DOI: 10.1070/RCR4833

Progress and prospects in the use of photocatalysis for the synthesis of organofluorine compounds

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Data on the synthesis of fluorinated organic compounds by photocatalysis are systematically considered and analyzed. The attention is focused on the mechanisms of photocatalytic reactions and the selectivity problem.
The bibliography includes 173 references.

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1. Introduction

The development of new methods for introducing a fluorine atom into organic compounds is crucial for advances in pharmaceutical chemistry and agrochemistry and plays a key role in the design of industrially important materials.[1–7] Photocatalysis is considered as one of promising methods for the synthesis of organofluorine compounds. This approach belongs to green methods for the functionalization of organic compounds, because such reactions are initiated by photon absorption and, unlike other catalytic methods, do not produce any environmentally harmful by-products.[8] Photocatalysis involves absorption of a light quantum by a catalyst rather than by a substrate (Fig. 1).[9] Then the photocatalyst activates the substrate to form different intermediates.

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Received 11 May 2018
Translation: T.N.Safonova

The photocatalysis can initiate homolytic C – X bond cleavage giving a radical or electron transfer to form radical cations or anions.[10] Radicals are highly reactive species and are involved in diverse reactions. However, the C – H bond is quite stable, and an organic compound is generally functionalized on thermal activation by the replacement of this bond with other bonds that are more prone to homolysis (C – Br, C – I, C – O, *etc.*) (Fig. 2). Photocatalytic activation can give rise to radicals *via* direct cleavage of a C – H bond and also can involve other reactive intermediate species in the reaction. In photocatalytic reactions, mild activation by a catalyst can be accomplished even under visible light irradiation ($\lambda > 400$ nm).[11–21]

In recent years, photocatalysis has been rapidly developed, as evidenced by a wide number of publications retrieved from the Web of Science database. The number of papers containing the word 'photocatalysis' published in

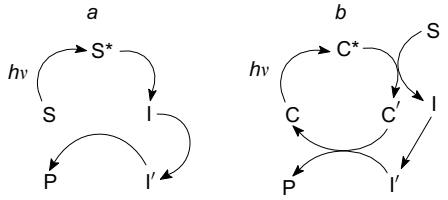


Figure 1. Photochemical (*a*) and photocatalytic (*b*) activation of a substrate (S) with light and a catalyst (C) giving intermediates (I, I′) and a product (P).

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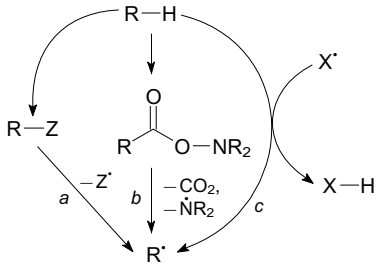


Figure 2. Types of thermal C–H bond activation.
(*a*, *b*) The replacement of a hydrogen atom in this bond by a good leaving group or an atom; *c*, the involvement of the X· radical in homolytic C–H bond cleavage.

the past ten years exceeds 27 000, and photocatalysis is receiving growing interest. Journals publish special issues on different aspects of photocatalysis.† A large number of reviews have recently addressed the use of photocatalysis in the synthesis of organic compounds.[18, 22–43] However, only some of them cover relevant aspects of the introduction of a fluorine atom into organic molecules. The goal of this review is to systematically consider and analyze the data published in the literature in the past 10–15 years on the application of photocatalysis in the synthesis of organofluorine compounds. Earlier studies are cited only when they are required for understanding the issue and highlighting new trends in this field. Special attention is focused on the reaction mechanisms and the selectivity problem of photocatalysis.

The following designations and abbreviations are used:
Acr — acridinium,
^{1}Ad — 1-adamantyl,
ANQ-2-SO_3H — anthraquinone-2-sulfonic acid,
bpy — 2,2′-bipyridine,
CFL — compact fluorescent lamp,
Cp — cyclopentadienyl,
Cy — cyclohexyl,
DABCO — 1,4-diazabicyclo[2.2.2]octane,
DBU — 1,8-diazabicyclo[5.4.0]undec-7-ene,
DCE — 1,2-dichloroethane,
DMAP — 4-dimethylaminopyridine,
DME — dimethyl ether,
DMF — dimethylformamide,
dtb-bpy — 4,4′-di-*tert*-butyl-2,2′-bipyridine,
Eosin Y — 2,4,5,7-tetrabromofluorescein disodium salt,
ET — electron transfer,
glyme — 1,2-dimethoxyethane,
HAT — hydrogen atom transfer,
HBpin — 4,4,5,5-tetramethyl-1,3,2-dioxaborolane,
Hex — n-hexyl,
LED — light-emitting diode,
Mes — mesityl,
Mes-Acr$^+$ — 9-mesityl-10-methylacridinium,
Naph — naphthyl,
nc-ZnS — nanocrystalline ZnS,
NFSI — *N*-fluorobenzenesulfonimide,
NPhth — phthalimido,
P — product,
phen — 1,10-phenanthroline,
PhthSCF_3 — trifluoromethylthiophthalimide,
ppyH — 2-phenylpyridine,
PQ — 9,10-phenanthrenequinone,
PyH — pyridine,
RB — Rose Bengal,
rt — room temperature,
S — substrate,
Selectfluor — 1-chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(tetrafluoroborate),
SET — single electron transfer,
TBADT — tetrabutylammonium decatungstate,
TEMPO — (2,2,6,6-tetramethylpiperidin-1-yl)oxyl,
Tf — triflate,
Th — thienyl,
TMEDA — tetramethylethylenediamine,
TMP — 2,2,6,6-tetramethylpiperidine,
Ts — tosyl,
TSSP — tetra(*p*-sulfonatophenyl)porphyrin,
Um — Umemoto reagent [2,8-difluoro-*S*-(trifluoromethyl)dibenzo[*b*,*d*]thiophenium trifluoromethanesulfonate].

† See, for example, *Eur. J. Org. Chem.*, (15) (2017), *Chin. J. Chem.*, (2) (2017), *Acc. Chem. Res.*, (10) (2016).

