, 112.3, 17.1, 13.1. <sup>19</sup>F NMR (564.63 MHz, CDCl<sub>3</sub>) δ: -58.58 (t, 2F), -102.70 (t, 2F), -112.99 (m, 2F), -120.36 (m, 2F), -120.87 (m, 2F), -121.48 (m, 2F). HRMS-EI+ (*M* + 1): calcd. For C<sub>14</sub>H<sub>10</sub>F<sub>12</sub>IN: 547.96663; found, 547.96651.

**2,3-Dimethyl-4-(1,1,2,2,3,3,4,4-octafluoro-4-iodobutyl)aniline (9).** Yellow oil. Yield = 37%. Isolated and purified mass obtained: 68 mg. TLC (CH<sub>2</sub>Cl<sub>2</sub> : *n*-hexane 8 : 2 v/v): *R*<sub>f</sub> = 0.77; <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ: 7.20 (d, *J* = 8.6 Hz, 1H), 6.60 (d, *J* = 8.6 Hz, 1H), 3.85 (b s, 2H), 2.32 (s, 3H), 2.10 (s, 3H). <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>) δ: 147.6, 137.6, 127.1, 121.8, 117.1, 112.3, 17.0, 13.1. <sup>19</sup>F NMR (564.63 MHz, CDCl<sub>3</sub>) δ: -57.77 (t, 2F),



–102.74 (t, 2F), –112.56 (m, 2F), –119.42 (m, 2F). HRMS-EI+ (M + 1): calcd. For C<sub>12</sub>H<sub>10</sub>F<sub>8</sub>IN: 447.97302; found, 447.96999.

**2,3-Dimethyl-6-(perfluorodecyl)aniline (10a).** White solid. Yield = 2%. TLC (CH<sub>2</sub>Cl<sub>2</sub> : *n*-hexane 1 : 1 v/v): R<sub>f</sub> = 0.88; <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ: 7.10 (d, *J* = 8.0 Hz, 1H), 6.66 (d, *J* = 8.0 Hz, 1H), 3.49 (b s, 2H), 2.31 (s, 3H), 2.09 (s, 3H). <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>) δ: 143.9, 141.2, 125.9, 122.0, 119.6, 109.8, 20.9, 12.6. <sup>19</sup>F NMR (564.63 MHz, CDCl<sub>3</sub>) δ: –59.21 (t, 2F), –81.03 (t, 3F), –113.20 (m, 2F), –121.02 (m, 2F), –121.98 (m, 8F), –122.89 (m, 2F), –126.32 (m, 2F). HRMS-EI+ (M + 1): calcd. For C<sub>18</sub>H<sub>10</sub>F<sub>21</sub>N: 640.04779; found, 640.04771.

**2,3-Dimethyl-4-(perfluorodecyl)aniline (10b).** Pale yellow solid. Yield = 4%. Isolated and purified mass obtained: 4.6 mg. TLC (CH<sub>2</sub>Cl<sub>2</sub> : *n*-hexane 1 : 1 v/v): R<sub>f</sub> = 0.60; <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ: 7.21 (d, *J* = 8.6 Hz, 1H), 6.61 (d, *J* = 8.6 Hz, 1H), 3.88 (b s, 2H), 2.33 (s, 3H), 2.10 (s, 3H). <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>) δ: 147.6, 137.7, 127.1, 121.9, 117.2, 112.3, 17.0, 13.1. <sup>19</sup>F NMR (564.63 MHz, CDCl<sub>3</sub>) δ: –80.73 (t, 3F), –102.69 (t, 2F), –120.37 (m, 2F), –121.79 (m, 10F), –122.67 (m, 2F), –126.08 (m, 2F). HRMS-EI+ (M + 1): calcd. For C<sub>18</sub>H<sub>10</sub>F<sub>21</sub>N: 640.04779; found, 640.04758.

