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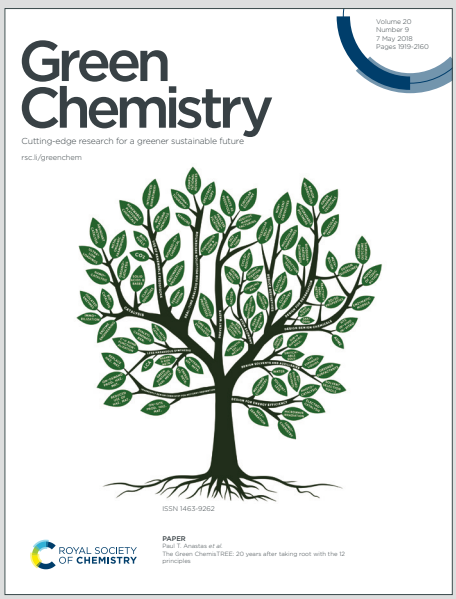

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Bioinspired Photocatalysed C-H Fluoroalkylation of Arenes in Water Promoted by Native Vitamin B_{12} and Rose Bengal

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The first perfluoroalkylation reaction of activated arenes (amino-substituted arenes and alkoxyarenes) has been achieved in water by employing the dyad Rose Bengal and hydrosoluble unmodified vitamin B_{12} (cyanocobalamin) as photocatalyst and co-catalyst, respectively. The reaction is performed under green LEDs irradiation and employs perfluoroalkyl bromides as perfluoroalkyl radical sources. In particular, the presence of vitamin B_{12} co-catalyst is found to be fundamental to elicit the formation of perfluoroalkyl radicals.

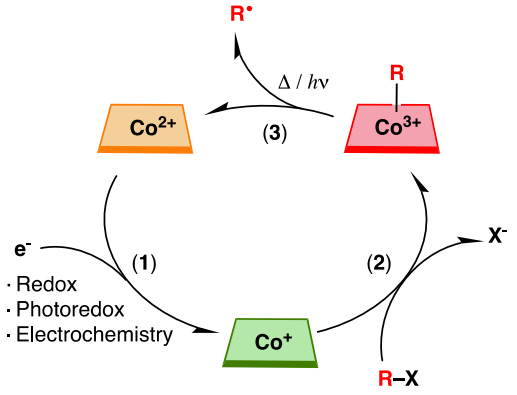
Introduction

New synthetic methodologies towards the synthesis of fluoroalkylated arenes are highly sought-after due to their unique properties, which enable their application in different areas such as medicinal chemistry, agrochemistry and materials science.[1] In this context, radical fluoroakylation reactions triggered by light-mediated catalytic cycles have come to the forefront in the last decade.[2]

As a matter of fact, the versatility of visible-light photoredox catalysis has brought about a myriad of applications in organic synthesis. These reactions are usually carried out under mild conditions and typically mediated by easily available metal-organic complexes or organic dyes that facilitate the conversion of visible light into chemical energy. Furthermore, the use of light sources such as LEDs, can drastically cut the reaction energetic costs. Photoredox catalysis is also quite permissive in terms of the functional group substituents present on the substrate. In addition, the use of water or water mixtures with organic solvents, is another key aspect of green procedures that has been embraced by academia and industry. In this regard, the combined use of light and water can offer new perspectives, enhancing the chemist's arsenal for functionalization reactions which are safe, low-cost, and with low environmental impact.

In modern organocatalysis, activation modes that emulate chemical reactions occurring in nature using low molecular weight organic photocatalysts are highly sought-after strategies. In this regard, catalytic active vitamin derivatives play a substantial role, as these vitamins also function as redox-active cofactors in enzyme catalysis, employing nature´s reactivity principles in laboratory environments.

Cobalt-catalysis[3] provides an environmentally benign and inexpensive alternative to numerous noble metal catalysed transformations. Cobalt complexes are known to catalyse unique reactions mediated by the different oxidation states achievable by the cobalt ion. Besides their application in C-H activation[4] and cross-coupling[5,6] reactions, alkyl radicals can be produced via homolytic cleavage of weak Co-C bonds (typical bond-dissociation energies 80-168 kJ / mol) either by light or heat (Scheme 1).[7,8] The latter exploits the reactivity of the low oxidation state of the cobalt ion – i.e., Co(I), which is known as a supernucleophilic species – with alkyl halides to form an alkyl-cobalt complex (R_{alkyl}-Co(III)). Co(I)-species are easily oxidised