2. Classification of photocatalysts and their characteristics

Photocatalysts used in the synthesis of organofluorine compounds can be classified according to their chemical

Table 1. Electrochemical parameters of the ground and excited states of selected photocatalysts and the absorption maxima or absorption ranges (see [a]).[23, 26, 32]

Photocatalyst (PC)	E_{red} (PC/PC$^{-\bullet}$)	E_{ox} (PC / PC$^{+\bullet}$)	E^*_{red} (PC*/PC$^{-\bullet}$)	E^*_{ox} (PC$^{+\bullet}$/PC*)	Absorption /nm (see [b])
Eosin Y	−1.14	0.72	1.18	−1.60	539
Rose bengal	−0.78	–	2.32	–	320–470
Benzophenone	−1.68	–	1.55	–	320–380
Phenanthrene	−2.49	1.83	1.10	−1.76	300–350
9,10-Dicyanoanthracene	−0.89		1.97		330–440
10-Methylacridinium cation	−0.43	–	2.32	–	320–470
$Ru(bpy)_3^{2+}$	−1.33	1.29	0.84	−0.86	450
$Ir(ppy)_3$	−2.19	0.77	0.31	−1.73	375

[a] The potentials are expressed in volts with respect to calomel electrode. [b] The absorption maximum or absorption range for irradiation used in the reaction.

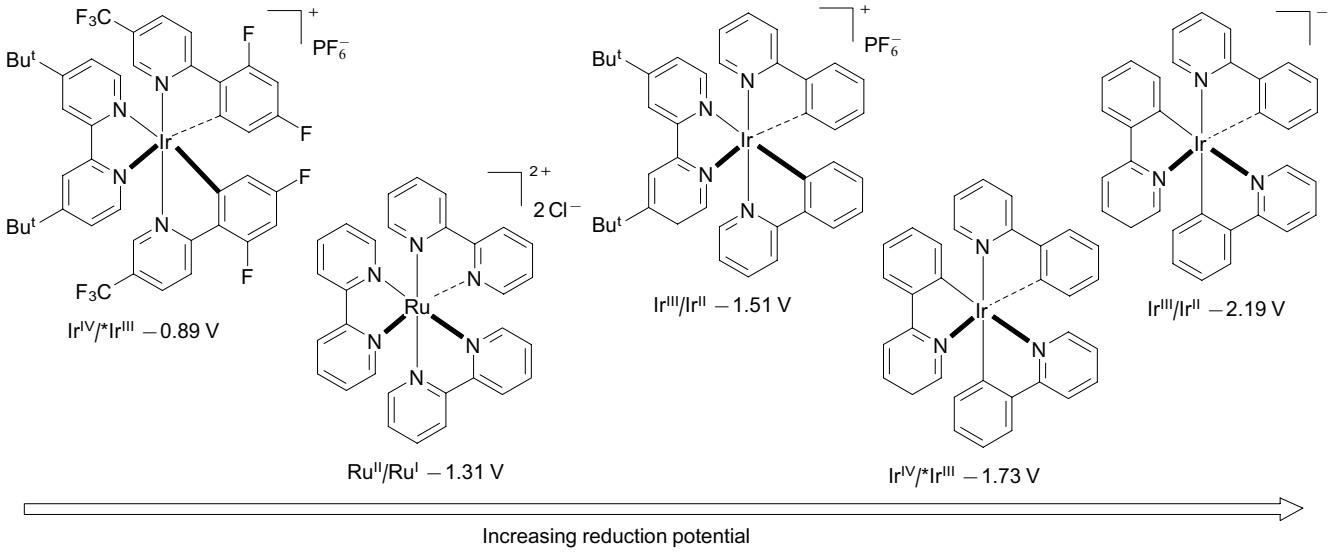
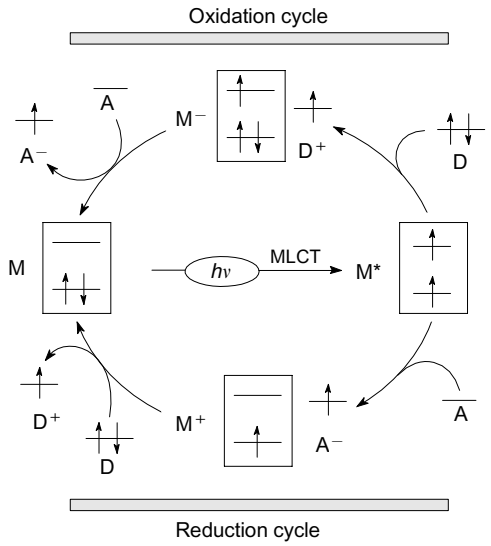


Figure 3. Influence of the ligand structure and the nature of metal on the reduction potential of the photocatalyst.



D is a donor, A is an acceptor, MLCT is metal-to-ligand charge transfer

Figure 4. Visible light-driven photocatalytic oxidation and reduction cycles.

nature and structure into inorganic, organic and organometallic ones. Inorganic photocatalysts [$Na_4W_{10}O_{32}$, $UO_2(NO_3)_2 \cdot 6H_2O$, TiO_2, ZnS, *etc.*] are rather rarely used in the synthesis of organofluorine compounds and generally require hard radiation for activation. Organic and organometallic photocatalysts are more widely employed since they allow fine tuning of electrochemical parameters and the use of different light sources depending on the characteristics of the absorption range or absorption maximum of the catalyst. Selected characteristics of the most popular catalysts are summarized in Table 1.[23,26,32] Most organic compounds are colourless and cannot absorb in the visible region ($\lambda > 400$ nm). By contrast, organometallic catalysts are generally capable of absorbing visible light. The redox potential of the catalyst required for the reaction can be controlled by varying the ligands and metal in organometallic photocatalysts (Fig. 3).[13,44]

The redox characteristics of a large number of organometallic photocatalysts capable of absorbing visible light are reported in reviews.[17,25]

Upon light excitation, the photocatalyst can act as an oxidizing or reducing agent depending on its structure, the fluorinating agent, the substrate and reaction conditions. Photocatalytic properties of organometallic catalysts, including their excited states, were studied in sufficient detail. These catalysts can be involved in both oxidation and reduction cycles.[32] The schematic representation of the action of these photocatalysts is shown in Fig. 4. When exposed to visible light, the catalyst is transformed into the triplet excited state, the lowest- and highest-energy singly occupied levels being involved in the oxidation or reduction, respectively, with the participation of a donor or an acceptor. This is followed by fluorination of the substrate with a fluorinating agent and the reduction of the catalyst.

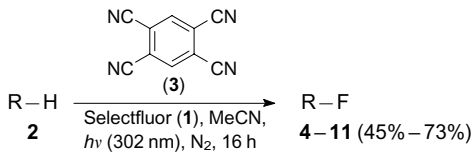
Numerous examples of application of photocatalysts of different nature, including organometallic catalysts, in the synthesis of organofluorine compounds are given below.