**2,5-Difluoro-4-(perfluorobutyl)aniline (11).** Yellow oil. Yield = 9%. Isolated and purified mass obtained: 2.5 mg. TLC (CH<sub>2</sub>Cl<sub>2</sub> : iso-octane 6 : 4 v/v): R<sub>f</sub> = 0.58; <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ: 7.11 (dd, *J* = 4.6 Hz, *J* = 11 Hz, 1H), 6.53 (dd, *J* = 4.5 Hz, *J* = 11.6 Hz, 1H), 4.20 (b s, 2H). <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>) δ: 156.6, 147.5, 139.9, 115.0 (m), 108.2, 103.8 (dd). <sup>19</sup>F NMR (564.63 MHz, CDCl<sub>3</sub>) δ: –81.01 (t, 3F), –108.30 (m, 2F), –116.62 (td, 1F), –123.00 (m, 2F), –125.93 (m, 2F), –140.51 (d, 1F). HRMS-EI+ (M + 1): calcd. For C<sub>10</sub>H<sub>4</sub>F<sub>11</sub>N 348.01681; found, 348.01690.

**2,5-Dibromo-4-(perfluorobutyl)aniline (12).** Yellow oil. Yield = 15%. Isolated and purified mass obtained: 53.4 mg. TLC (CH<sub>2</sub>Cl<sub>2</sub> : petroleum ether 4 : 6 v/v): R<sub>f</sub> = 0.60; <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ: 7.58 (s, 1H), 7.05 (s, 1H), 4.49 (b s, 2H). <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>) δ: 147.9, 134.2, 120.7, 120.5, 117.6, 106.9. <sup>19</sup>F NMR (564.63 MHz, CDCl<sub>3</sub>) δ: –80.95 (t, 3F), –105.73 (t, 2F), –120.58 (m, 2F), –125.81 (m, 2F). HRMS-EI+ (M + 1): calcd. For C<sub>10</sub>H<sub>4</sub>F<sub>9</sub>Br<sub>2</sub>N: 467.85668; found, 467.85669.

**2-Chloro-6-methyl-4-(perfluorobutyl)aniline (13).** Dark amber oil. Yield = 15%. Isolated and purified mass obtained: 13.7 mg. TLC (CH<sub>2</sub>Cl<sub>2</sub> : iso-octane 4 : 6 v/v): R<sub>f</sub> = 0.56; <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ: 7.36 (s, 1H), 7.15 (s, 1H), 4.36 (b s, 2H), 2.24 (s, 3H). <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>) δ = 144.5, 127.2, 126.0, 123.0, 118.6, 117.9, 18.1. <sup>19</sup>F NMR (564.63 MHz, CDCl<sub>3</sub>) δ: –81.09 (t, 3F), –109.72 (t, 2F), –122.71 (m, 2F), –125.64 (m, 2F). HRMS-EI+ (M + 1): calcd. For C<sub>11</sub>H<sub>7</sub>F<sub>9</sub>ClN: 360.01233; found, 360.01241.

**2,5-Dichloro-3-(perfluorobutyl)aniline (14).** Dark amber oil. Yield = 16%. Isolated and purified mass obtained: 58 mg. TLC (CH<sub>2</sub>Cl<sub>2</sub> : iso-octane 3 : 7 v/v): R<sub>f</sub> = 0.73; <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ: 7.45 (d, *J* = 2.3 Hz, 1H), 7.24 (d, *J* = 2.3 Hz, 1H), 4.75 (b s, 2H). <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>) δ: 142.6, 141.2, 132.9, 127.6, 121.9. <sup>19</sup>F NMR (564.63 MHz, CDCl<sub>3</sub>) δ: –80.89 (t, 3F), –109.07 (t, 2F), –122.49 (m, 2F), –125.78 (m, 2F). HRMS-EI+ (M + 1): calcd. For C<sub>10</sub>H<sub>4</sub>Cl<sub>2</sub>F<sub>9</sub>N: 379.95771; found, 379.95784.

**Ethyl-4-amino-3-(1,1,2,3,3,4,4,4-octafluoro-2-methylbutyl)-benzoate (ref. 4), (15).** White solid, mp 89–90 °C. TLC (CH<sub>2</sub>Cl<sub>2</sub>/iso-octane 1 : 1 v/v): R<sub>f</sub> = 0.6; <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ: 8.03 (d, *J* = 2 Hz, 1H), 7.94 (dd, *J* = 10 Hz, *J* = 5 Hz, 1H), 6.70 (d, *J* = 10 Hz, 1H), 4.66 (b s, 2H), 4.33 (q, *J* = 7 Hz, 2H), 1.37 (t, *J* = 7 Hz, 3H). <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>) δ: 165.6, 149.5, 134.2, 131.6 (t, CF<sub>2</sub>), 119.8, 118.4, 117.4, 116.9, 110.0 (t, CF<sub>2</sub>), 60.8, 14.3. <sup>19</sup>F NMR (564.603 MHz, CDCl<sub>3</sub>) δ: –81.00 (t, 3F), –109.06 (t, 2F), –122.74 (m, 2F), –125.83 (m, 2F). HRMS-EI+ (M + 1): calcd. For C<sub>13</sub>H<sub>11</sub>F<sub>9</sub>NO<sub>2</sub>: 384.06406; found, 384.06535.