Scheme 1: Alkyl radical formation catalysed by a cobalt complex

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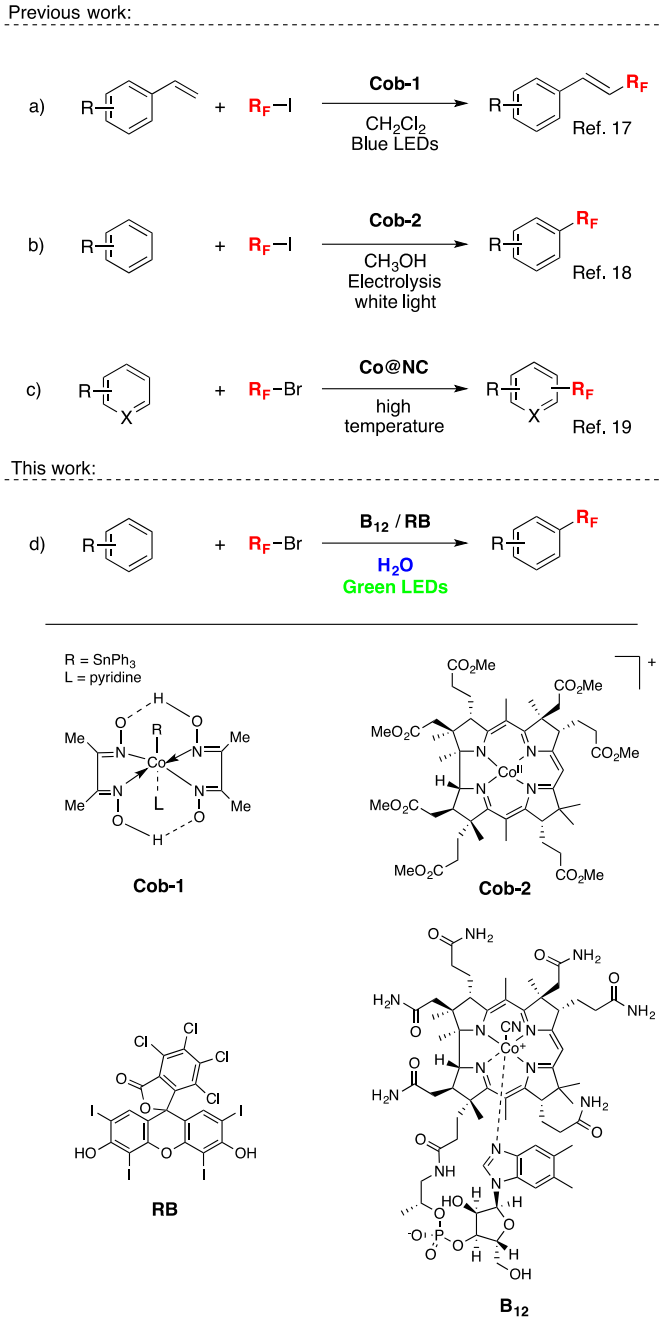
in the presence of oxygen and typically generated in-situ by reduction of a stable Co(II)-species through a chemical, electrochemical or photoredox process.[9,10] Visible light irradiation or heat then induces a homolytic cleavage of the carbon-cobalt σ- bond of the alkyl-cobalt complex to form an alkyl radical and Co(II) species according to the sequence of reactions summarized in Scheme 1. This general reaction mechanism is at the base of the catalytic activity of porphyrin-type and oxime cobalt complexes, along with vitamin B_{12} derivatives.[9]

Vitamin B_{12} is a cobalt coordination complex and one of the very few organometallic molecules present in nature which occurs in several forms called cobalamins. Among the former ones, cyanocobalamin (B12, Scheme 2) is most used in vitamin supplements and pharmaceuticals. Vitamin B_{12} has been well known as a crucial co-enzyme in many biological processes since its first isolation in 1948 and further structure characterization in 1956.[11] Indeed, enzymatic reactions such as dehalogenation, isomerisation, and methyl transfer are mediated by its two active coenzyme forms: methylcobalamin and 5-deoxyadenosylcobalamin and depend on the formation and cleavage of the Co–C bond. Due to its unique redox properties, vitamin B_{12} has inspired the development of different cobalt-containing complexes utilised in organic synthesis as catalysts for Co-mediated reactions.[8]



Scheme 2. Co-catalysed fluoroalkylation reactions

For instance, photoredox dehalogenation reactions employing cobalamin derivatives[12–14] have been reported, as well as cross-coupling reactions of alkyl halides with phenylacetylene and its derivatives catalysed by a cobalamin derivative with $[Ir(dtbbpy)(ppy)_2]PF_6$ as photocatalyst at room temperature.[15] Also the acylation of alkenes employing 2-*S*-pyridyl thioesters as acylating agents can be conducted in the presence of porphyrin-type Co catalysts using blue LEDs irradiation.[16]

