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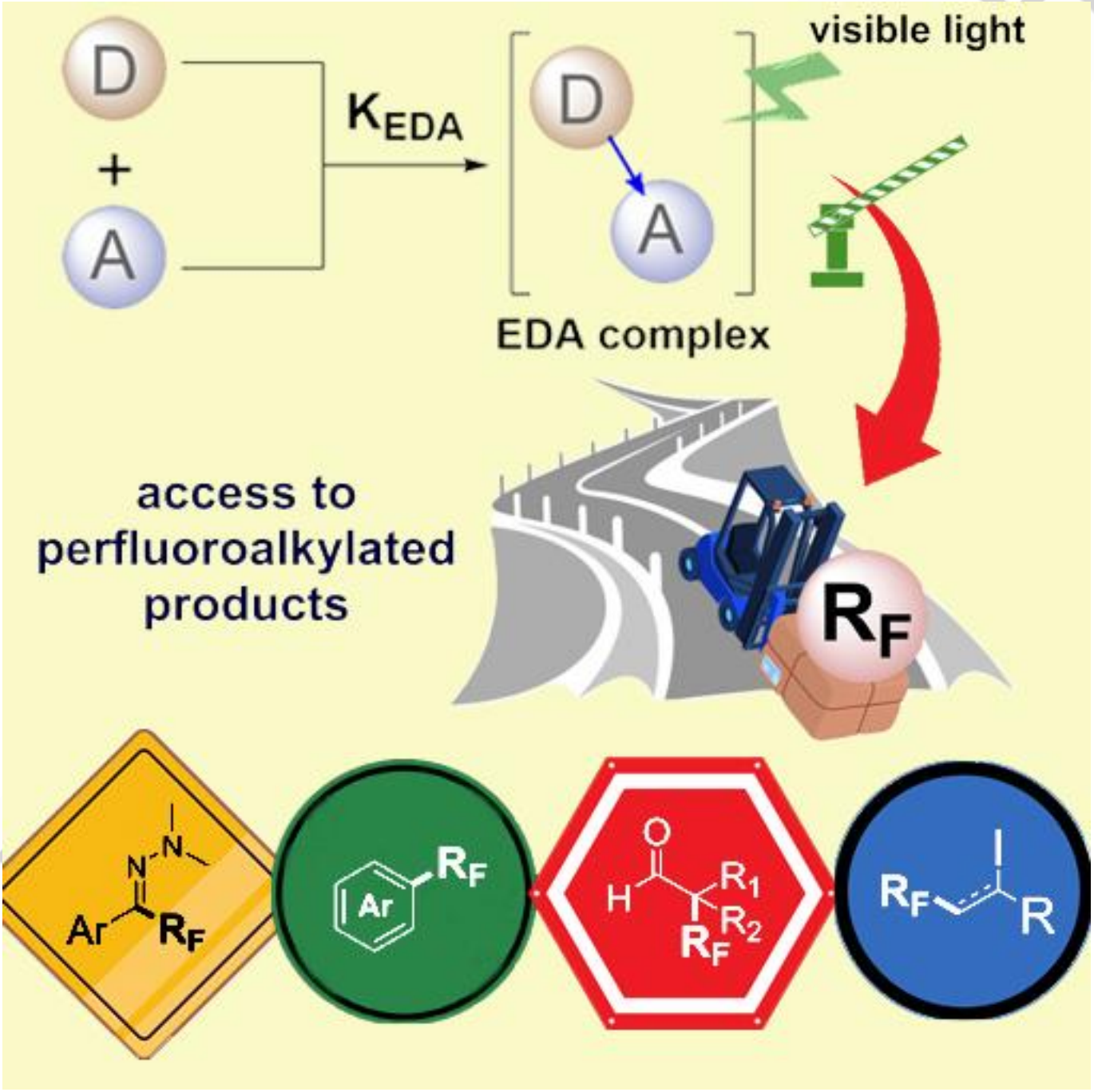
REVIEW

Perfluoroalkylation Reactions by Electron Donor-Acceptor Complexes: Recent Advances

Damian E. Yerien,[a] Sebastian Barata-Vallejo*[a,b] and Al Postigo*[a]



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REVIEW

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Abstract: This Perspective analyses the perfluoroalkylation reactions by electron donor-acceptor (EDA) complexes since 2018, while summarizes, in Tables 1-3, the vast majority of representative perfluoroalkylation reactions of various classes of organic compounds by EDA complexes and halogen-bonding interactions. Numerous intriguing reaction methodologies and valuable synthetic instances have emerged. We aim to delve into these new examples comprehensively, while also contemplating the future directions in the field. Subsequent sections will elaborate on the perfluoroalkylation of (hetero)aromatic compounds, carbon-carbon multiple bonds, perfluoroalkylation of carbonyl compounds, and perfluoroalkylation of isocyanides, covering their synthetic scope and mechanistic insights.

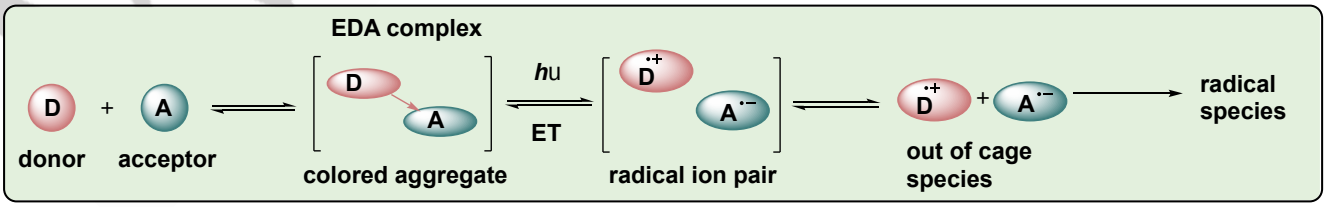
1. Introduction

Electron donor-acceptor complexes (EDA complexes) are identified by weak absorption bands in the UV/Vis spectrum or by a change in color when mixing two colorless reagents. Some of these complexes have been proposed to initiate organic transformations when exposed to visible light or through thermal activation. While detailed mechanistic understanding is lacking, they often exhibit charge transfer characteristics and similar spectral properties. Lima, Jürberg, and Paixao[1] recently revisited the photophysical properties and synthetic applications of high-energy-excited EDA complexes, along with some visible light-activated EDA complexes. Their discussion includes theories of Electron Transfer (ET), considerations of kinetics and thermodynamics, fluorescence quenching, solvent effects, and molecular orbital descriptions of EDA complexes. These complexes essentially arise from the interaction of electron deficient and electron rich partners, which interplay in the ground state as association complexes, which can be excited either by light or thermally, eliciting radical species.

Despite studies of the photophysics of EDA complexes since the 1950s,[2] applications in organic synthetic chemistry are recent, probably due to synthetically unproductive back electron transfer (BET)[3] events that take place upon excitation of the complex. This could, in part, be avoided by providing one of the partners with a leaving group, capable of competing with BET.

Excellent review articles[4–8] on different EDA complexes explain the general molecular orbital comparison between direct photo- excitation and the excitation of an EDA complex.[7,9] Sulfonium salts (as prospective thiophene leaving groups),[9,10] have been employed as suitable acceptors in EDA complexes, supplying radicals in most effective ways, a feature which has recently been recognized. *N*-alkoxyphthalimides,[11] maleimides,[12] or hypervalent iodine reagents,[13] have also been introduced as suppliers of radical species upon association with properly electron configured partners and ulterior visible light excitation.

In the case of organic halides (a special class of EDA complex or halogen bonding complex, XB complexes),[14–18] the generation of radicals takes place according to a mechanism such as that shown in Scheme 1.[19,20]



Scheme 1. EDA-complex-driven photoinitiation: **A** = acceptor, **D** = donor

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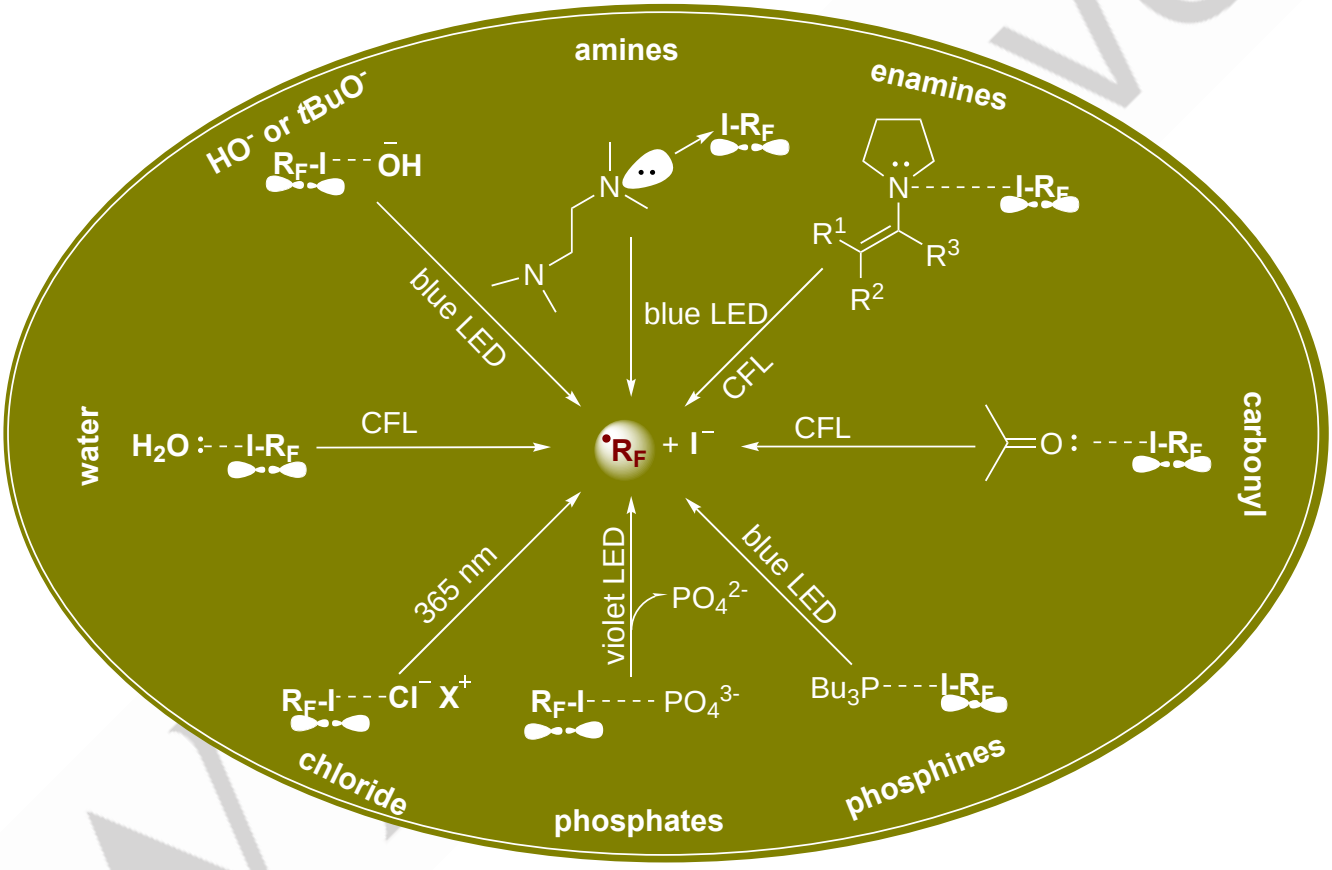
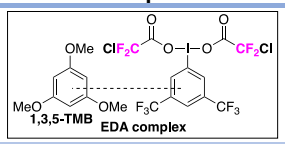
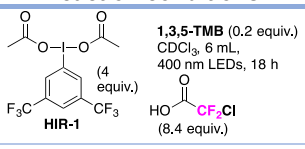
Perfluoroalkyl iodides,[21,22] denoted as R_F-I and known for their profound σ-hole, engage in the formation of EDA complexes[23] with Lewis bases (LB) through halogen bonding (XB).[24,25] Upon exposure to visible light, this interaction triggers an electron transfer (SET) process from the electron pair of the Lewis base to the σ* antibonding orbital of R_F-I, resulting in the generation of corresponding R_F radicals. Various small organic molecules or ionic species such as *NH*-heterocycles,[26,27] amines,[28,29] enamines,[30] carbonyl compounds,[31,32] phosphines,[33–36] phosphates,[37] phenols,[38] hydroquinones,[38] chloride ions,[39]or even water[40,41] can act as organic catalysts, forming EDA complexes with perfluoroalkyl iodides.[42–44] R_F-I bonds can also be activated by bases like K*t*OBu and HO^-, which efficiently produce R_F radicals under illumination.[1] Scheme 2 provides a selected summary of the EDA complexes reported with R_F-I for efficient generation of R_F radicals.