**2-((Perfluorobutyl)thio)aniline (16).** Pale yellow oil. Yield > 95%. Isolated and purified mass obtained: 66.2 mg. TLC (CH<sub>2</sub>Cl<sub>2</sub> : iso-octane 1 : 1 v/v): R<sub>f</sub> = 0.63; <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ: 7.47 (d, *J* = 7.8 Hz, 1H), 7.28 (t, *J* = 7.3 Hz, *J* = 8.2 Hz, 1H), 6.77 (d, *J* = 8.2 Hz, 1H), 6.74 (t, *J* = 7.3 Hz, *J* = 7.8 Hz, 1H), 4.45 (b s, 2H). <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>) δ: 151.1, 140.0, 133.4, 118.8, 115.8, 104.5. <sup>19</sup>F NMR (564.63 MHz, CDCl<sub>3</sub>) δ: –81.05 (t, 3F), –87.05 (t, 2F), –120.37 (m, 2F), –125.54 (m, 2F). HRMS-EI+ (M + 1): calcd. For C<sub>10</sub>H<sub>6</sub>F<sub>9</sub>NS: 344.00772; found, 344.00801.

**5-(Perfluorobutyl)pyrimidine-2,4,6-triamine (17).** Pale yellow oil. Yield > 48%. Isolated and purified mass obtained: 56.2 mg. <sup>1</sup>H NMR (600 MHz, DMSO-*d*<sub>6</sub>) δ: –<sup>13</sup>C NMR (151 MHz, DMSO-*d*<sub>6</sub>) δ: 162.4, 162.5. <sup>19</sup>F NMR (564.63 MHz, DMSO-*d*<sub>6</sub>) δ: –80.41 (t, 3F), –101.47 (m, 2F), –122.77 (m, 2F), –125.35 (m, 2F). HRMS-EI+ (M + 1): calcd. For C<sub>8</sub>H<sub>6</sub>F<sub>9</sub>N<sub>5</sub>: 344.04795; found, 344.04799.

**2,6-Diamino-5-(perfluorobutyl)pyrimidin-4-ol (18).** Pale yellow oil. Yield > 64%. Isolated and purified mass obtained: 39.8 mg. <sup>1</sup>H NMR (600 MHz, DMSO-*d*<sub>6</sub>) δ: 5.74 (s). <sup>13</sup>C NMR (151 MHz, DMSO-*d*<sub>6</sub>) δ: 206.5 (C=O from tautomer), 167.3 (from oxo tautomer), 163.1 (from oxo tautomer), 160.6, 160.3, 157.5, 156.3, 155.0 (from oxo tautomer). <sup>19</sup>F NMR (564.63 MHz, DMSO-*d*<sub>6</sub>) δ: –79.10 (t, 3F) (from oxo tautomer), –80.45 (t, 3F), –102.34 (m, 2F) (from oxo tautomer), –111.83 (m, 2F), –121.54 (m, 4F), –122.38 (m, 2F), –125.35 (m, 2F). HRMS-EI+ (M + 1): calcd. For C<sub>8</sub>H<sub>5</sub>F<sub>9</sub>N<sub>4</sub>O: 345.03196; found 345.03205.

**5-(Perfluorobutyl)pyridin-2-amine (19).** Pale yellow oil. Yield > 23%. Isolated and purified mass obtained: 19.8 mg. <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ: 8.26 (s, 1H), 7.56 (1H, d, *J* = 3 Hz), 6.53 (d, 1H, *J* = 3 Hz), 4.86 (broad s, 2H). <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>) δ: 160.6, 147.7, 136.3, 114.8, 107.8. <sup>19</sup>F NMR (564.63 MHz, CDCl<sub>3</sub>) δ: –81.07 (t, 3F), –110.57 (m, 2F), –123.02 (m, 2F), –125.59 (m, 2F). HRMS-EI+ (M + 1): calcd. For C<sub>9</sub>H<sub>5</sub>F<sub>9</sub>N<sub>2</sub>: 313.03090; found 313.03081.