However, despite their wide-spread use as catalysts there are only a handful of Co-catalysed fluoroalkylation or fluorination reactions reported in the literature. Tang, Xu, Feng, and collaborators[17] have developed the monofluoroalkylation and the perfluoroalkylation of styrene derivatives employing (triphenyltin)cobaloxime catalyst under blue LEDs irradiation in dichloromethane as a solvent; the reaction gives excellent *E*-stereoselectivity (Scheme 2a). In 2017, Ono, Hisaeda and collaborators[18] have reported the electrochemical perfluoroalkylation of activated arenes and heteroarenes in organic solvents employing a vitamin B12 derivative. The Co(I) species necessary to reduce the perfluoroalkyl iodides R_F-I is prepared *in-situ* by controlled-potential electrolysis of a Co(II)-containing vitamin B_{12} derivative. Critically, the system both necessitates electrochemical and photochemical inductions and uses perfluoroalkyl iodides R_F-I as perfluoroalkylating source (Scheme 2b). In a more recent report, the use of a Co nanocatalyst in a thermally-activated (130 °C) reaction allowed the perfluorohexylation of (hetero)arenes with perfluorohexyl bromide in neat conditions with high excess of substrates in moderate to high yields (Scheme 2c).[19]

On the other hand, electron-rich arenes such as aniline derivatives, have been recently substituted with perfluoroalkyl groups by ruthenium-liganded thermal catalysis,[20] molybdenum catalysis ($Mo(CO)_6$),[21] or copper (Cu_2O) catalysis[22] in organic solvents at very high temperatures. Visible light photocatalysis has been employed in the recent past as a resourceful strategy to achieve the perfluoroalkylation of anilines with Ir(*fac*-(ppy)$_3$ as photocatalyst,[23] ruthenium photocatalysis,[24] or with organic dye Rose Bengal as photocatalyst.[25] However, all these attempts and transformations were carried out in organic solvents in homogeneous or heterogeneous mixtures and employing perfluoroalkyl iodides as fluoroalkylating reagents.

Although there are precedents in the literature of some photocatalytic fluoroalkylation reactions in water,[26] there are no examples of aromatic substitutions with R_F groups by photocatalysis in this medium; furthermore there are no reported examples on the use of native vitamin B_{12} in photocatalysed (fluoro)alkylation reactions of aromatics. Consequently, the exploration of unmodified vitamin B_{12}-photocatalysed substitutions of arenes with fluoroalkyl groups in water can be considered a major improvement for achieving homolytic aromatic substitution reactions with perfluoroalkyl groups.

We herein report the first photocatalysed fluoroalkylation of electron-rich arenes (anilines and alkoxy-substituted benzene rings) with perfluoroalkyl bromides in water employing Rose Bengal as photocatalyst and unmodified vitamin B_{12} (cyanocobalamin) as co-adjuvant catalyst (Scheme 2d). To the best of our knowledge, unmodified vitamin B_{12} has never been reported as a catalyst in (photo)catalytic substitution reactions of aromatics likely due to its poor solubility in organic solvents, nor perfluoroalkyl bromides as perfluoroalkyl radical precursors have ever been employed in photocatalysis.

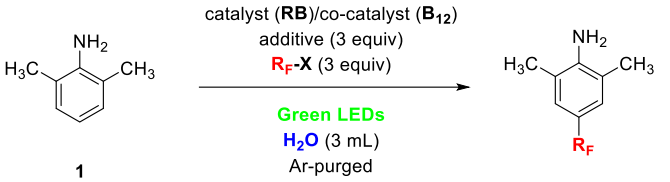
Results and discussion

To start with, we conducted a series of optimization studies employing 2,6-dimethylaniline **1** as model substrate in order to achieve the best reaction conditions (Table 1).