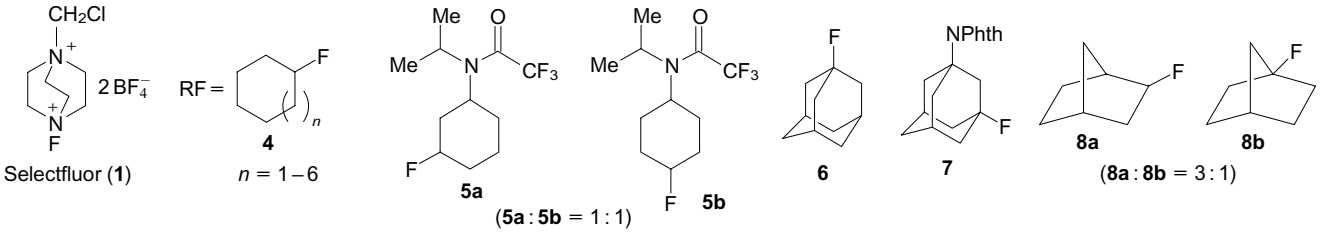
3. Formation and transformation of the F–C(sp^3) bond

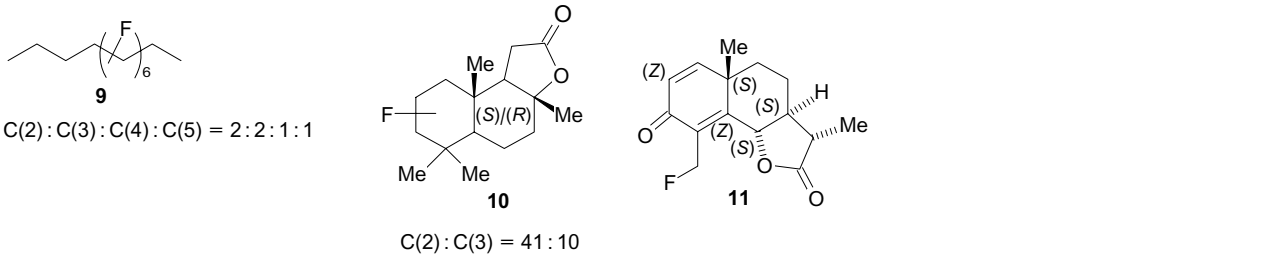
Most photocatalytic transformations of the C(sp^3)–H bond into C(sp^3)–F were performed using NF reagents, with 1-chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(tetrafluoroborate) (Selectfluor) (**1**) being most commonly applied.[45–50] The photocatalytic replacement of a C–H bond by C–F in cyclic and natural compounds **2** was accomplished using Selectfluor in the presence of 1,2,4,5-tetracyanobenzene (**3**) giving products **4**–**11** in good yields with moderate selectivity (Scheme 1).[51]

It is assumed that upon photoexcitation, tetracyanobenzene (**3**) oxidizes the substrate to radical cation **12**. The reaction of the latter with the solvent affords radical **13**, which abstracts a fluorine atom from Selectfluor (**1**) (Scheme 2).

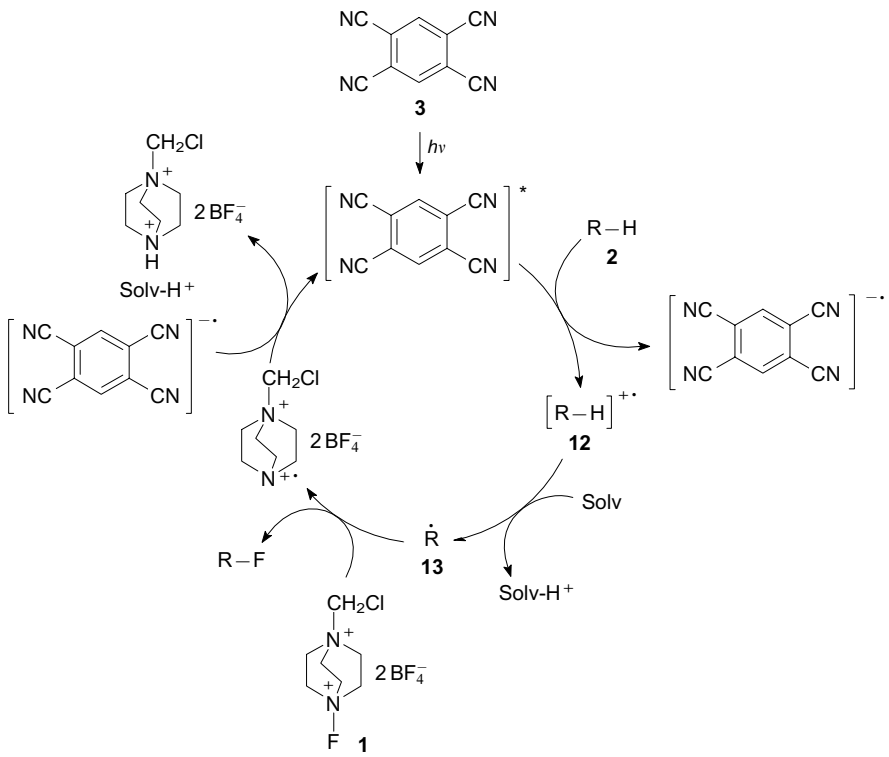
Scheme 1







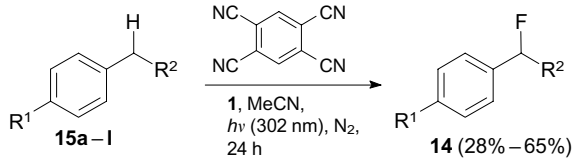
Scheme 2



In many cases, the selectivity of fluorination is determined by relative stability of the resulting alkyl radicals (tertiary > secondary > primary), the involvement of the radical site in the conjugation and, besides, by steric factors. For example, n-dodecane is fluorinated predominantly at the atoms from C(2) to C(5) rather than at C(1) (product **9**). Exceptions are the fluorination of norbornane, in which the unfavourable formation of a radical site at the bridgehead position could occur (products **8a**,**b** are formed instead), and the fluorination of compounds in which the tertiary or secondary carbon centre is shielded by a bulky group (products **5**, **10**, **11**). The predominant formation of compound **11** can be attributed to high stability of the corresponding allyl-type radical taking into account steric accessibility of the methylene moiety.