Since our last review article on electron donor-acceptor complexes in perfluoroalkylation reactions in 2018,[45] many interesting reaction protocols and useful synthetic examples have been published. In this Perspective we wish to discuss such examples in detail and envisage the future directions in the field. In the next sections, the perfluoroalkylation of (hetero)aromatic compounds, perfluoroalkylation of carbon-carbon multiple bonds, perfluoroalkylation of carbonyl compounds, and the perfluoroalkylation of isocyanides will be discussed in terms of synthetic scope and mechanistic aspects. In Tables 1-3, those examples treated in this Perspective as well as all other known examples we have knowledge of perfluoroalkylation reactions of organic compounds by EDA complexes are reported.



Scheme 2. Selected EDA complexes documented in the literature that result in the generation of R_F radicals from perfluoroalkyl iodides R_F-I. CFL: Compact fluorescent light. Adapted with permission from *ACS Catal*. **2023**, *13*, 7756−7794. Copyright 2023 American Chemical Society.

Table 1. Perfluoroalkylation reactions of (hetero)aromatic compounds by EDA complexes

Entry	Substrate	Complex	Reaction conditions	Product	Ref.
1					[13]

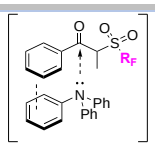
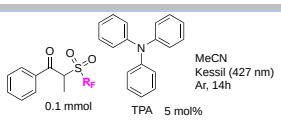
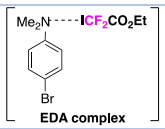
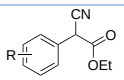
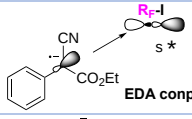
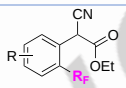
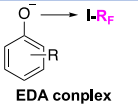
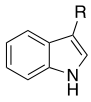
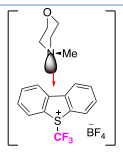
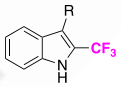
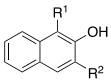
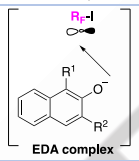
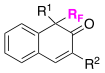
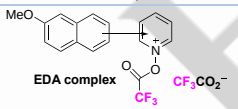
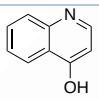
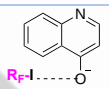
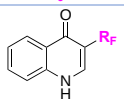
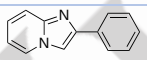
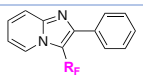
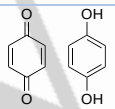
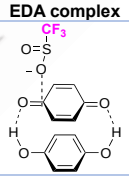
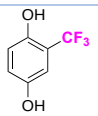
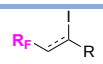
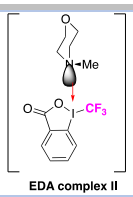
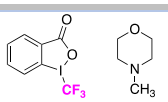
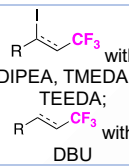
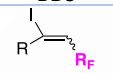
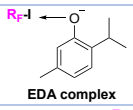
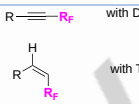
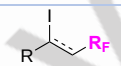
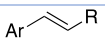
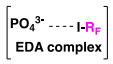
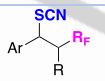
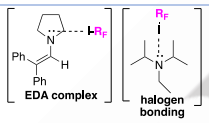
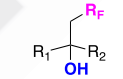
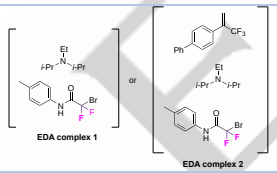
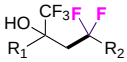
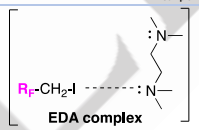
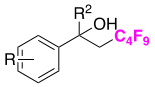
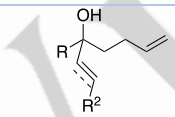
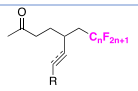
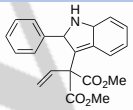
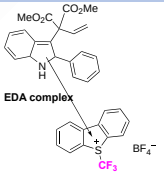
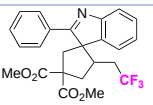
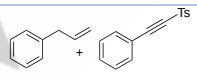
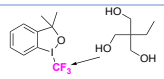
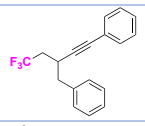
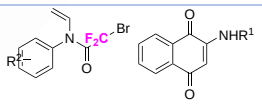
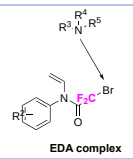
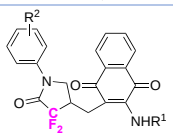
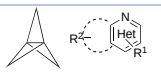
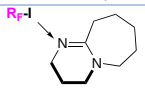
2					[46]
3		**EDA complex**	R_FI (3 equiv.) **KOH** (1.5 equiv.) Blue LEDs H_2O, Ar, 20 h		[47]
4		TEEDA-----**I-R_F** **EDA complex**	**TEEDA** (3 equiv.) CFL (25 W) THF, r.t. **R_F-I** (3 equiv.)		[48]
5		 **EDA complex**	**ICF_2CO_2Et** (1.3 equiv.) Na_2CO_3 (1.5 equiv.) DMSO (3 mL) Ar, rt. 427 nm LED, 16 h		[49]
6		 **EDA conplex**	**TMG** (2.5 equiv.) **R_F-I** (2.5 equiv.) 23 W CFL, MeCN/Hex_f (5:1)		[42,50]
7		 **EDA conplex**	**TMG** (2.5 equiv.) **R_F-I** (2.5 equiv.) 23 W CFL, MeCN		[51]
8		 **EDA complex**	Umemoto´s reagent (2 equiv.) *N*-methylmorpholine (2.5 equiv.) DMF, r.t.		[52]
9		 **EDA complex**	Cs_2CO_3 (2 equiv.) **R_F-I** (3 equiv.) white light H_2O (3 equiv.) DMF, r.t., 2 h		[53]
10		 **EDA complex**	4.5 W 450 nm laser $CaCl_2$, $MeNO_2$, 0 °C		[3]
11		 **EDA complex**	**R_F-I** (1.5 equiv.) *t*-BuONa (2 equiv.) DMF Green LEDs		[54]
12		TMEDA------**I-R_F** or DBU -------**I-R_F** **EDA complex**	**I-R_f** (2.1 equiv.) TMEDA (2 equiv.) or DBU (2 equiv.) Blue LEDs 24 W		[55,56]
13			TFE / water (1: 1) (0.2 M) CF_3SO_2Na Blue LEDs r.t., 12 h		[84]

Table 2. Perfluoroalkylation reactions of carbon-carbon multiple bonds and constrained cyclic compounds by EDA complexes.

Entry	Substrate	Complex	Reaction conditions	Product	Ref.
1		**EDA complex**	**Bu_4NCl**, Hg lamp (6 W) **R_F-I** (1.2 equiv.) CH_3OH, 1.5 h r.t, Ar		[39]
2		 **EDA complex**	**R_F**I (3 equiv.) **KOH** (1.5 equiv.) Blue LEDs H_2O, Ar, 20 h		[47]

3		 EDA complex II	 pyrrolidin-2-one, 25 °C, N_2		[57]
4		**DIPEA or TMEDA or DBU or TEEDA** ·····**CF_3I**	**CF_3-I** (3 equiv.) **Base** (2 equiv.) MeCN or DMF or THF CFL, 25 W	 with DIPEA, TMEDA or TEEDA; with DBU	[48,58,59]
5		**Bn_2-NH** ----- **R_F-I** **EDA complex**	**Bn_2NH** MeCN **R_F-I** Blue LED, r.t.		[60]
6		 EDA complex	**Base**, Blue LEDs DMF or THF	 with DMF; with THF	[61]
7		H_2O ------> I-R_F **EDA complex**	I-R_F **H_2O** / toluene = 9:1 Blue LEDs, 65°C, 12h		[41]
8			**K_3PO_4** (3 equiv.) **R_F-I** (3 equiv.) CuCl (10 mol%) **TMSNCS** (3 equiv.) CH_3CN (2 mL) Violet LEDs (24 W) Ar, 4 h		[37]
9		 EDA complex; halogen bonding	**R_F-I** (3 equiv.) Diphenylacetaldehyde (10 mol%) Pyrrolidine (40 mol%) DIPEA (2 equiv.) DCE (2.5 mL); O_2 (0.8 eq.); Ar White LEDs (2.5 W); 24 h		[44,62]
10		 EDA complex 1; or; EDA complex 2	 **DIPEA**,DMA Ar (trace air) Blue LEDs, rt. 36-72 h		[63]
11		 EDA complex	**TMEDA** Blue LEDs ***n*-C_4F_9I** DMSO air, 24 h RT		[64]
12		**DABCO** ------ **C_nF_{2n+1} -I** **EDA complex**	K_3PO_4 (2 equiv.) **DABCO** (1.2 equiv.) *hu* (400 Watt) 50 °C **C_nF_{2n+1}I** (1.8 equiv.)		[65–67]
13		 EDA complex	Blue LEDs DCE, r.t.		[27]
14		 EDA complex	2,4,6-trimethylpyridine MeCN, 60 °C Togni´s reagent		[68]
15		 EDA complex	PMDETA (2 equiv.) DMSO (2 mL) N_2, Blue LEDs		[69]
16			Blue LEDs		[70,71]

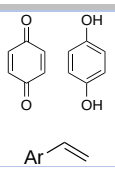
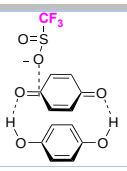
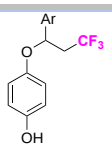
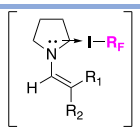
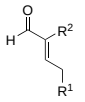
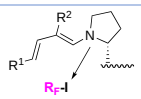
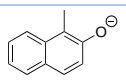
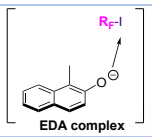
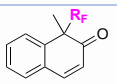
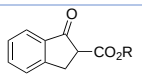
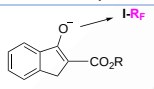
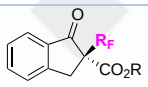
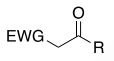
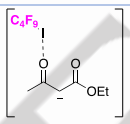
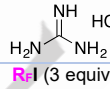
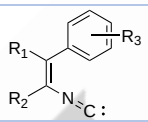
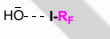
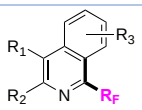
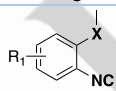
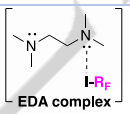
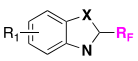
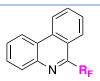
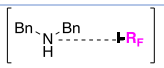
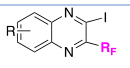
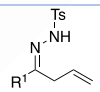
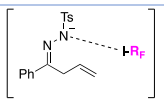
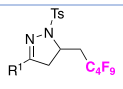
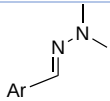
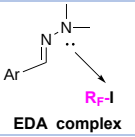
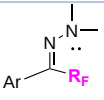
17			MeCN (0.2 M) with less than 1% water CF_3SO_2Na (1 mmol) Blue LEDs		[84]

Table 3. Perfluoroalkylation of carbonyl compounds, isocyanides and hydrazones.