We commenced our investigation with the use of perfluorohexyl bromide *n*-C_6F_{13}-Br as *n*-$C_6F_{13}^{\bullet}$ radical source and the system RB / B12, as catalyst and co-catalyst respectively, for the perfluorohexylation of 2,6-dimethylaniline **1**. Irradiation of an argon-purged water mixture of **1**, RB / B12 and *n*-C_6F_{13}-Br, utilising Cs_2CO_3 as additive/electron donor with high power LEDs (λ = 525 nm, 3 Watts) led to the formation of traces of product **2** both in the presence or absence of co-catalyst B12 (entries 1 and 2, Table 1). Gratifyingly, when the reaction was performed utilising *N,N,N´,N´*-tetramethylethylenediamine (TMEDA) as additive/electron donor, quantitative yields of 4-perfluorohexyl-2,6-dimethylaniline **2** were obtained (entry 3, Table 1). On the other hand, only traces of **2** were formed in the absence of co-catalyst B12 (entry 4, Table 1). In our previous report[25] we had informed the RB-photocatalysed perfluoroalkylation of aniline derivatives in MeCN as solvent utilising Cs_2CO_3 as additive/electron donor. However, TMEDA seemed to act as a better sacrificial donor in this system (cf. with ref. [25]) (entry 3, Table 1), affording quantitative yields of **2**.

The photocatalysed reactions employing other light sources (blue LEDs, λ = 450 nm, or a compact fluorescent lamp, CFL lamp) in the presence of B12 and absence of photocatalyst RB did not result in any product either (Table 1, entries 12 and 13), purporting to the relevance of RB as photocatalyst and B12 as co-catalyst in these perfluoroalkylation reactions. This latter result is very interesting since it rules out the formation of the reduced Co(I) species in the absence of RB as photocatalyst, that would ensue the reduction of R_F-Br.[18]

Table 1. Optimization of reaction conditions. Use of 2,6-dimethylaniline **1** (0.2 mmol) as substrate, perfluorohexyl bromide (3 equiv), under Ar-atmosphere in water (3 mL) as solvent, in the presence of additive (3 equiv), catalyst Rose Bengal (RB, 5 mol%) and co-catalyst B_{12} (cyanocobalamin, 5 mol%). Reaction carried out under green LEDs irradiation with constant stirring for 20 hrs.



1
0.2 mmol

R_F = *n*-C_6F_{13} **(2)**
R_F = *n*-C_8F_{17} **(3)**

Entry	R_F-X	Additive	Catalyst (5 mol %) / Co-catalyst (5 mol %)	Product, yield (%)
1	*n*-C_6F_{13}-Br	Cs_2CO_3	RB / B_{12}	**2**, <5
2	*n*-C_6F_{13}-Br	Cs_2CO_3	RB / -	**2**, <5
3	*n*-C_6F_{13}-Br	TMEDA	RB / B_{12}	**2**, >99
4	*n*-C_6F_{13}-Br	TMEDA	RB / -	**2**, <5
5	*n*-C_6F_{13}-Br	-	- /-	-
6	*n*-C_6F_{13}-Br	TMEDA	- / B_{12}	-
7	*n*-C_6F_{13}-Br	TMEDA	RB / Co (II)[a]	**2**, <5
8	*n*-C_6F_{13}-Br	TMEDA	RB / B_{12}	**2**, >99[b]
9	*n*-C_6F_{13}-Br	TMEDA	RB / B_{12}	**2**, 50[c]
10	*n*-C_6F_{13}-Br	TMEDA	RB / B_{12}	**2**, >99[d]
11	*n*-C_6F_{13}-Br	TMEDA	RB / B_{12}	**2**, >99[e]
12	*n*-C_6F_{13}-Br	TMEDA	- / B_{12}	-[f]
13	*n*-C_6F_{13}-Br	TMEDA	- / B_{12}	-[g]
14	*n*-C_6F_{13}-Br	TMEDA	RB / B_{12}	**2**, >99[h]
15	*n*-C_6F_{13}-Br	TMEDA	RB / B_{12}	**2**, >99[i]
16	*n*-C_6F_{13}-Br	TMEDA	RB / B_{12}	**2**, >99[j]
17	Enflurane[k]	TMEDA	RB / B_{12}	-
18	*n*-C_6F_{13}-I	TMEDA	RB / B_{12}	**2**, 95
19	*n*-C_8F_{17}-Br	TMEDA	RB / B_{12}	**3**, >99
20	*n*-C_8F_{17}-I	TMEDA	RB / B_{12}	**3**, 95