Benzyl fluorides **14** were synthesized under similar conditions (Scheme 3).[52] The reaction proceeds with satisfac-

Scheme 3



14: R^1 = H: R^2 = H (**a**), Me (**b**), CH_2OAc (**c**),  (**d**), CH_2CHO (**e**), $CH_2CH{=}CHCO_2H$ (**f**), $CH_2C(O)CH_2CH_2Ph$ (**g**), CH_2SO_2Ph (**h**); R^2 = H: R^1 = Ph (**i**), Pr^i (**j**), CN (**k**), Br (**l**)

tory selectivity in moderate yields, the lowest yields being observed for compounds **14k** (28%) and **14l** (36%).

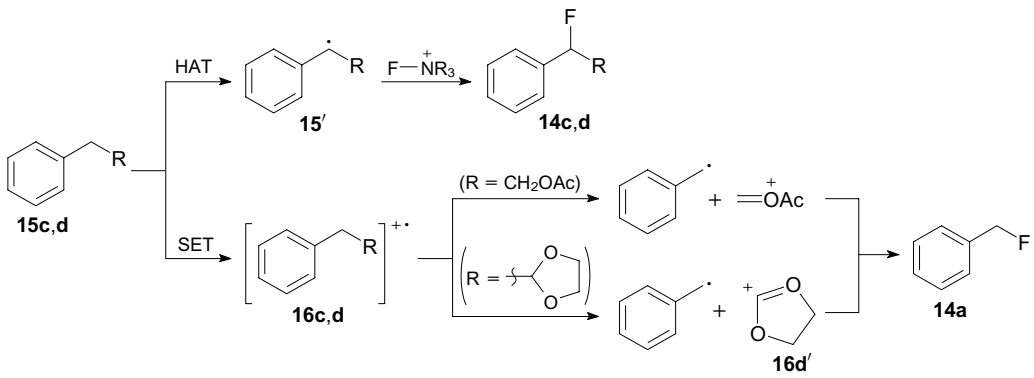
In order to elucidate the mechanism of this reaction, the following model compounds were used: 1-phenylethyl acetate (**15c**) and 2-benzyl-1,3-dioxolane (**15d**). It was expected that these compounds can form radical cations accompanied by elimination of benzyl radical **15′** and stable cations. In the case of radical cation **16d** generated from compound **15d**, the elimination should occur more easily due to the formation of more stable cation **16d′** (Scheme 4).

The photofluorination of compounds **15c**,**d** affords a mixture of fluorinated derivatives **14c** : **14a** and **14d** : **14a** in a ratio of ~5 : 1 and 2 : 1, respectively. This is consistent with the SET radical-cation mechanism of the reaction. This mechanism was also proposed for the photofluorination of 1,4-dioxaspiro[4.5]decane derivatives **17a**–**f** (Scheme 5).[53]

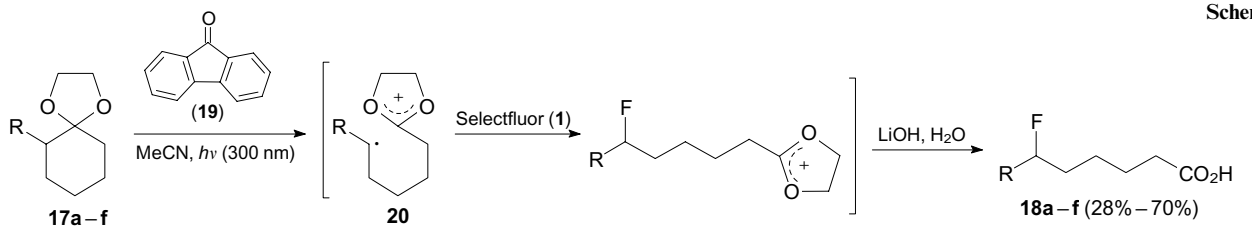
Among the photocatalysts used (1,2,4,5-tetracyanobenzene, 1,4-dicyanobenzene, acetophenone, anthraquinone, xanthone, 9-fluorenone), 9-fluorenone (**19**) provided the highest yields of acids **18a**–**f**. High selectivity of the reaction is due to structural features of the starting compounds, the oxidation of which produces stable radical cation **20**.

The visible light-induced photocatalytic conversion of the C–H bond in the benzylic position of compounds **15** and **21** was performed using Selectfluor (**1**) in the presence of ketones as photocatalysts (Scheme 6).[54] 9-Fluorenone (**19**) catalyzes mainly the formation of monofluorinated

Scheme 4

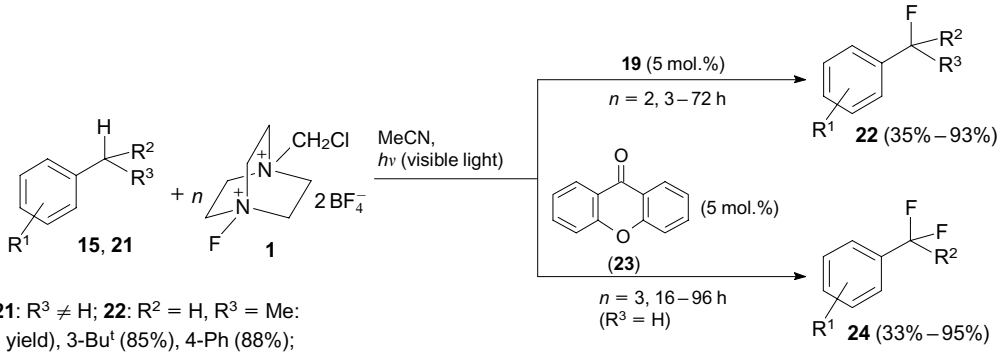


Scheme 5



R = Ph (**a**), 4-MeC_6H_4 (**b**), 4-$Bu^tC_6H_4$ (**c**), 4-FC_6H_4 (**d**), 4-ClC_6H_4 (**e**), 2-BrC_6H_4 (**f**)