Entry	Substrate	Complex	Reaction conditions	Product	Ref.
1			R_FI (1.1 equiv.) (2.1 equiv.) CH_2Cl_2 (2.5 mL), Ar CFL, 16 h		[72,73]
2		 EDA complex	R_F-I (0.2 mmol) *cis*-catalyst M (20 mol%) 2,6-lutidine (1.2 equiv.) Blue LEDs, Et_2O (0.7 M) -10 °C, 20 h		[74]
3		 EDA complex	white light R_F-I		[75]
4		 EDA complex	phase transfer catalyst Cs_2CO_3 , $C_6H_5Cl/8F_{18}$ (2:1), 25 °C, R_F-I		[32]
5			ambient light C_4F_9-I NaOH (4.1 equiv.) MeCN, R.T. 		[76]
6		 EDA complex	R_FI (3 equiv.) **KOH** (1.5 equiv.) Blue LEDs THF, Ar, 36 h		[47]
7		 EDA complex	R_F-I (2 equiv.) **TMEDA** (2 equiv.) THF (2 mL) Blue LEDs (25 W) 30 °C, N_2		[77]
8			**TEEDA** (1.5 equiv.) CFL (25 W) THF I-C_4F_9		[48]
9			**Bn_2NH** Blue LEDs MeCN, RT R_F-I		[78]
10			TMG (1.5 equiv.) ambient light MeCN, RT I-R_F		[79]
11		 EDA complex	Imidazole (3 equiv.) MeCN, R_F-I (2 equiv.) r.t.		[80]

10.1002/cptc.202400112

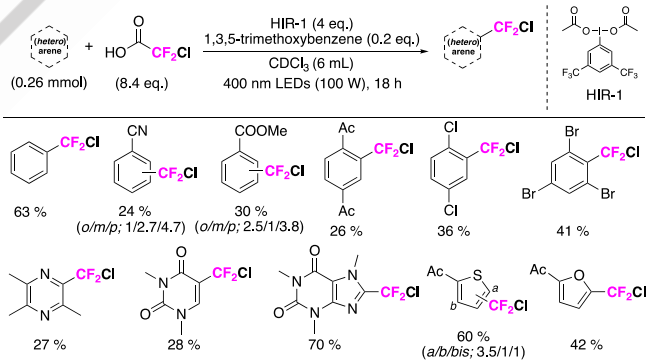
Damian E. Yerien was born in Argentina and obtained his Biochemistry degree from University of Buenos Aires in 2014. He obtained his Ph.D. degree (2019) at the University of Buenos Aires studying synthetic and mechanistic aspects of radical perfluoroalkylation reactions through photoredox catalysis, under the direction of Prof. Dr. Al Postigo. He is currently a National Argentine Research Council research member and a Teaching Assistant at the Department of Chemical Sciences, Faculty of Pharmacy and Biochemistry, University of Buenos Aires.

Sebastián Barata-Vallejo was born in General Villegas (Argentina) and holds degrees in Pharmacy (2007) and Biochemistry (2010). He obtained his Ph.D.degree (2012) at the University of Buenos Aires, studying radical reactions in aqueous and microheterogeneous media under the supervision of Prof. A. Postigo. He has been a research fellow and held several postdoctoral positions at the Istituto per la Sintesi Organica e la Fotoreattività (ISOF), Consiglio Nazionale delle Ricerche (CNR), Bologna, Italia, under the supervision of Dr. C. Chatgilialoglu, studying biomimetic radical reactions and their mechanisms. He is currently a researcher at the National Council for Scientific and Technical Investigation, CONICET (Argentina), research associate at ISOF-CNR, Bologna, Italy, and assistant professor at the Chemical Sciences Department, Faculty of Pharmacy and Biochemistry, University of Buenos Aires. His research activities focus on radical organic chemistry, in particular carbon- and sulfur-centered radicals reactivity, fluoroalkylation reactions by radical pathways and photocatalysis.

Al Postigo was born in Argentina and obtained his M.Sc. degree from the University of Buenos Aires in 1986. He moved to Canada in 1990, and obtained his Ph.D. from McMaster University in 1994, under the direction of Prof. Dr. W. J. Leigh. After postdoctoral positions in Canada, he returned to Argentina and worked with Prof. Dr. R. Rossi at the University of Córdoba in the area of radical ion reactions. He held assistant and associate professorship positions at the University of Córdoba, University of Buenos Aires, and University of Belgrano. He is currently full professor of Organic Chemistry at the Department of Chemical Sciences, Faculty of Pharmacy and Biochemistry, University of Buenos Aires. His interests are in the areas of radical chemistry, both carbon-centered radicals and metal-centered radicals. He is devoted to studying radical reactions of these species in water and non-conventional media.

2. Perfluoroalkylation of (Hetero)Aromatic Compounds

Prakash and collaborators[13] presented a visible-light mediated chlorodifluoromethylation of arenes and heteroarenes enabled by a new EDA complex consisting of *bis*(chlorodifluoroacetoxy)iodoarene and 1,3,5-trimethoxybenzene. This mild and easy operational methodology employs readily accessible reagents and is compatible with various functional groups as well as different *N*,*O* and *S*-heterocycles as shown in Scheme 3. Improved reaction yields are obtained when replacing $CHCl_3$ with $CDCl_3$ as solvent. This is probably due to the increased bond strength of the C-D bond compared to the C-H bond, leading to a reduction in solvent-mediated hydrogen atom transfer (HAT) quenching of the active $^{\bullet}CF_2Cl$ species. The authors perform a series of mechanistic studies for demonstrating the radical nature of the reaction and proposed a mechanism according to the Scheme 4. Initially a ligand exchange occurs between the hypervalent iodine reagent (**HIR-1**, Scheme 4) and chlorodifluoroacetic acid affording the hypervalent iodine specie **A** (Scheme 4). 1,3,5-Trimethoxybenzene and **A** form an EDA complex which upon irradiation (400 nm) provides radical anion **B** and radical cation **C**. Radical anion **B** decomposes through a decarboxylation process and yields a $^{\bullet}CF_2Cl$ radical which reacts with the arene substrate yielding cyclohexadienyl radical **D** (Scheme 4). Cyclohexadienyl radical **D** undergoes a single electron transfer process with radical cation **C** affording 1,3,5-trimethoxybenzene and Wheland intermediate **E** which upon deprotonation gives the desired reaction product (Scheme 4).[13] Figure 1 shows the presence of an EDA complex between **A** and 1,3,5-trimethoxybenzene).



Scheme 3. Selected examples of the visible-light mediated chlorodifluoromethylation of (hetero)arenes enabled by a hypervalent iodine EDA complex.

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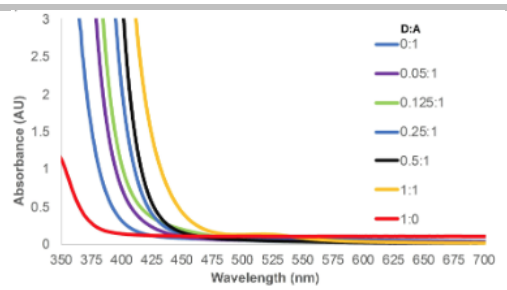
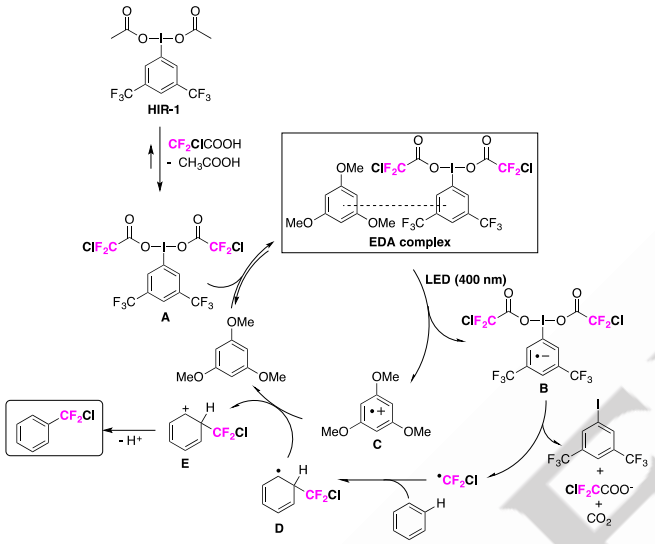
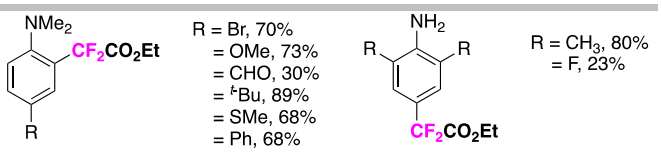


Figure 1. UV-visible spectra of EDA complex at different concentrations of Donor (i.e.: 1,3,5-trimethoxybenzene) and Acceptor (i.e.: *bis*(chlorodifluoroacetoxy)iodoarene) (Reproduced from Open Access Article: *Eur. J. Org. Chem*. **2022**, *2022*, e202200607)

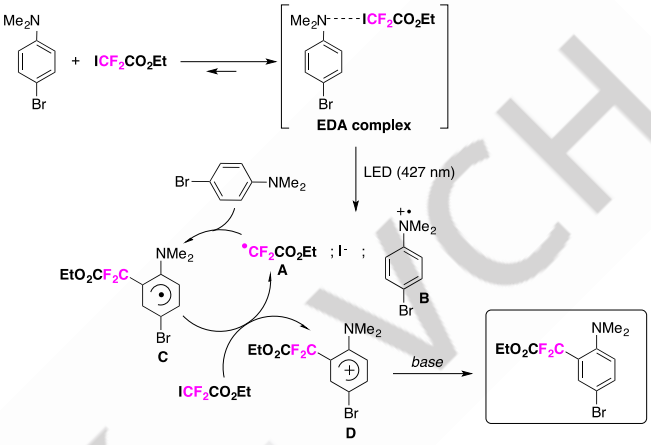


Scheme 4. Proposed mechanism for the visible-light mediated chlorodifluoromethylation of (hetero)arenes enabled by a hypervalent iodine EDA complex.