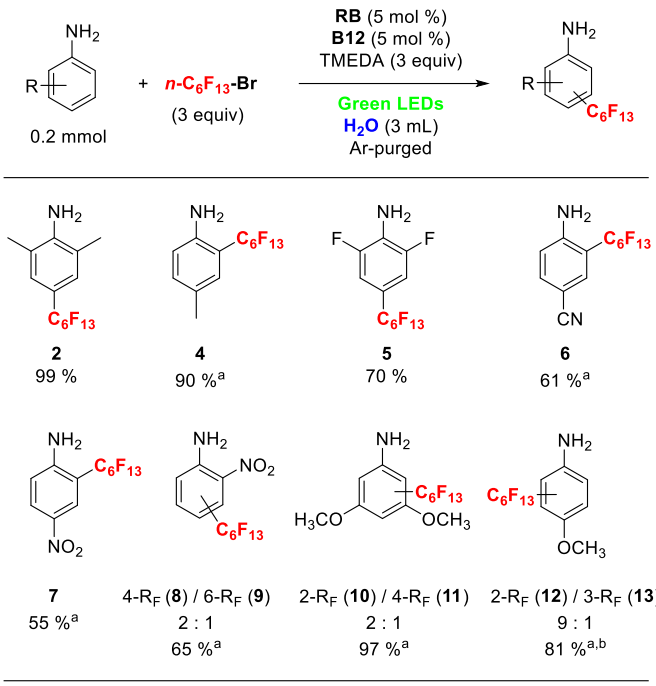
[a] $CoCl_2.6H_2O$ used as Co-catalyst. [b] Without argon purging. [c] Without stirring. [d] The *n*-C_6F_{13}-Br was previously purged with argon (see ESI). [e] Reaction performed in oxygen-saturated solution. [f] Blue LED (λ = 430 nm) as light source. [g] 40 W CFL bulb as light source. [h] Reaction perform in MeCN as reaction solvent. [i] Reaction perform in MeCN: H_2O (1:1) as reaction solvent. [j] The co-photocatalyst used is hydroxycobalamin. [k] Reaction using 2-chloro-1-(difluoromethoxy)-1,1,2-trifluoroethane as pefluoroalkylating reagent.

As expected, the absence of photocatalyst and co-catalyst did not afford product **2** (entries 5 and 6, Table 1). The use of $CoCl_2$ as co-catalyst, did not yield product either (entry 7, Table 1). Surprisingly, the reactions in the presence of air or oxygen-saturated solutions led to product **2** in quantitative yield (entries 8 and 11, Table 1, (the solubility of oxygen in water is 1.34×10^{-3} M at 22 °C).

When hydroxycobalamin (an analogue of vitamin B12 cyanocobalamin) was used as co-catalyst, a quantitative yield of product **2** was obtained (entry 16, Table 1).

Attempts at using 2-chloro-1-(difluoromethoxy)-1,1,2-trifluoroethane as fluoroalkyl chloride in the fluoroalkylation of 2,6-dimethylaniline **1** under the standard reaction conditions

Table 2. Scope of the photocatalysed (RB / B12) perfluorohexylation reaction of anilines (0.2 mmol) in the presence of TMEDA (3 equiv) in Ar-purged water under green LEDs irradiation. Reaction time: 20 hrs under constant stirring at room temperature.



[a] Water : Acetonitrile (1:1) used as solvent. [b] 1 equiv of n-C_6F_{13}-Br

failed, as the corresponding product was not observed (entry 17, table 1), probably due to the much stronger BDE of R_F-Cl as compared to R_F-Br. On the other hand, when employing 1-iodotridecafluorohexane as n-$C_6F_{13}^{\bullet}$ radical source product **2** was obtained in 95% yield (entry 18, Table 1).

Gratifyingly, the reaction also performed well when employing n-C_8F_{17}-Br and n-C_8F_{17}-I as fluoroalkyl radical sources affording excellent yields of 4-perfluorooctyl-2,6-dimethylaniline **3** (entries 19 and 20, Table 1).

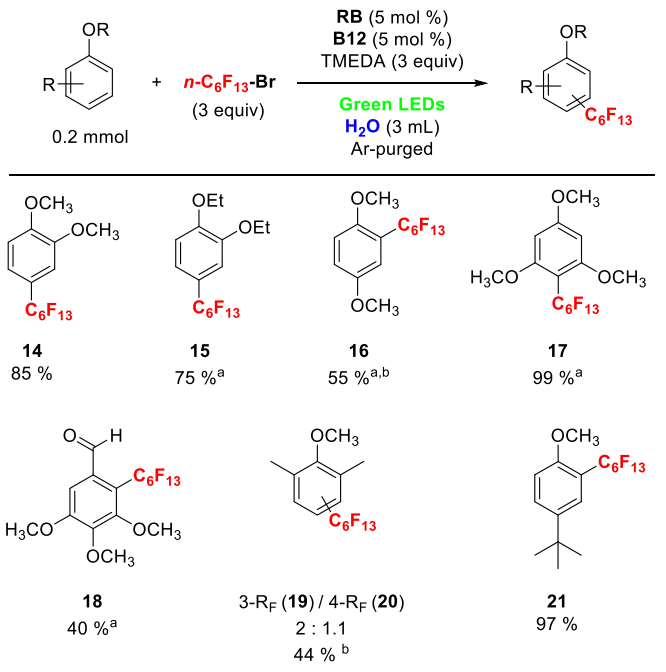
With the optimized reaction conditions in hand, we undertook the fluoroalkylation of aniline derivatives in water photocatalysed by the system Rose Bengal / B12, according to Table 2.