Scheme 6

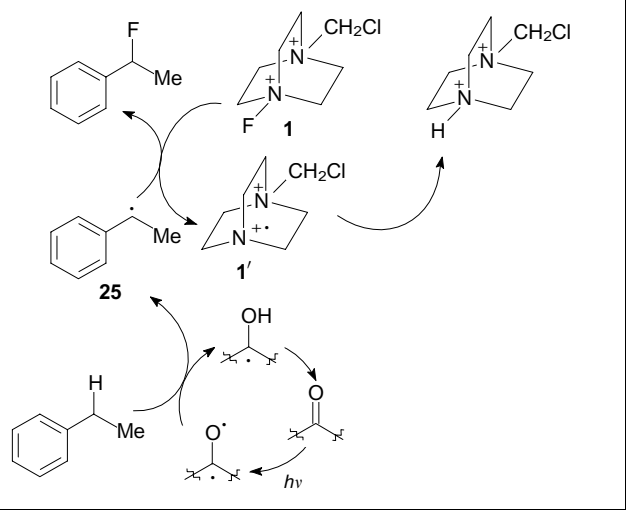


15: R^3 = H, **21**: $R^3 \neq$ H; **22**: R^2 = H, R^3 = Me:
R^1 = H (85% yield), 3-Bu^t (85%), 4-Ph (88%);
R^1 = R^2 = H, R^3 = CH_2Cl (35%); R^1 = 4-Ph, R^2 = R^3 = H (93%);
R^2 = R^3 = Me: R^1 = H (72%), 4-Ph (64%);
24: R^2 = Me: R^1 = H (83%), 3-Bu^t (33%), 4-F (95%), *etc.*

derivatives **22**, while xanthone (**23**) catalyzes the formation of difluorinated products **24**. The employment of 4,4′-dimethoxybenzophenone or 3,6-dimethoxyxanthone results in a decrease in the selectivity of the reaction.

It was assumed that the reaction affords benzyl radical **25** and radical cation **1′** generated through transformation of Selectfluor (**1**) (Scheme 7).

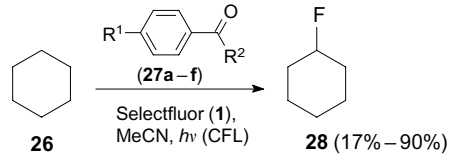
Scheme 7



Interestingly, the photocatalytic photofluorination of different benzyl compounds with reagents **1** in a continuous-flow system using a compact fluorescent lamp (CFL, 30 W) as a light source in the presence of xanthone (**23**) affords exclusively monofluorinated products in 60%–89% yields.[55]

Ketones **27a**–**f** proved to be efficient photocatalysts for the fluorination of cyclohexane (**26**) with Selectfluor (**1**) promoted by CFL irradiation (Scheme 8).[56] The yield of fluorocyclohexane **28** significantly depends on the structure of the catalyst and is generally 59%–90%. The lowest yields are observed with 4-nitroacetophenone (**27c**, 18%) and 4,4′-bis(dimethylamino)benzophenone (**27f**, 17%).

Scheme 8

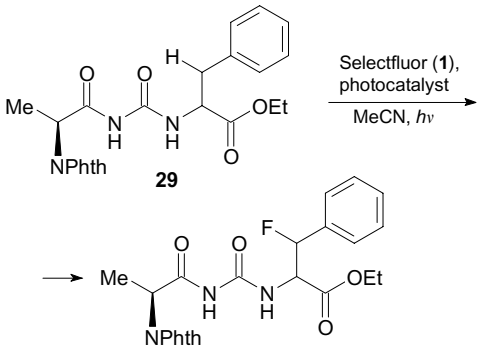


27: R^2 = Me: R^1 = H (**a**), OMe (**b**), NO_2 (**c**), Me (**d**), CF_3 (**e**);
$R^1 = Me_2N$, R^2 = 4-$Me_2NC_6H_4$ (**f**)

Amino acids, peptides and their derivatives, *e.g.*, dipeptide **29**, are also photofluorinated with Selectfluor at the benzyl moiety with high regioselectivity. The efficiency of fluorination depends on the structure of the substrate and the catalyst (**3**, **19**, **23**, **30**–**34**) and on the light source, the highest yields of fluorinated products being achieved in the presence of visible light-activated 5-dibenzosuberenone as the photocatalyst (Scheme 9).[57]

As was shown by the photochemical fluorination of phenylalanine derivatives, phthalimide and trifluoroacetyl moieties are the most efficient N-protecting groups, while

Scheme 9

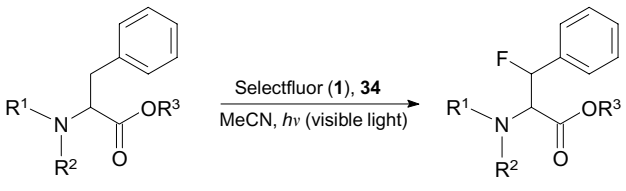


Photocatalyst (mol.%)		Light wavelength /nm	Yield (%)
1,4-Dicyanobenzene (**30**)	(10)	300	18
1,4-Dicyanobenzene (**30**)	(20)	300	42
1,2,4,5-Tetracyano-	(5)	300	21
benzene (**3**)	(10)	300	33
1-Cyanonaphthalene (**31**)	(20)	300	Traces
Benzophenone (**27g**)	(20)	300	40
9-Fluorenone (**19**)	(20)	300	10
Xanthone (**23**)	(10)	300	39
Xanthone (**23**)	(5)	Visible light (CFL, 14 W)	39
Anthraquinone (**32**)	(10)	300	38
Anthraquinone (**32**)	(20)	300	42
9,10-Phenanthrene-	(10)	300	22
quinone (**33**)	(20)	300	21
5-Dibenzosuberenone (**34**)	(5)	Visible light (CFL, 14 W)	73

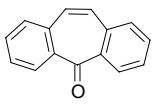
methyl or ethyl groups involved in the ester moiety CO_2R^1 are the best C-protecting groups (Scheme 10).

Anthraquinone (**32**) proved to be an efficient photocatalyst for selective fluorination of unactivated alkanes and cycloalkanes with Selectfluor under light irradiation with a fluorescent lamp (11 W). This method was used to synthesize fluorinated compounds **36**–**38** in 39%–68% yields.[58]

Scheme 10

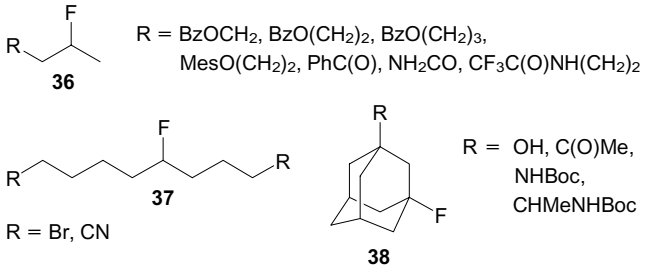


34 =



NR^1R^2	R^3	Yield (%)	NR^1R^2	R^3	Yield (%)
$NHC(O)CF_3$	Me	74	NPhth	Bu^t	31
$NHC(O)CF_3$	Et	60	NPhth	Ph_3C	28
NPhth	Me	78	NPhth	^{1}Ad	20
NPhth	Et	80			