Vallribera and collaborators[49] performed the photocatalyst-free difluoroacetylation of aniline derivatives mediated by the photoactivation of an EDA complex between the aniline substrate and ethyl difluoroiodoacetate reagent. The reaction tolerates different functional groups affording the corresponding difluoroacetylated products in moderate to very good yields (Scheme 5). The authors[49] after performing several mechanistic studies proposed the reaction mechanism depicted in Scheme 6. Initially an EDA complex between the aniline substrate and ICF_2CO_2Et reagent is formed and upon illumination (427 nm) yields fluorinated radical **A,** I^- and radical cation **B** (Scheme 6). Fluorinated radical **A** reacts with the aniline substrate yielding cyclohexadienyl radical **C** (Scheme 6) which is further oxidized by ICF_2CO_2Et reagent propagating the radical chain and affording Wheland intermediate **D** (Scheme 6) which upon proton loss gives the reaction product.



Scheme 5. Selected examples for the photocatalyst-free difluoroacetylation of aniline derivatives mediated by the photoactivation of an EDA complex between the aniline substrate and ethyl difluoroiodoacetate reagent.



Scheme 6. Proposed reaction mechanism for the difluoroacetylation of aniline derivatives mediated by the photoactivation of an EDA complex between the aniline substrate and ethyl difluoroiodoacetate reagent.

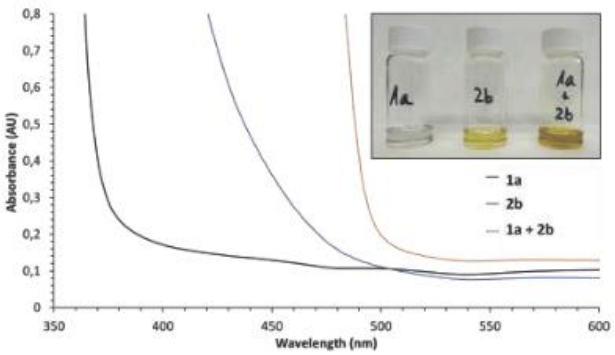


Figure 2. UV-visible spectra of **1a** (4-bromo-*N,N*-dimethylaminobenzene), **2b** (ethyl 2,2-difluoro-2-iodoacetate) and the mixture of **1a:1b** (Reproduced from Open Access Article: *J. Org. Chem*. **2023**, *88*, 12585-12596)

Figure 2 shows the UV-visible spectra of a 1: 1 mixture of 4-bromo-*N,N*-dimethylaminobenzene and ethyl 2,2-difluoro-2-iodoacetate, illustrating a distinctive UV absorbance from the reagents.

In a 2023 report, Li and colleagues[46] introduced a highly efficient approach for the C_{Ar}-H perfluoroalkylation of arenes and heteroarenes. This method relies on the formation of an EDA complex between triaryl amines and α-perfluorosulphonylpropiophenone, with the reaction facilitated under blue light irradiation in acetonitrile as the solvent.

The optimized conditions and substrate scope are detailed in Scheme 7. Perfluoroalkylation of an electron-rich compound, such as 1,2,3-trimethoxybenzene, exhibited excellent yields for perfluorohexylation and perfluorooctylation, with moderate yields observed for the reaction with C_4F_9. Even less electron-rich

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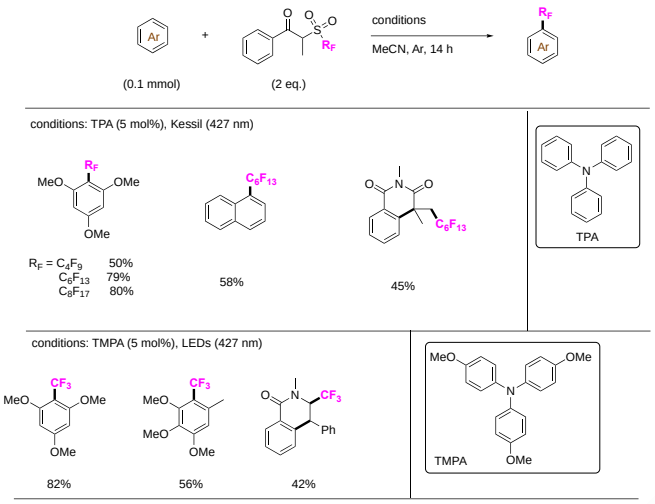
compounds, such as benzene and naphthalene, demonstrated reactivity under the reaction conditions. Additionally, the study explored the late-stage fluoroalkylation of compounds with biological and supramolecular significance, including caffeine, a naproxen derivative, and dibenzo-18-crown 6-ether, resulting in the desired products (not shown).

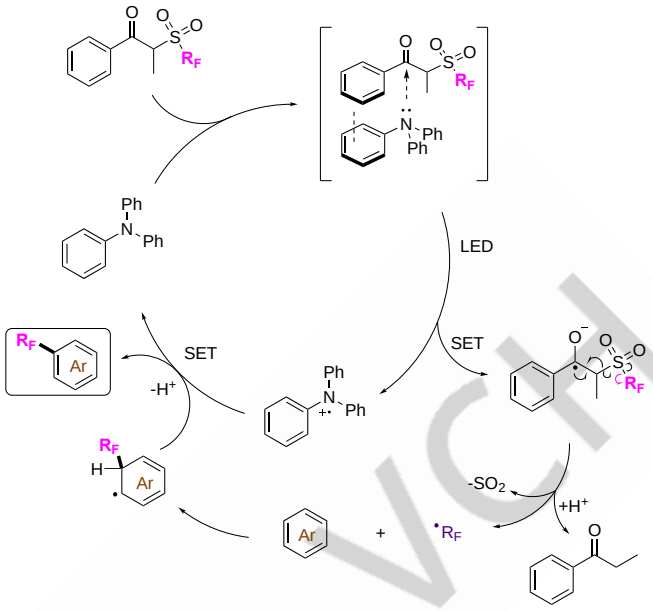


Scheme 7. Catalytic EDA complex fluoroalkylation of aromatic compounds: selected examples.

To achieve the trifluoromethylation of aromatic compounds - a highly sought-after moiety in medicinal chemistry - the authors utilized a more electron-rich amine, *tris*(4-methoxyphenyl)amine, in the presence of a CF_3 reagent, as illustrated in Scheme 7, bottom. 1,2,3-trimethoxybenzene was trifluoromethylated with a very good yield, also several examples of *N*-containing heterocyclic were presented with moderate to good yields.

To gain insights into the mechanistic aspects of the reaction, the authors[46] conducted several experiments. The UV-vis analysis of a mixture containing *tris*(4-methoxyphenyl)amine (TPA) and α-perfluorosulphonylpropiophenone revealed an immediate shift in absorption, indicating a process of charge transfer. Following a 10-minute irradiation of this mixture with blue light, a new absorption band at 660 nm appeared, likely attributed to the formation of the triphenylamine radical cation. Transient absorption studies using laser flash photolysis (LFP) were also conducted. Upon excitation at 355 nm in an Ar-deoxygenated solution of TPA in the presence of α-perfluorosulphonylpropiophenone, a band at 660 nm was observed, consistent with previous reports for the $TPA^{\bullet+}$ radical cation. The formation of the perfluoroalkyl radical was also confirmed by trapping experiments.

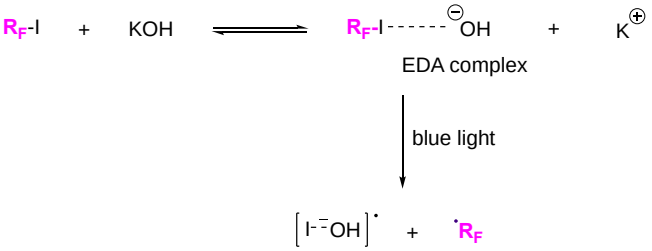
The proposed mechanism for the reaction is illustrated in Scheme 8. *Tris*(4-methoxyphenyl)amine (TPA) and the perfluoroalkylating reagent containing propiophenone form a charge transfer complex. Upon excitation with blue light (427 nm), a single electron transfer process (SET) occurs, generating a radical pair comprising $TPA^{\bullet+}$ and the radical anion of the perfluoroalkylating reagent. This radical anion decomposes into SO_2, an enolate, and the perfluoroalkyl radical. Finally, the perfluoroalkyl radical engages in a homolytic aromatic substitution (S_HA) process with the arene.



Scheme 8. Catalytic EDA complex perfluoroalkylation of aromatic compounds: proposed mechanism.

In a recently published report, Wang, Neumann, Cheng, Beller, and co-workers[47] have introduced a versatile system designed to facilitate the addition of perfluoroalkyl radicals to electron-rich π bonds. This method relies on the activation of perfluoroalkyl iodides using straightforward inorganic bases, such as potassium hydroxide or potassium carbonate.[81]

According to the mechanistic proposal shown in Scheme 9, the reaction between perfluoroalkyl iodides and the base leads to formation of an EDA complex by halogen bonding interaction. This complexation facilitates the homolytic cleavage of the relatively weaker C-I bond within the complex under mild irradiation conditions, resulting in the simultaneous formation of a perfluoroalkyl radical and an iodine radical.



Scheme 9. Proposed mechanism for the perfluoroalkyl radical formation assisted by KOH.

The C-H perfluoroalkylation of electron-rich aromatic and heteroaromatic compounds was investigated. The authors[47] reported the perfluoroalkylation reactions of aniline, pyrrole, and indole derivatives. Additionally, the authors explored the perfluoroalkylation of tryptophan-containing short peptides, yielding products in moderate to good yields, as illustrated in Scheme 10.

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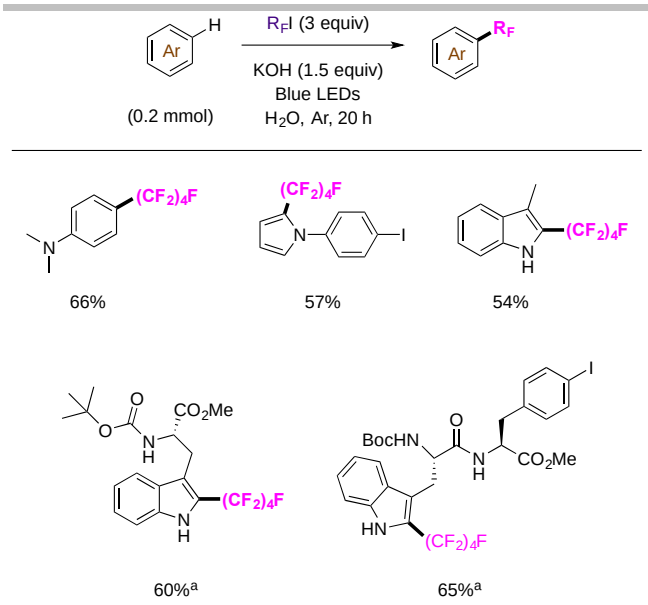
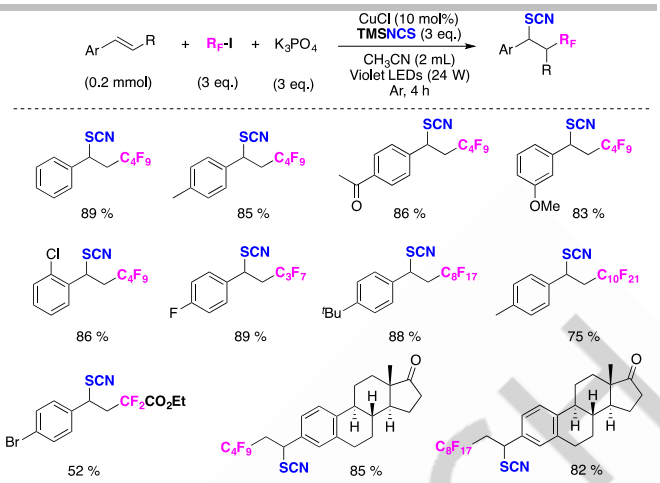


a- CH_2Cl_2 used as solvent

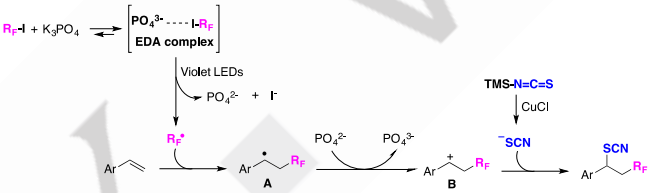
Scheme 10. C-H perfluoroalkylation of electron-rich arenes and heteroarenes.