From Table 2, it is observed that under the reaction conditions studied 2,6-dimethylaniline **1** afforded excellent quantitative yields of product **2**. Gratifyingly, 4-methylaniline rendered 90% yield of product **4** (i.e.: 2-perfluorohexyl-4-methyl-aniline). The reactions of 4-methylaniline as well as all other solid substrates were performed in a water : acetonitrile (1:1) solvent mixture in order to solubilize the solid substrates and maximize product yields.

Encouraged by the results obtained for the perfluorohexylation of 2,6-dimethylaniline and 4-methylaniline we deemed proper to test our system employing aniline substrates substituted with electron-withdrawing groups. When 2,6-difluoroaniline was used, a 70% yield of 4-perfluorohexyl-2,6-difluoroaniline **5** was obtained. 4-Aminobenzonitrile afforded a 61% yield of 4-amino-3-(perfluorohexyl)benzonitrile **6**. When 4-nitroaniline was employed as substrate a 55% yield of 2-perfluorohexyl-4-nitroaniline **7** was obtained. 2-Nitroaniline provided a 65% combined product yield of 4-perfluorohexyl-2-nitroaniline **8** and 6-perfluorohexyl-2-nitroaniline **9** in a 2 : 1 ratio. The results obtained with the nitro-substituted anilines represent a major improvement when compared with the protocols available in the literature. For instance, in a previous publication[25] employing n-C_4F_9-I as R_F source, RB as photocatalyst, Cs_2CO_3 as sacrificial donor, in acetonitrile as solvent and upon visible light illumination, 4-nitroaniline failed to react completely and 2-nitroaniline afforded only a 5% yield of 6-perfluorobutyl-2-nitroaniline. This notorious increase in product yields from the 2-nitro- and 4-nitroaniline substrates obtained with the current methodology as opposed to the reactions carried out in acetonitrile as solvent[25] reflects on the relevance of water as reaction medium in the photocatalytic process.

As expected, electron rich 3,5-dimethoxyaniline reacted successfully providing a 97% combined product yield of 2-perfluorohexyl-3,5-dimeyhoxyanilline **10** and 4-perfluorohexyl-3,5-dimethoxyaniline **11** in a 2 : 1 ratio. When 4-methoxyaniline was employed as substrate an 81% combined yield of 2-perfluorohexyl-4-methoxyaniline **12** and 3-perfluorohexyl-4-methoxyaniline **13** was obtained, in a 9 : 1 ratio. [25]. This particular result made us consider the possibility of all-alkoxy - substituted arenes as candidate substrates in the context of this novel reaction system. Encouraged by the results obtained with the aniline derivatives we then undertook the photocatalysed perfluoroalkylation of methoxy-substituted arenes under the optimized reaction conditions, according to Table 3.

Table 3. Scope of the photocatalysed (RB / B12) perfluorohexylation reaction of alcoxy-substituted benzenes (0.2 mmol) in the presence of TMEDA (3 equiv) in argon purged water under green LEDs irradiation. Reaction time: 20 hrs under constant stirring at room temperature.



[a] Water : acetonitrile (1:1) used as solvent. [b] 0.6 mmol of substrate and 1 equiv of n-C_6F_{13}-Br

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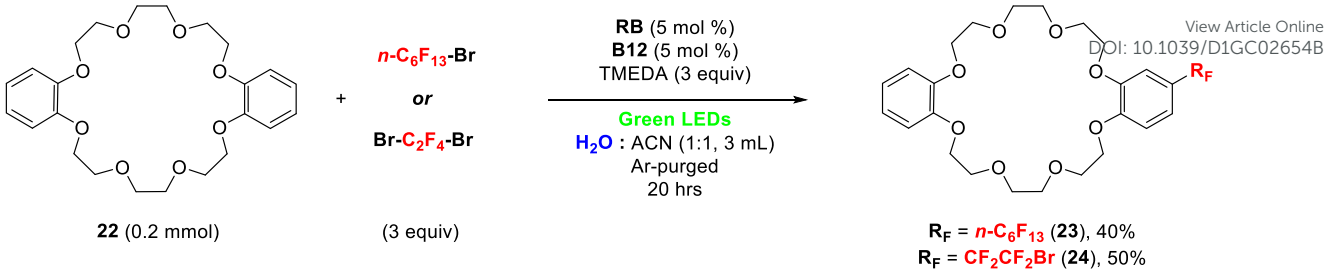