Structures 36 – 38



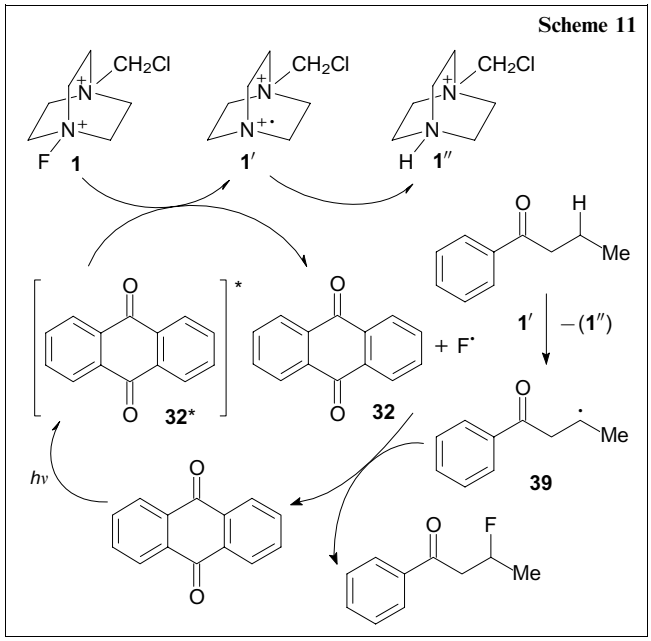
The presumptive mechanism involves energy transfer between anthraquinone (**32***) in the triplet state and Selectfluor (**1**) followed by the C – H bond cleavage in the substrate and generation of radical **39**, which reacts with a fluorine atom (Scheme 11). The key step is the reaction of bulky radical dication **1′** with the substrate at the most sterically accessible position to form a secondary or tertiary radical. An interesting feature of this reaction is the formation of radical **39** containing the radical site in the β rather than α position with respect to the carbonyl group.

The fact of 'avoidance' of the carbonyl group was observed in other photocatalytic fluorination reactions of aliphatic and cyclic carbonyl compounds. It was shown that the carbonyl group deactivates the adjacent position towards photocatalytic fluorination of natural (*e.g.*, steroid **40**) and other compounds with a rigid mono-, di- or polycyclic structure, as well as exocyclic aliphatic ketones, a hydrogen atom being replaced with a fluorine atom mainly in the β or γ position with respect to the C=O group (Scheme 12, compounds **41** – **48**).[59]

Apart from Selectfluor (**1**), *N*-fluorobenzenesulfonamide (NFSI, **49**) can be employed as a fluorine source.[60] The reaction using compound **49** in the presence of tetrabutylammonium decatungstate (TBADT, **50a**) as the photocatalyst produced fluorinated benzyl derivatives **22a** – **e**, as well as cyclic and acyclic compounds **51** – **60** (Scheme 13).[19, 61]

In the case of cyclic and acyclic compounds, higher selectivity of fluorination is achieved by introducing a fluorine atom into sterically accessible methine or methylene moieties, the sites distant from the carbonyl group being preferable.

Scheme 11

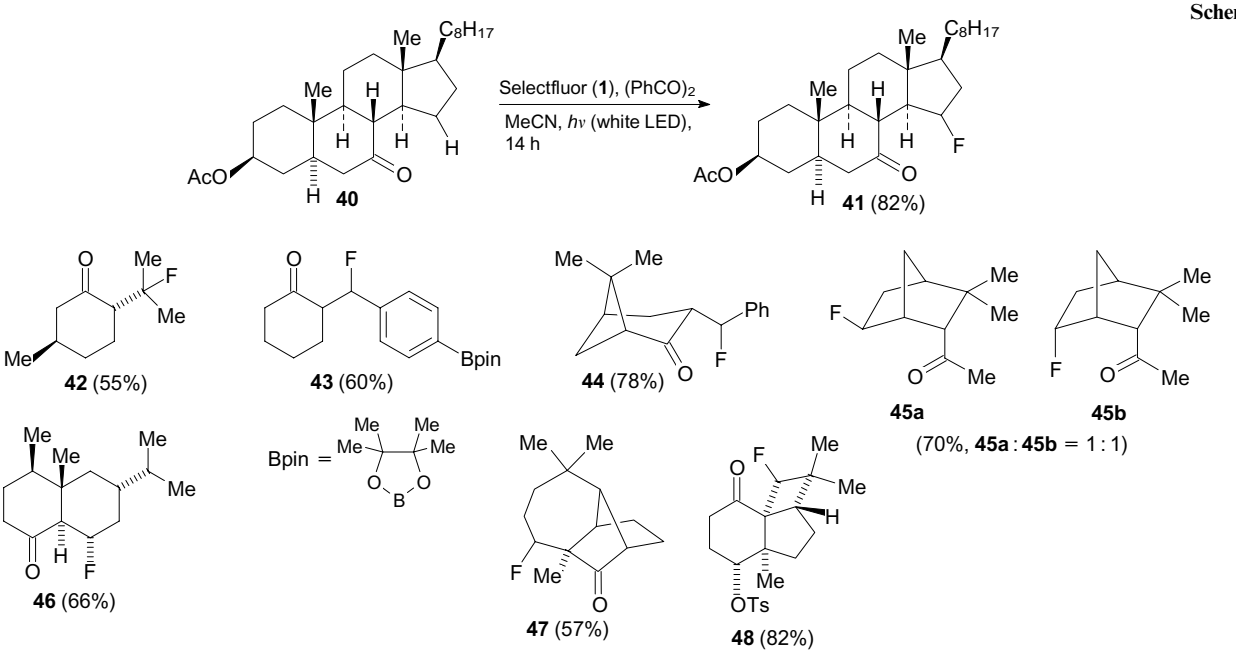


Acridinium salts **61** can be employed as photocatalysts for selective fluorination of alkylbenzenes with Selectfluor.[62] This method was used to synthesize a wide range of fluorinated benzyl derivatives **22** (Scheme 14).