3.- Perfluoroalkylation of Carbon-carbon Multiple Bonds

Guo and colleagues [37] reported on a visible-light induced fluoroalkylthiocyanation of alkenes *via* EDA complexes between K_3PO_4 and perfluoroalkyl iodides (R_FI), employing trimethylsilyl isothiocyanate (TMSNCS) as thiocyanate source. Aromatic alkenes bearing electron-donating and electron-withdrawing groups at the *o*-, *m*-, or *p*- positions all performed well under standard conditions shown in Scheme 11. Various functional groups, such as –^{t}Bu, –OCH_3, –F, –Cl, –Br, –Ac, and –Ph were all well-tolerated, and the reaction performed on an estrone derivative afforded the desired products with good yield (Scheme 11). However, when aliphatic alkenes were employed as substrates under standard conditions only the iodoperfluoroalkylation ATRA[82] reaction products were obtained. The authors attribute the distinct reaction pathways observed in aliphatic and aryl alkenes to the differing properties of the benzyl and non-benzyl radical intermediates. Based on the mechanistic investigations, the authors propose a plausible reaction mechanism (Scheme 12). Initially, K_3PO_4 and R_FI forms a colored EDA complex which upon violet-light irradiation generates the electron-deficient $R_F^{\bullet}$ radical along with I^- and PO_4^{2-}. The $R_F^{\bullet}$ radical is subsequently trapped by the alkene, forming the benzylic intermediate **A** (Scheme 12), which undergoes oxidation by the PO_4^{2-} anion to generate the carbocation species **B** (Scheme 12). The carbocation intermediate **B** reacts with the nucleophilic ^-SCN anion, ultimately yielding the desired product.[37]



Scheme 11. Selected examples for the visible light-induced fluoroalkylthiocyanation of alkenes *via* EDA complexes.



Scheme 12. Proposed reaction mechanism for the visible light-induced fluoroalkylthiocyanation of alkenes *via* EDA complexes.

Yajima and colleagues [44] presented a methodology for the hydroxyperfluoroalkylation of electron-deficient conjugated olefins. In this approach, an *in situ* generated enamine forms a photoactive EDA complex with perfluoroalkyl iodides and upon irradiation $R_F^{\bullet}$ radical formation is facilitated. Optimization studies demonstrate that *N,N*-di*iso*propylethylamine (DIPEA)[83] additive is also necessary for maximizing product yields as it also promotes $R_F^{\bullet}$ radical generation *via* halogen-bonding. Optimized reactions conditions for this transformation as well as the substrate scope are shown in Scheme 13. The reaction performs well with substrates such as methacrylates bearing different ester groups as well as employing different styrenes with electron-donating or electron-withdrawing groups at the *p*-position (Scheme 13). To gain insight into the reaction mechanism, the authors conducted various studies, including radical trapping with (2,2,6,6-Tetramethylpiperidin-1-yl)oxyl (TEMPO), the use of labeled reagents such as $^{18}O_2$ and $H_2{}^{18}O$, and ^{19}F NMR titration experiments to determine the association constant (K_a) between R_FI and the enamine catalyst, as well as DIPEA. A simplified plausible reaction mechanism for this transformation is shown in Scheme 14. The authors propose that both enamine and DIPEA are involved in $R_F^{\bullet}$ radical generation. In a catalytic cycle, enamine **A** (Scheme 14) formation results from the condensation of diphenylacetaldehyde and pyrrolidine, followed by the generation of a photoactive EDA complex with R_FI. Upon visible-light irradiation of the EDA complex, $R_F^{\bullet}$ radicals, I^-, and enamine radical cations **B** (Scheme 14) are produced. The enamine catalyst **A** is regenerated through a SET process with I^-. Simultaneously, DIPEA engages in a halogen bonding interaction with R_FI leading, upon visible-light irradiation, to the generation of

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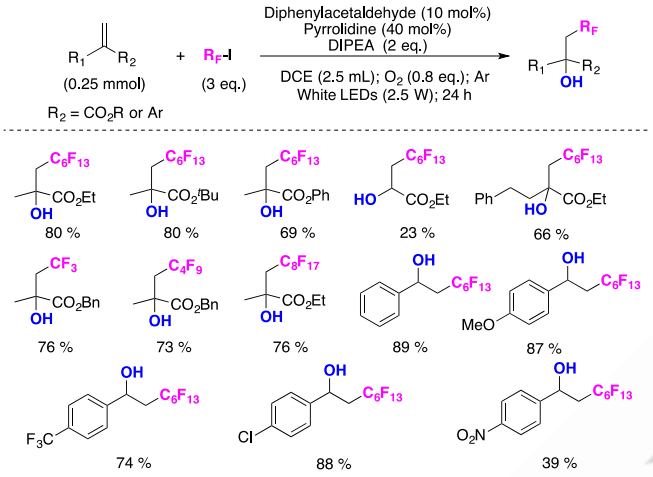
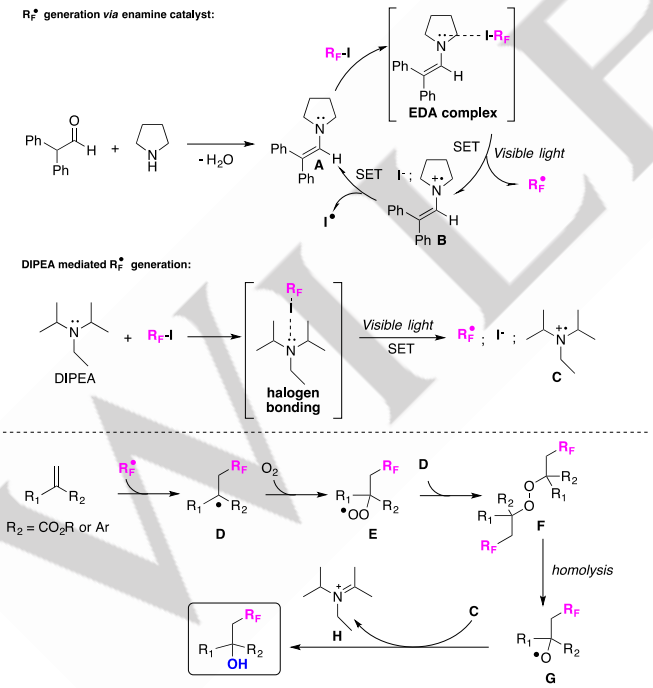
$R_F^{\bullet}$ radicals along with I^- and DIPEA radical cation **C** (Scheme 14). Subsequently, $R_F^{\bullet}$ radicals react with the substrate, and the resulting radical intermediate **D** (Scheme 14) is promptly trapped by molecular oxygen, forming peroxyl radical intermediate **E** (Scheme 14). Considering that less than 1.0 eq. of O_2 is sufficient for the reaction, the authors propose that the reaction mechanism involves the formation of dimer **F** (Scheme 14), arising from the radical-radical recombination reaction between **D** and **E.** Finally, dimer **F** homolyzes to yield radical adduct **G** (Scheme 14) which abstract a hydrogen atom from DIPEA radical cation **C** affording the reaction product.[44]



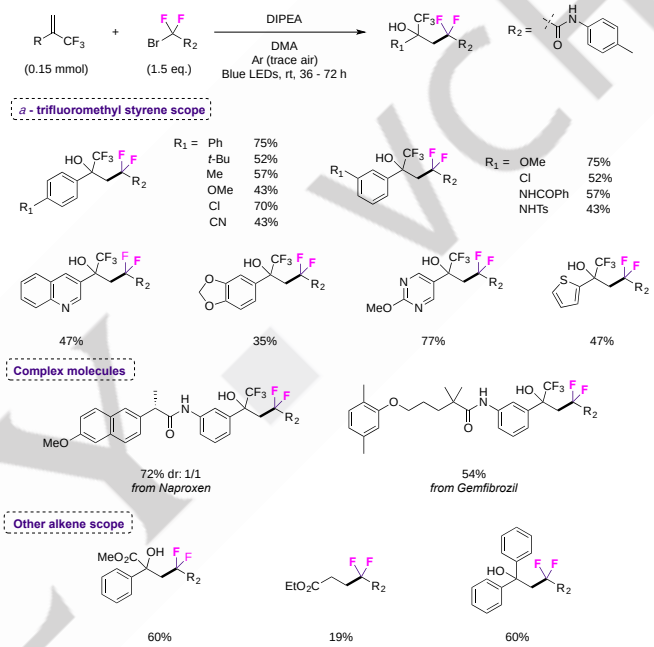
Scheme 13. Selected examples for the hydroxyperfluoroalkylation of electron-deficient conjugated olefins using enamine catalyst.



Scheme 14. Proposed reaction mechanism for the hydroxyperfluoroalkylation of electron-deficient conjugated olefins using enamine catalyst.

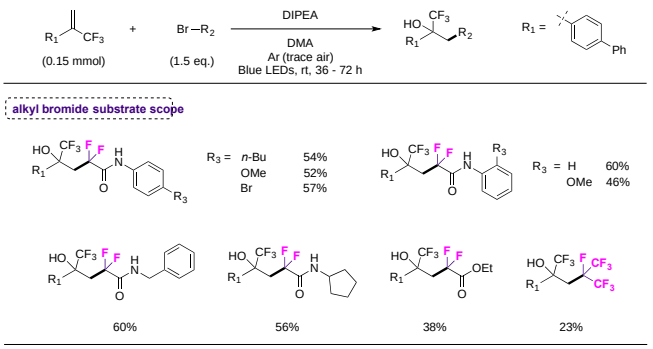
The process of irradiation electron donor-acceptor (EDA) complexes, which are formed by pairing an electron-poor halide with an electron-rich compound like an amine or enamine, leads to the generation of alkyl radicals by inducing the fragmentation of the alkyl halide. Xiang, Chen, Yang, and co-workers[63] exploit this strategy for achieving visible light-induced hydroxydifluoroalkylation of alkenes.

In this photocatalyst-free protocol, the radical source is derived from alkyl halides containing fluorine atoms. *N,N*-Di*iso*propylethylamine (DIPEA) serves as the electron donor in *N,N*-Dimethylacetamide (DMA) as solvent. The reaction takes place in the presence of trace amounts of oxygen and is initiated by irradiation with blue LEDs. The optimized conditions and the substrate scope involved are illustrated in Scheme 15, along with some selected examples of the alkene scope of the reaction.



Scheme 15. Hydroxydifluoroalkylation of alkenes: alkene scope. Selected examples.