**3-(Perfluorobutyl)pyridin-4-amine (21).** Yield > 25%. Isolated and purified mass obtained: 19.9 mg. <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ: 8.37 (s, 1H), 8.27 (d, 1H, *J* = 3 Hz), 6.57 (d, 1H, *J* = 3 Hz), 4.78 (broad s, 2H). <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>) δ: 152.6, 151.6, 150.2, 150.0, 111.4. <sup>19</sup>F NMR (564.63 MHz, CDCl<sub>3</sub>) δ: –80.96 (t, 3F), –109.48 (broad s, 2F), –123.05 (broad s, 2F), –125.74 (brad s, 2F). HRMS-EI+ (M + 1): calcd. For C<sub>9</sub>H<sub>5</sub>F<sub>9</sub>N<sub>2</sub>: 313.03090; found 313.03099.

**4-(Perfluorobutyl)pyridine-2,3-diamine (22).** Yield > 12%. Isolated and purified mass obtained: 10 mg. <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ: 7.01 (d, 1H, *J* = 2 Hz), 6.94 (d, 1H, *J* = 2 Hz), 4.38 (broad s, 2H), 3.60 (broad s, 2H), 3.82 (s, =NH), 3.75 (s, =NH). <sup>13</sup>C NMR (151 MHz, CDCl<sub>3</sub>) δ: 148.6, 135.6, 132.1, 120.9, 115.1.



$^{19}\text{F}$  NMR (564.63 MHz,  $\text{CDCl}_3$ )  $\delta$ :  $-80.99$  (t, 3F),  $-113.22$  (m, 2F),  $-122.75$  (m, 2F),  $-125.76$  (m, 2F). HRMS-EI+ ( $M + 1$ ): calcd. For  $\text{C}_9\text{H}_6\text{F}_9\text{N}_3$ : 328.04180; found 328.04210.

**5-Methyl-4-(perfluorobutyl)pyridin-2-amine (23).** Yield > 47%. Isolated and purified mass obtained: 51 mg.  $^1\text{H}$  NMR (600 MHz,  $\text{DMSO-d}_6$ )  $\delta$ : 8.07 (s, 1H), 7.47 (s, 1H), 6.07 (broad s, 2H), 3.33 (s, 3H).  $^{13}\text{C}$  NMR (151 MHz,  $\text{DMSO-d}_6$ )  $\delta$ : 154.6, 152.9, 142.3, 137.7, 120.6, 16.4.  $^{19}\text{F}$  NMR (564.63 MHz,  $\text{DMSO-d}_6$ )  $\delta$ :  $-80.5$  (t, 3F),  $-108.86$  (m, 2F),  $-122.23$  (m, 2F),  $-125.34$  (m, 2F). HRMS-EI+ ( $M + 1$ ): calcd. For  $\text{C}_{10}\text{H}_7\text{F}_9\text{N}_2$ : 327.04655; found 327.04669.

**5-Bromo-3-(perfluorobutyl)pyridin-2-amine (24).** Yield > 50%. Isolated and purified mass obtained: 53 mg.  $^1\text{H}$  NMR (600 MHz,  $\text{DMSO-d}_6$ )  $\delta$ : 8.31 (s, 1H), 7.79 (s, H), 6.65 (broad s, 2H).  $^{13}\text{C}$  NMR (151 MHz,  $\text{DMSO-d}_6$ )  $\delta$ : 155.2, 153.3, 139.2, 104.1, 99.5.  $^{19}\text{F}$  NMR (564.63 MHz,  $\text{DMSO-d}_6$ )  $\delta$ :  $-80.49$  (t, 3F),  $-109.39$  (m, 2F),  $-122.21$  (m, 2F),  $-125.27$  (m, 2F). HRMS-EI+ ( $M + 1$ ): calcd. For  $\text{C}_9\text{H}_4\text{BrF}_9\text{N}_2$ : 390.94141; found 390.94151.

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