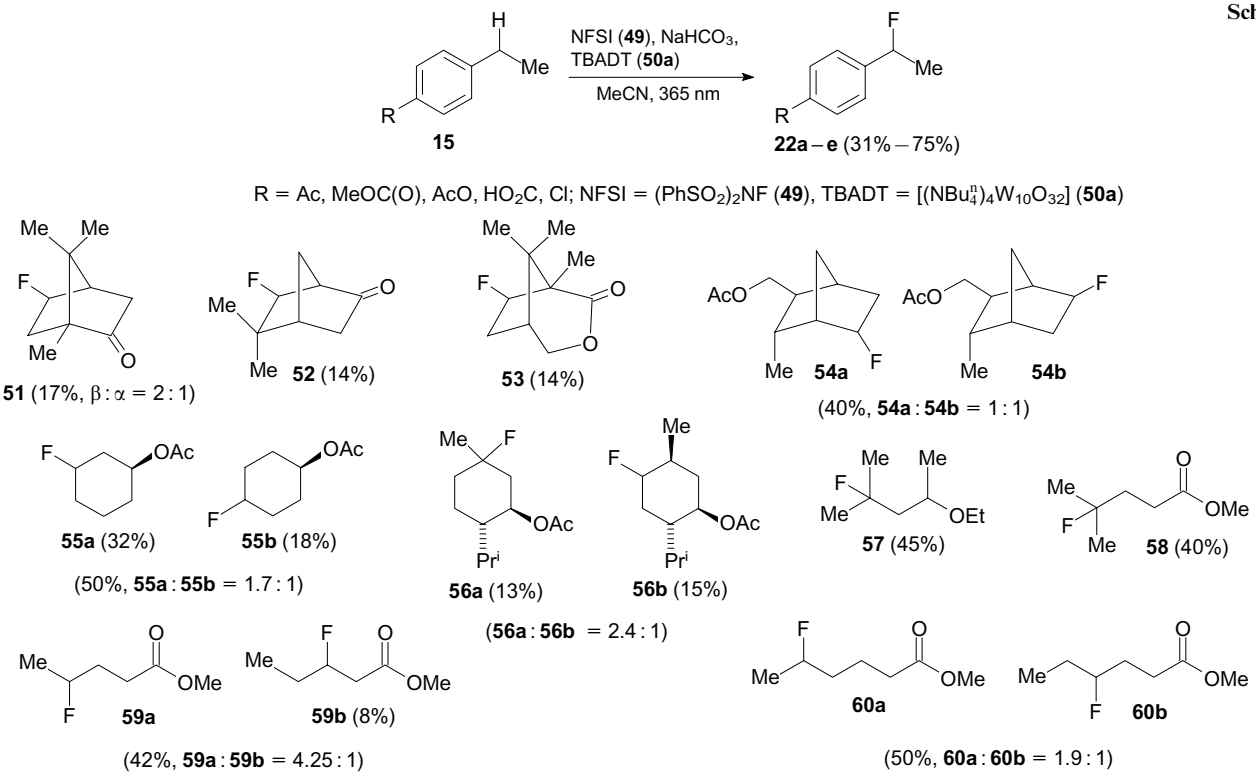
Besides the formation of benzyl radicals **A**, this reaction is assumed to involve benzyl cations **B** (Scheme 15). A significant isotope effect ($k_H/k_D = 2.3$) observed in the fluorination of compounds $PhCR_2Me$ (R = H, D) indicates that the C – H bond cleavage is the rate-limiting step.

A photocatalyst based on uranyl nitrate hexahydrate (**62**) proved to be highly active for fluorination of alkanes and cycloalkanes with NFSI (**49**) but it is unsuitable for fluorination of simple ketones and alkylarenes (Scheme 16).[63] The latter fact is apparently attributed to high oxidizing ability of the $[UO_2]^{2+}$ dication (similar to that of F_2) and also to ability of simple ketones and

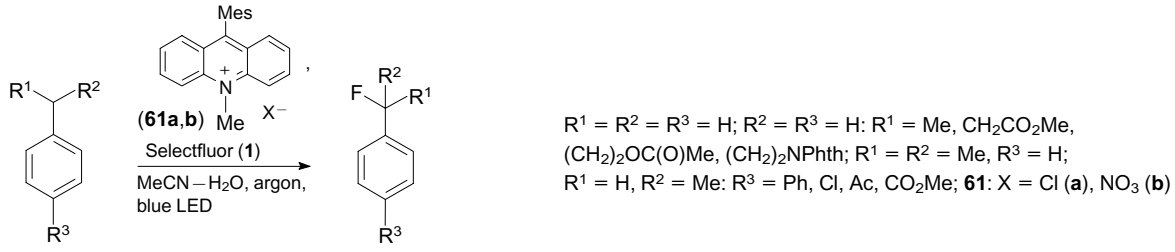
Scheme 12



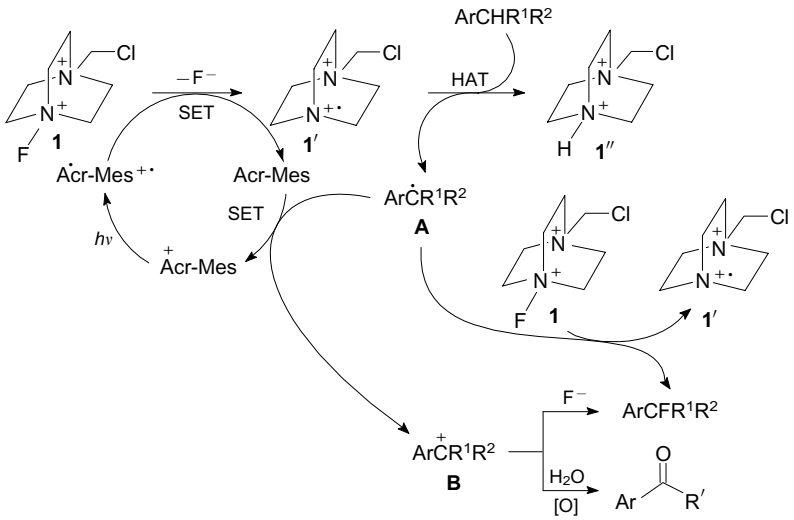
Scheme 13



Scheme 14



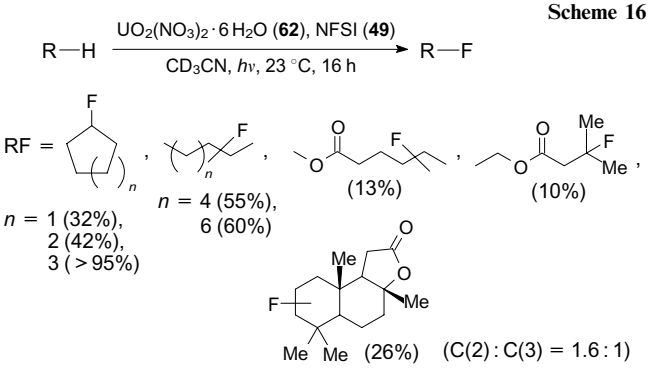
Scheme 15



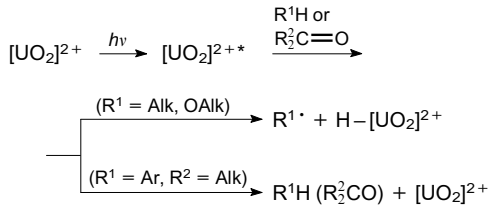
alkylarenes to efficiently quench the excited state $[UO_2]^{2+*}$ (Scheme 17).