Several substituted α-trifluoromethylstyrenes were tested with moderate to good yields. The authors achieved two noteworthy outcomes by isolating two products containing biologically relevant units. Additionally, the substitution of the α-trifluoromethyl group with other electron-withdrawing groups, such as esters, proved to be effective in the reaction. Additionally, the investigation of the alkyl bromide scope was conducted, and the outcomes are summarized in Scheme 16.



Scheme 16. Hydroxydifluoroalkylation of alkenes: alkyl bromide scope. Selected examples.

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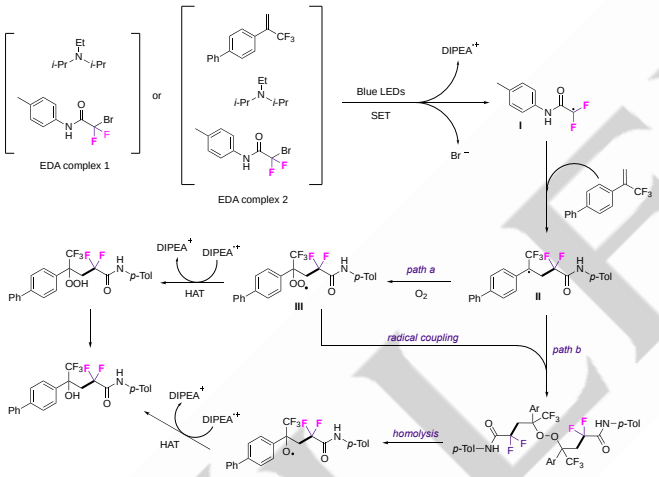
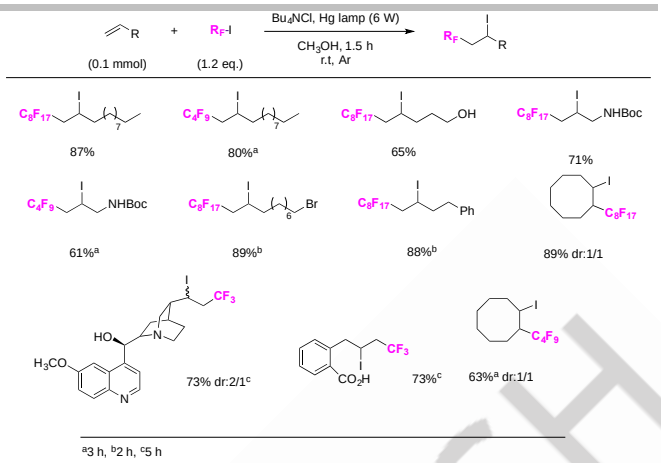
In order to propose a reaction mechanism, the authors conducted a series of control experiments. Upon adding α-trifluoromethylstyrene to a solution of DIPEA and 2-bromo-2,2-difluoro-*N*-phenylacetamide, a significant bathochromic displacement is observed in the UV-vis absorption spectrum. This observation suggests the likely formation of an EDA complex in the mixture. This observation was also supported by the titration of the complex performed by ^{19}F and ^{1}H NMR spectroscopy. The introduction of radical scavengers, such as TEMPO or butylated hydroxytoluene (BHT) into the reaction mixture resulted in a depletion of product accumulation.

The proposed reaction mechanism for this reaction is depicted in Scheme 17. Direct photoexcitation of EDA complex 1 or 2 leads to the formation of the radical intermediate I by fragmentation of the C-Br bond. Upon radical addition of I to a doble bond, the radical adduct II is formed. The trifluoroalkyl radical II could be trapped by molecular oxygen to form a peroxyl radical (III) who can subsequently transform into the desire product by hydrogen atom transfer from DIPEA$^{\bullet+}$ followed by cleavage of the peroxide bound (pathway a). Another possibility (path b) is the dimerization of the radical III and the homolysis of the O-O bond followed by hydrogen atom abstraction gave the final product.



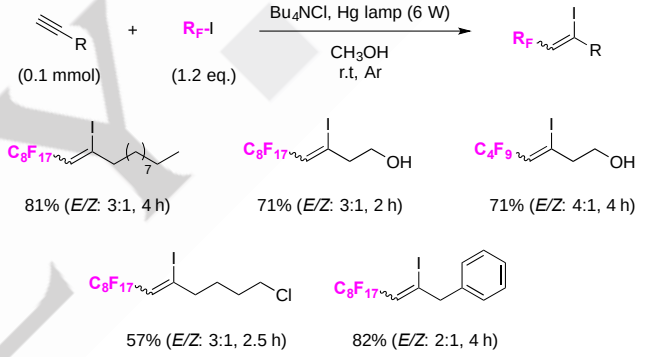
Scheme 17. Hydroxydifluoroalkylation of alkenes: mechanistic proposal.

In their 2018 report, Jean-Marc Vicent and co-authors[39] introduced a method for iodoperfluoroalkylation of alkenes and alkynes. This process is facilitated by the direct irradiation of an EDA complex, which is formed between perfluoroalkyl iodides and chloride ions. Scheme 18 illustrates the optimized reaction conditions. Perfluoroalkyl iodides serve as sources of perfluoroalkyl radicals, while NaCl or tetrabutylammonium chloride (Bu_4NCl) is added in catalytic amounts to provide chloride ions. The reaction takes place in deoxygenated methanol as the solvent, under irradiation with low-intensity UVA light irradiation. The reaction protocol was effectively applied to terminal alkenes with diverse functional groups, including alcohols, alkyl bromides, carbamates, amines, and carboxylic acids. Additionally, the authors explored the reaction with an internal alkene, employing cyclooctene as the substrate. In all cases, the desired products were obtained in high yields, as depicted in Scheme 18.



Scheme 18. Iodoperfluoroalkylation of alkenes: scope.

Scheme 19 illustrates the iodoperfluoroalkylation reaction applied to terminal alkynes. Numerous iodoperfluoroalkylated alkenes were successfully obtained with good to excellent yields within a reaction time ranging from 2 to 4 hours. The stereoselectivity for the *E*-isomers was generally low to moderate.



Scheme 19. Scope of the iodoperfluoroalkylation of alkynes.

The authors performed titration experiments using ^{19}F NMR, utilizing the halogen bonding interaction between chloride ions and I-C_8F_{17} in organic solvents. In $CDCl_3$, a 1:1 complex was observed between I-C_8F_{17} and Bu_4NCl, with a constant K_a = 4.8-5.0 M^{-1}. As anticipated, in a solvent with higher competition for halogen bonding, such as CD_3OD, the constant values were notably smaller, falling below < 1 M^{-1}. However, it's worth noting that despite the reduced constants, a significant interaction is still observable through shifts in the signals in the NMR spectrum.

In a recently released publication, Wang, Neumann, Cheng, Beller[47] and their colleagues have introduced a versatile system aimed at streamlining the addition of perfluoroalkyl radicals to electron-rich π bonds. This approach hinges on activating perfluoroalkyl iodides using simple inorganic bases like potassium hydroxide.

As depicted above (*vide supra*, section aromatics), the proposed mechanism suggests that the interaction between perfluoroalkyl iodides and the base generates an EDA complex through halogen bonding. This complexation facilitates the breaking of the relatively weaker C-I bond within the complex

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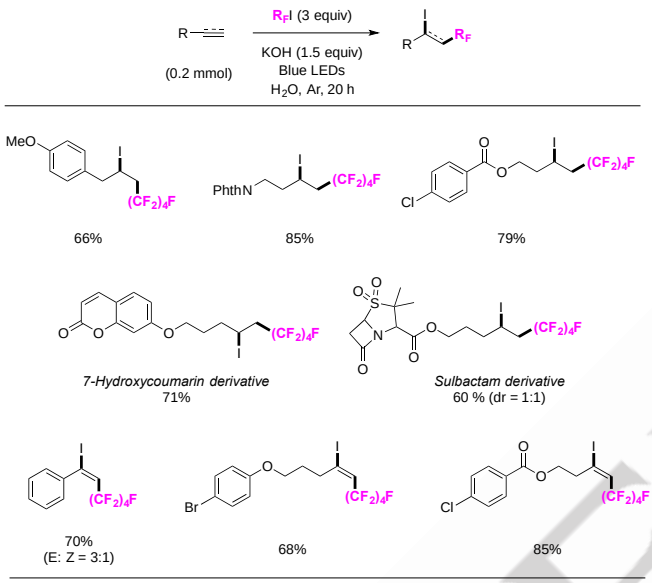
under mild irradiation conditions, leading to the simultaneous generation of a perfluoroalkyl radical and an iodine radical.

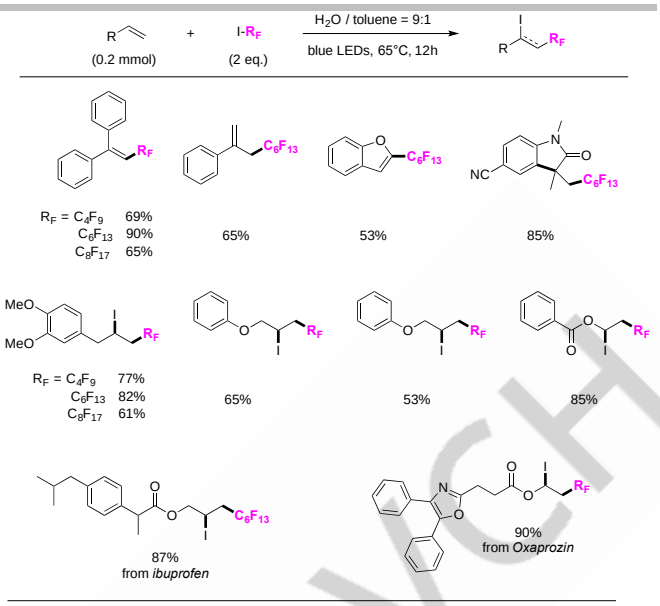
Moreover, under the same conditions as described previously, the perfluoroalkyl radical can react with terminal alkenes and alkynes,[47] resulting in the formation of iodoperfluoroalkylated alkanes and iodoperfluoroalkylated alkenes, respectively, through a 1,2-addition process. Scheme 20 illustrates the substrate scope of these reactions, indicating that various functional groups are well-tolerated. The versatility of the method is highlighted by successful reactions with substrates derived from natural products or drugs, yielding the desired products.



Scheme 20. Addition of Perfluoroalkyl radical to alkenes and alkynes: Selected examples.

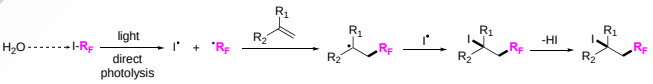
Li, Wang, Chen, and their colleagues[41] devised a methodology for activating the C-I bond through direct photolysis facilitated by an EDA (electron donor-acceptor) complex. This complex is formed through halogen bonding between perfluoroalkyl halides and water. This procedure offers a more environmentally friendly and practical option compared to other methods that rely on superstoichiometric quantities of electron donors or the utilization of Lewis bases. The authors endeavor to react perfluoroalkyl radicals with double bonds of alkenes and aromatic compounds.

The reaction conditions and scope are shown in Scheme 21. The protocol employs perfluoroalkyl iodides as $^{\bullet}R_F$ source in water: toluene as solvent mixture, under irradiation with blue LEDs at 65 °C. Several derivatives of styrene proved suitable for this reaction, yielding the desired products in good to excellent yields. The $^{\bullet}C_6F_{13}$ radical also exhibited successful reactions with benzofuran and substituted *N*-arylacrylamides. In the latter case, the outcome was the formation of cyclic products. Iodo perfluoroalkylation products were isolated for various substrates containing other functional groups, such as ethers and esters. Additionally, a range of biologically relevant compounds bearing terminal alkenes were tested, including derivatives of Ibuprofen and Oxaprozin, achieving excellent yields.