Scheme 3. Late-stage perfluorohexylation of dibenzo-24-crown-8 (**22**)

When 1,2-dimethoxybenzene was used as substrate under the standard reaction conditions (Table 3), an 85% yield of 4-perfluorohexyl-1,2-dimethoxybenzene **14** was obtained. 1,2-Diethoxybenzene afforded 75% yield of 4-perfluorohexyl-1,2-diethoxybenzene **15**. 1,4-Dimethoxybenzene afforded 55% yield of 2-perfluorohexyl-1,4-dimethoxybenzene **16**.

When 1,3,5-trimethoxybenzene was used as substrate under the standard reaction conditions, a 99% yield of 2-perfluorohexyl-1,3,5-trimethoxybenzene **17** was obtained. 3,4,5-Trimethoxybenzaldehyde afforded a 40% yield of 2-perfluorohexyl-3,4,5-trimethoxybenzaldehyde **18**.

2,6-dimethylanisole afforded a 44% combined yield of 3-perfluorohexyl-2,6-dimethylanisole **19** and 4-perfluorohexyl-2,6-dimethylanisole **20** in a 2 : 1.1 ratio. Products **19** and **20** were both identified as a mixture (see ESI).

Under the standard reaction conditions (Table 3), 1,4-dimethoxybenzene and 2,6-dimethylanisole afforded disubstitution products. However, altering the reaction stoichiometry (0.6 mmol of substrate and 1 equivalent of n-C_6F_{13}-Br) only monosubstituted products from 1,4-dimethoxybenzene (product **16**) and 2,6-dimethylanisole (products **19** and **20**) were obtained, thus avoiding disubstitution (entry b, Table 3).

4-*Tert*-butylanisole, according to the reaction conditions, afforded 97% yield of 2-perfluorohexyl-4-tert-butylanisole **21**.

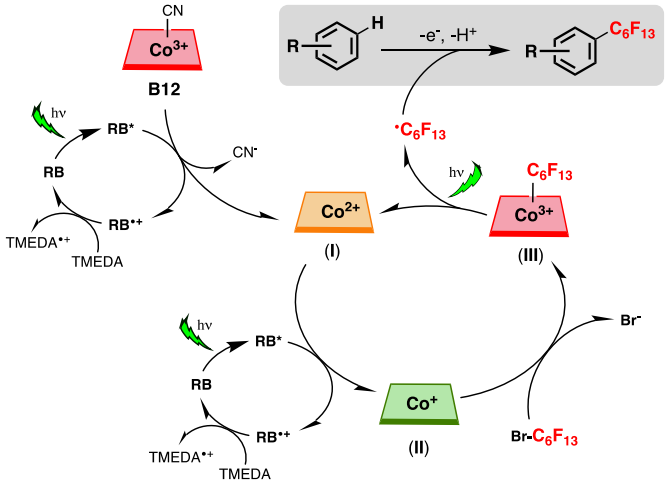
The utility of the methodology described is further highlighted by the late-stage fluoroalkylation of dibenzo-24-crown-8 (**22**), as shown in Scheme 3. These results proved that this photocatalytic system is applicable as a simple and rapid means to access functionalized crown ethers, which represent one of the most exploited class of macrocycles for the development of supramolecular and interlocked architectures.[27] Under optimized reaction conditions and employing *n*-C_6F_{13}-Br as fluoroalkyl radical source, a 40 % yield of the mono-perfluorohexylated dibenzo-24-crown-8 (**23**) was obtained with minimal purification efforts. Gratifyingly, when 1,2-dibromotetrafluoroethane was assessed as fluoroalkyl radical source and under optimized reaction conditions, a 50% yield of mono-2-bromo-1,1-2,2-tetrafluoroethylated dibenzo-24-crown-8 (**24**) was obtained.

In order to estimate the greenness of the photocatalytic methodology in water herein presented, Sheldon's E-Factor (EF)[28] and complete E-Factor (cEF)[29] were both calculated for the perfluorohexylation of 2,6-xylidine (**1**) and compared with those obtained applying an alternative methodology[25] previously published by some of us (see ESI for details). Satisfyingly, an EF of 7.7 and a cEF of 83.4 were obtained applying the methodology reported in this work as opposed to an EF of 20.1 and a cEF of 290.0 calculated for the previously reported protocol[25] in acetonitrile as solvent.