Scheme 21. Selected examples for the iodoperfluoroalkylation of alkenes by H_2O : R_F-I EDA complex.

Based on UV-vis spectra measurements and titration of the EDA complex conducted by the authors, they proposed a mechanism depicted in Scheme 22. Initially, the photoexcitation of the EDA complex enables the photolysis of the C-I bond, resulting in the corresponding perfluoroalkyl radical. The electrophilic radical then adds to a terminal position of the substrate, producing a radical adduct. The iodoperfluoroalkylation product may be formed through the coupling of the radical adduct with an iodine radical. If the iodoperfluoroalkylation product is unstable, the authors suggest that elimination of HI could lead to the formation of the perfluoroalkylated alkene.



Scheme 22. Photolysis of perfluoroalkyl iodides assisted by water, proposed mechanism.

4.- Perfluoroalkylation of Carbonyl Compounds at the α and γ-Positions

Yajima and collaborators [72] reported on a visible-light induced perfluoroalkylation of the α-position of aldehydes *via* enamine intermediates. The reaction is facilitated by the EDA complexation of enamines and perfluoroalkyl iodides which enables perfluoroalkyl radicals formation upon visible-light irradiation. The system is compatible with a variety of aldehydes and perfluoroalkyl iodides, allowing the synthesis of diverse quaternary α-perfluoroalkyl aldehydes (Scheme 23). Regarding some mechanistic aspects of the reaction, the authors proposed the formation of an enamine intermediate **A** (Scheme 24) by reaction of the aldehyde with a secondary amine additive, followed by EDA complexation of the enamine with the perfluoroalkyl iodide. Irradiation of the EDA complex employing a commercial fluorescent lamp (CFL) induces an electron transfer process yielding perfluoroalkyl radicals, iodide anion and the

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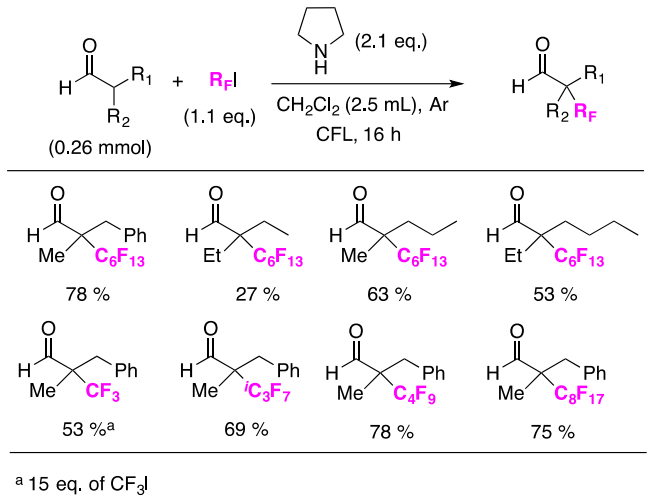
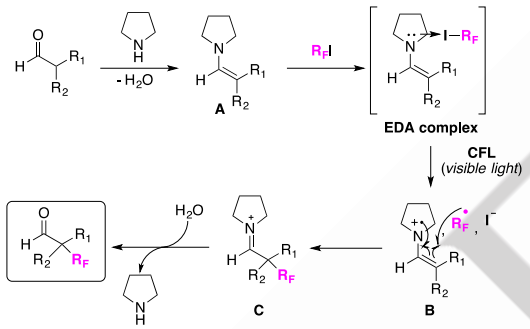
enamine radical cation **B** (Scheme 24). Perfluoroalkyl radicals then react with the enamine radical cation **B** affording a perfluoroalkylated iminium ion **C** (Scheme 24) which is further hydrolyzed to yield the quaternary perfluoroalylated aldehyde.[72]



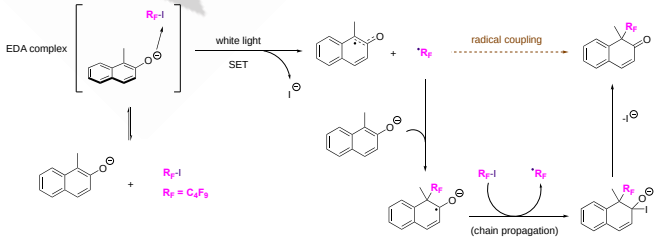
[a] 15 eq. of CF_3I

Scheme 23. Selected examples of the photocatalyst free visible-light induced synthesis of α-perfluoroalkyl aldehydes.



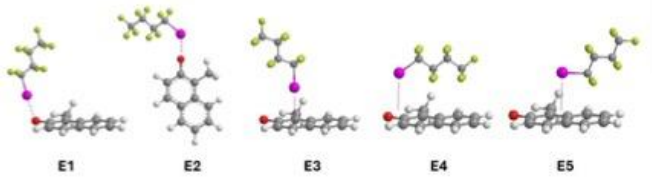
Scheme 24. Proposed mechanism for the photocatalyst free visible-light induced synthesis of α-perfluoroalkyl aldehydes.

The widely accepted notion is that Electron Donor-Acceptor (EDA) complexes can be photoactivated through visible-light intermolecular charge transfer (IECT) excitation. This process induces an electron transfer process, potentially leading to the formation of radical species. However, there are limited mechanistic insights into these types of reactions.[1–3] In a paradigmatic example, Ma, Chen, Lin, and colleagues[20] investigated the dearomative perfluoroalkylation of β-naphthol (Scheme 25). They employed electronic structure calculations at the CASPT2//CASSCF/PCM level of theory to conduct a comprehensive mechanistic investigation.



Scheme 25. Visible-light dearomative perfluoroalkylation of β-napthol mediated by an EDA complex.

The study involved the examination of five distinct complexes that could potentially form between the naphtoxide anion and the perfluoroalkyl iodide (Scheme 26). Among these complexes, two were formed through a halogen-bonding interaction (E1 and E2, Scheme 26) another involved a polar-π interaction (E3, Scheme 26), and the remaining two complexes were formed by dipole-dipole interactions (E4-5, Scheme 26). In each case, both the ground-state and excited-state properties of these complexes were characterized. Additionally, the relaxation pathways of these Electron Donor-Acceptor (EDA) complexes were thoroughly examined.

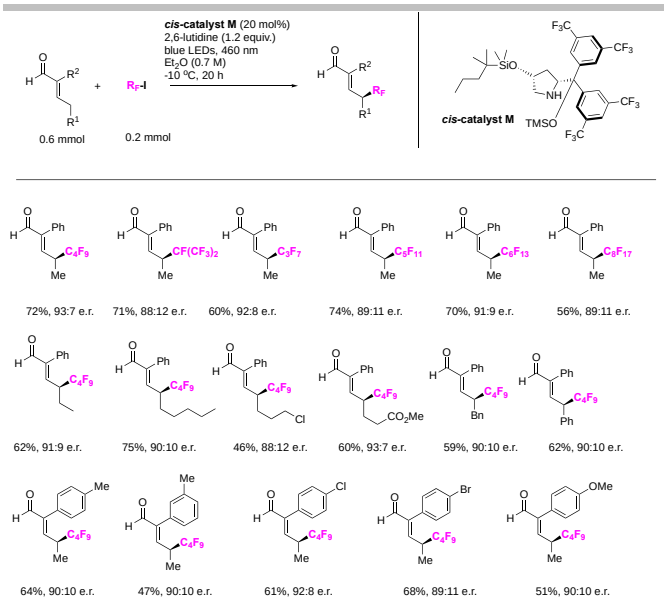


Scheme 26. EDA complexes E1-E5.

The authors concluded that the energy level of the intramolecular charge transfer (IACT) / intermolecular charge transfer (IECT) in the Electron Donor-Acceptor (EDA) complexes can be modulated by the noncovalent interaction between the naphtoxide and the perfluoroalkyl iodide. As the noncovalent interactions weaken, the calculated Boltzmann-weighted UV-vis absorption spectrum exhibits a broad range from UVA (<380 nm) to visible light (>500 nm). Consequently, the most stable complexes (E1-E2) can only absorb UVA irradiation either via IACT or IECT excitations, whereas the less stable complexes (E3-5) can be activated solely by IECT excitation.

In the former case, where radicals are formed at a similar rate, radical dimerization is anticipated to be dominant. On the other hand, in the latter cases (irradiation above 500 nm), the propagation chain is more likely because only a small quantity of complexes E3-5 can be promoted to the excited state. As a result, radical coupling is minimized in this scenario due to the very low concentrations of radicals.

Baletti, Melchiorre and colleagues[74] have recently pioneered the development of the first enantioselective methodology enabling the remote incorporation of perfluoroalkyl-containing stereogenicity. This approach harnesses the capability of chiral catalytic dienamines to form photoactive electron donor–acceptor (EDA) complexes with perfluoroalkyl iodides, which, upon blue irradiation, initiate radical generation via a SET mechanism. The crucial factor for achieving exceptional levels of enantiocontrol and precise site selectivity at the more distant γ position of enals was the utilization of a sterically hindered *cis*-4-hydroxyprolinol-derived catalyst. The scope of the transformation is shown in Scheme 27.



Scheme 27. Scope of the enantioselective γ-perfluoroalkylation of enals.

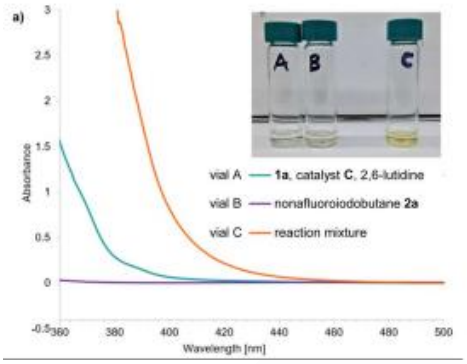
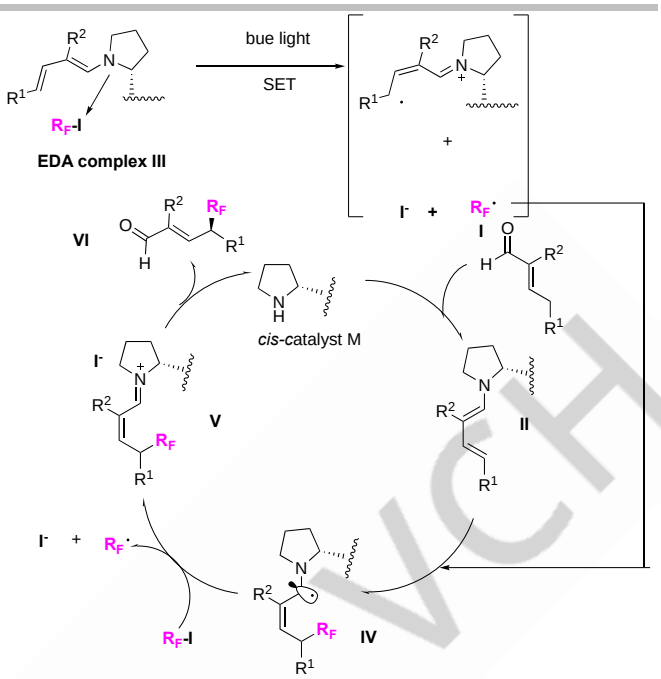


Figure 3. UV-visible spectra of (*E*)-2-phenylpent-2-enal and catalyst (i.e.: (*S*)-2-(*bis*(3,5-bis(trifluoromethyl)phenyl)((trimethylsilyl)oxy)methyl)pyrrolidine), nonafluoroiodobutane, and the mixture (Reproduced from Open Access Article: *Chem. Sci.*, **2023**, *14*, 4923-4927)

The authors[74] through several mechanistic studies (UV-vis. Experiments (Figure 3), quantum yield measurements, etc.) postulated a mechanism such as that shown in Scheme 28. In terms of mechanism, upon light irradiation of the EDA complex **III**, an intracomplex single electron transfer (SET) event occurs, resulting in the generation of perfluoroalkyl radical **I** after cleavage of the C–I bond (Scheme 28). Subsequently, the electrophilic R_F **I** radical is captured by the chiral dienamine **II** in a regio- and stereoselective manner. The ensuing α-amino radical **IV** may then either transfer an electron to compound R_F-I via SET or abstract an iodine atom from R_F-I through atom-transfer radical addition (ATRA), thus regenerating the perfluoroalkyl radical **I** and sustaining the radical chain reaction. Hydrolysis of the resulting iminium ion intermediate **V** liberates product **VI** while regenerating the organocatalyst.