To throw some light into the reaction mechanism a radical inhibition experiment with TEMPO (2,2,6,6-tetramethyl-1-piperidinyloxy), a well-known radical scavenger, was performed. Under standard conditions employing **1** as substrate in the presence of TEMPO (3 equiv), product **2** formation was completely suppressed and a TEMPO-C_6F_{13} adduct was detected by ^{19}F-NMR (see ESI for details). This result strongly supports the operation of a radical pathway in the reaction mechanism and demonstrates the presence of *n*-$C_6F_{13}^{\bullet}$ radicals in the catalytic cycle.

We also undertook steady-state UV-vis absorption spectra studies of aqueous solutions containing Rose Bengal, B12 and TMEDA before and after green LEDs irradiation under Ar atmosphere. It was pleasing to observe that upon irradiation the characteristic absorption bands of B12 disappeared along with appearance of distinctive cob(I)alamin bands[30] (see ESI for details).

According to the investigations performed and the information available in the literature,[8,31] a plausible reaction mechanism is proposed in Scheme 4. Initially, B12 undergoes one electron reduction promoted by a RB oxidative photocatalytic cycle affording, upon cyanide loss, cob(II)alamin (**I**, Scheme 4); this one-electron reduction process has been extensively studied by means of pulse radiolysis techniques in aqueous solutions by Blackburn and collaborators.[30] The aforementioned proposal is also in agreement with the results obtained from the fluorescence quenching of RB upon addition



Scheme 4. Proposed reaction mechanism

of B12; a Stern–Volmer quenching rate constant of 1.77 x 10^4 M^{-1} was obtained which indeed confirms the ET step under our reaction conditions (see ESI for details). Also, as observed from Table 1 (entries 12 and 13) the photocatalysed reactions employing R_F-Br as fluoroalkylating agent in the presence of B12 and absence of photocatalyst RB did not render any product, indicating that no reduced Co(I) species can be formed in the absence of RB as photocatalyst, supporting the RB-oxidative electron transfer to Co species.[18]

The reaction pathway continues with further reduction of cob(II)alamin[30] (**I**, Scheme 4) by an additional RB oxidative photocatalytic cycle to afford cob(I)alamin (**II**, Scheme 4) that rapidly reacts with *n*-C_6F_{13}Br providing the Co(III)-C_6F_{13} complex (**III**, Scheme 4) and a bromide anion. The Co(III)-C_6F_{13} complex (**III**, Scheme 4) upon light irradiation[18] releases a *n*-$C_6F_{13}^{\bullet}$ radical and regenerates the cob(II)alamin (**I**, Scheme 4), completing the cobalt mediated co-catalytic cycle. The *n*-$C_6F_{13}^{\bullet}$ radical formed reacts with the arene via a homolytic aromatic substitution mechanism[25] affording the perfluorohexylated reaction product. Part of the reaction success is due to the excellent stability of RB in the reaction media, allowing the electron transfer process from the electron donor TMEDA to the ultimate electron acceptor *n*-C_6F_{13}Br with the aid of B12. This whole electron transfer process can be understood as a simplified biomimetic model of long-range electron transfer within vitamin B12-dependent reductive dehalogenases, which serve as terminal reductases in organohalide-respiring bacteria.[32]

Conclusions

The methodology described in this paper enables fluoroalkylation reactions in water of electron rich arenes by the dyad RB / B12 as catalyst and co-catalyst, respectively. The use of B12 is amply justified to produce fluoroalkyl radicals from perfluoroalkyl bromides, since in its absence, the reaction does not render any product. The role of RB catalyst in the perfluoroalkylation of electron-rich arenes in water with perfluoroalkyl bromides is to produce the super-nucleophilic Co(I) species that effects the very reduction of perfluoroalkyl bromides to perfluoroalkyl radicals, in oxidative photoredox cycles. The method is shown to be superior to other reported photocatalytic perfluoroalkylation strategies when employing substrates with electron-attracting groups such as nitro, where moderate-to-good yields of perfluoroalkylated products are obtained. This methodology allowed the synthesis and characterization of 15 new fluorinated products. In summary, we have developed the first photocatalysed fluoroalkylation reaction of arenes in a heterogeneous water system, that employs perfluoroalkyl bromides as fluoroalkyl radical precursors. Native non-modified vitamin B12 has been employed for the first time in fluoroalkylation reactions, as an activation mode that emulates Nature's biological chemistry.

Author contributions

DEY performed the experiments. AP, MB and SBV wrote the paper. All authors participated in conceptualization, analysed the data, discussed the results, and commented on the manuscript.

Conflicts of interest

There are no conflicts to declare.

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