Scheme 28. Postulated reaction mechanism.

5.- Perfluoroalkylation of Isocyanides

Yu and colleagues [77] developed a visible-light induced radical perfluoroalkylation/cyclization cascade reaction to access 2-perfluoroalkylbenzothiazoles/benzoselenazoles mediated by EDA complexes. The reaction employs commercially available fluoroalkyl radical sources such as perfluoroalkyl iodides ($C_nF_{2n+1}I$, n = 3-8, 10), ICF_2COOEt, ICF_2CF_2Cl or ICF_2CF_2Br, simple 2-*iso*cyanoaryl thio or selenoethers as substrates, *N,N,N′,N′*-tetramethylethane-1,2-diamine (TMEDA) as electron donor in THF as solvent, under blue LEDs irradiation in a N_2 atmosphere. With the optimized conditions in hand, the authors [77] performed the synthesis of a different 2-perfluoroalkylbenzothiazoles/benzoselenazoles in very good to excellent yields as shown in Scheme 29. Based on different mechanistic studies carefully performed for the synthesis of 2-perfluoroalkylbenzothiazoles the authors proposed a reaction mechanism shown in Scheme 30. Initially, the interaction between TMEDA and perfluoroalkyl iodide gives rise to a photoactive EDA complex which upon blue LEDs irradiation yields $R_F^{\bullet}$ radicals along with I^- and TMEDA radical cation **A** (Scheme 30). The electrophilic $R_F^{\bullet}$ radical adds to the terminal carbon of the isocyano functionality of the substrate to give imidoyl radical **B** which undergoes an intramolecular cyclization to form sulfonium radical **C**. Beginning from **C** (Scheme 30), there are two potential reaction routes (*I* and *II*, Scheme 30). Through route *I*, **C** undergoes an initial oxidation by TMEDA radical cation **A**, resulting in the formation of sulfonium cation **D** through an intermolecular Single Electron Transfer (SET) process. A nucleophilic attack of I^- on the methyl carbon in cation **D** then gives rise to the formation of the desired reaction product and MeI. In an alternative approach, through pathway *II*, radical **C** reacts with radical cation **A** through a concerted proton-coupled electron transfer (PCET) process. This results in the formation of the

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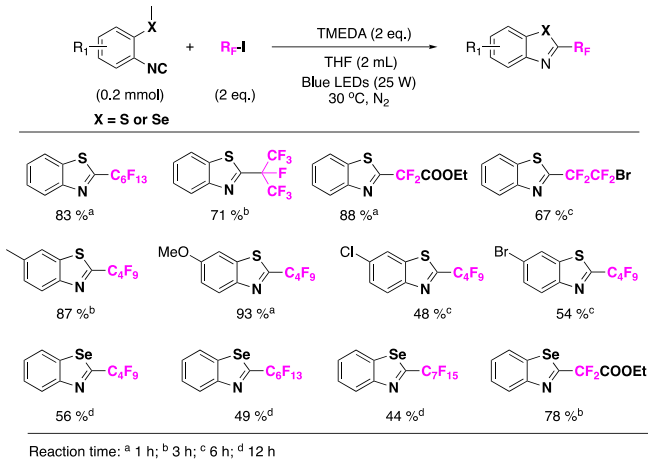
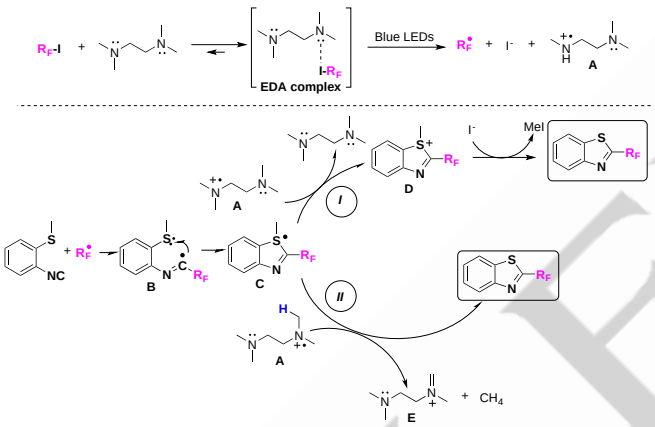
desired reaction product and the iminium ion **E**, accompanied by the liberation of CH_4.[77]



Scheme 29. Selected examples for the visible-light induced radical perfluoroalkylation/cyclization to access 2-perfluoroalkylbenzothiazoles / benzoselenazoles.

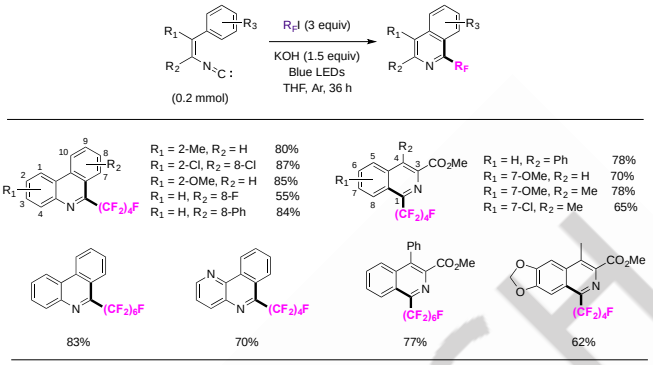


Scheme 30. Proposed reaction mechanism for the visible-light induced radical perfluoroalkylation / cyclization to access 2-perfluoroalkylbenzothiazoles.

In a recently published report, Wang, Neumann, Cheng, Beller,[47] and their colleagues have presented a versatile system aimed at facilitating the addition of perfluoroalkyl radicals to electron-rich π bonds. This technique relies on activating perfluoroalkyl iodides using simple inorganic bases such as potassium hydroxide.

The reaction between perfluoroalkyl iodides and the base results in the formation of an Electron Donor-Acceptor (EDA) complex through halogen bonding interaction. This complexation enables the homolytic cleavage of the relatively weaker C-I bond within the complex under mild irradiation conditions, leading to the simultaneous generation of a perfluoroalkyl radical and an iodine radical.

The authors[47] perform the addition of perfluoroalkyl radical to *iso*nitriles, followed by intramolecular homolytic aromatic substitution (S_HA) to synthesize perfluoroalkylated phenanthridines and *iso*quinolines. As is depicted in Scheme 31, using 3 equivalents of perfluoroalkyl iodide in presence of 1.5 equivalents of KOH under blue light irradiation, several 2-*iso*cyanobiphenyls and vinyl isocyanide bearing various substitution patterns reacted smoothly with IC_4F_9.



Scheme 31. Perfluoroalkyl phenanthridines and *iso*quinolines synthesis assisted by halogen bonding interaction: Selected examples.

6.- Conclusions and Outlook

In this Review perfluoroalkylation reactions of organic compounds by excitation of EDA complexes that have newly been studied and introduced since 2018 are presented. These synthetically useful transformations involve perfluoroalkylations of (hetero)aromatic compounds, unsaturated aliphatic compounds, perfluoroalkylation at the α- and γ-positions of carbonyl compounds, and isocyanides. Alongside these recent studies, comprehensive Tables summarize all the synthetically useful perfluoroalkylation reactions that have been studied through the use of EDA and halogen-bonding complexes through the last decades.

Notoriously, employing EDA complexes to achieve perfluoroalkylation reactions of organic substrates appears to represent a novel approach in perfluoroalkylation chemistry. These methods operate without the need for (metal)organo photocatalysts, utilize visible light irradiation, and in recent instances, demonstrate the viability of employing these complexes in catalytic quantities.

Beyond the typical EDA complexes through halogen bonding interactions, recent years have witnessed the emergence of EDA complexes where the leaving groups in the electron-poor partners were other than the classic iodide from perfluoroalkyl iodides, such as iodonium compounds (i.e.: *bis*(chlorodifluoroacetoxy)iodoarene), sulfonium compounds (such as α-perfluorosulphonylpropiophenone), Umemoto´s reagents, perfluoroacyl pyridinium *N*-oxide salts, etc. These protocols enlarge the scope of generation of perfluoroalkyl radicals, other than the perfluoroalkyl iodides sources. These new sources of EDA complexes function as catalytic electron donors between triaryl amines and α-perfluorosulphonylpropiophenone, establishing as new archetypes in the realm of catalytic complex activation.

Also recently, new enantioselective donors, such as thexyldimethylsilyl protected *cis*-catalyst M for the enantioselective γ-perfluoroalkylation of enals significantly augment the scope and use of the EDA methodology.

It seems appropriate at this stage to envisage the course of progression in the use of EDA complexes for perfluoroalkylation reactions, above all, the invention of new and more versatile leaving groups other than halides, for generating the incipient R_F radical, that could bypass back electron transfer processes more efficiently. Probably, the search for new catalytic donors that conform EDA complexes will pave the way in coming research. Also, a methodology that has not been taken fully advantage of is the installation of flow systems and light-activated EDA complexes, particularly considering that protocols employing EDA complexes take longer times that standard photocatalysis with appropriate (metal)organic photocatalysts, probably due to slow release of the incipient radical and shorter reaction chains.

7.- Acknowledgements

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Keywords: EDA complex • perfluoroalkylation reactions • halogen bonding interactions• perfluoroalkylation of hetero(aromatic) compounds • perfluoroalkylation of carbon-carbon multiple bonds

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REVIEW

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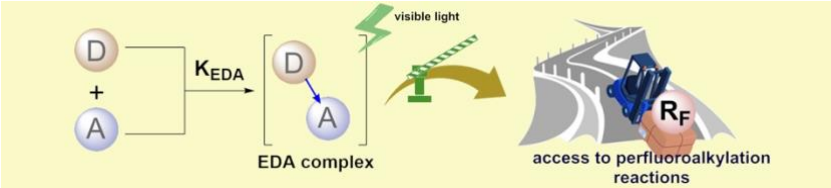

New EDA complexes beyond the classic halogen-bonding interactions between perfluoroalkyl iodides and Lewis bases have emerged as efficient sources of perfluoroalkyl radicals for perfluoroalkylation reactions of organic substrates. The perfluoroalkylation reactions of (hetero)aromatic compounds, unsaturated aliphatic, carbonyl-containing- and isocyanide substrates are reported.