A combination of the photocatalyst TBADT (**50b**) with NF reagents [NFSI (**49**) or Selectfluor (**1**)] was applied to introduce a fluorine atom into compounds with an unactivated C(sp^3)–H bond (derivatives of leucine, furan, bicyclo[2.2.1]heptane, *etc.*).[60] In particular, the photocatalytic fluorination of leucine methyl ester salt **63** affords γ-fluorinated derivative **64** (in high yield), which is a crucial

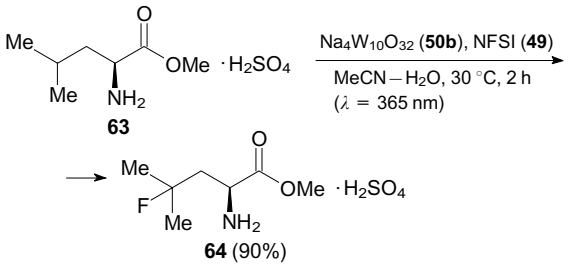
Scheme 16



Scheme 17



Scheme 18

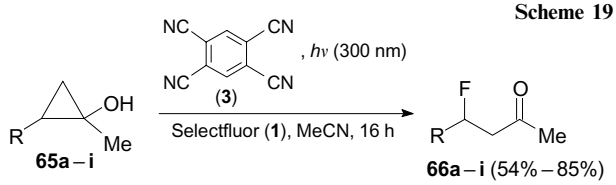


intermediate in the synthesis of odanacatib, a promising agent for the treatment of osteoporosis (Scheme 18).[64]

Methods were developed for the photocatalytic fluorination accompanied by the C–C bond cleavage in the cyclopropane moiety. Thus, the photocatalytic reaction of 1-hydroxy-1-methyl-2-R-cyclopropanes **65a–i** with tetracyanobenzene (**3**) and Selectfluor (**1**) gives β-fluorinated carbonyl compounds **66a–i** in good yields with high regioselectivity (Scheme 19).[65] The proposed mechanism involves the photoexcitation of the catalyst, electron transfer giving radical cation **65′** and cyclopropane ring opening accompanied by the CR–C(Me)OH bond cleavage (Scheme 20). High selectivity of the reaction is apparently attributed to the formation of the secondary radical site due to the cleavage of this bond.

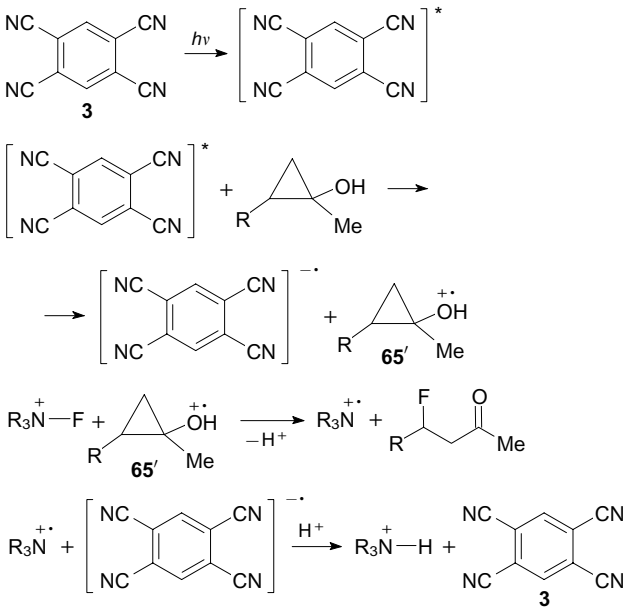
The C–F bond formation *via* the C–C bond cleavage can occur through decarboxylation. The first example of

Scheme 19



R = Cy (**a**), cyclo-C_8H_{15} (**b**), cyclo-$C_5H_9CH_2$ (**c**), cyclo-$C_6H_{11}CH_2$ (**d**), Ph (**e**), $PhCH_2$ (**f**), $Ph(CH_2)_2$ (**g**), $Me(CH_2)_4$ (**h**), $Me(CH_2)_8$ (**i**)

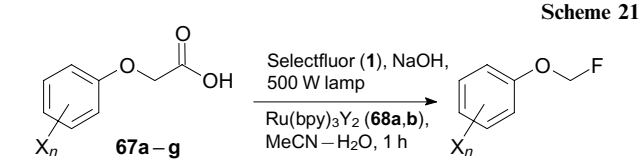
Scheme 20



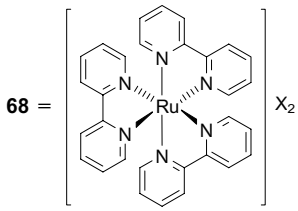
photocatalytic fluorination involving decarboxylation of aryloxyacetic acids **67a–g** with Selectfluor was reported by Rueda-Becerril *et al.*[66] The authors used the complexes $Ru(bpy)_3Cl_2$ (**68a**) and $Ru(bpy)_3(PF_6)_2$ (**68b**) as the photocatalyst (Scheme 21).

The proposed mechanism involves the oxidation of anion **69**, decarboxylation of intermediate **70** giving radical **71** and the reaction of the latter with a fluorinating agent (**1**) (Scheme 22) producing fluoromethoxy ethers **72a–h**.

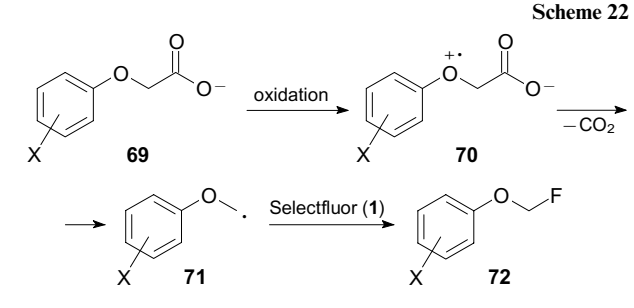
Scheme 21



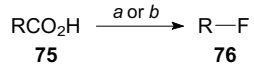
X_n = H (**a**), 4-Ph (**b**), 4-Bu^t (**c**), 4-F (**d**), 4-Br (**e**), 2,4-Bu^t_2 (**f**), 2,4,6-Me_3 (**g**);



Scheme 22

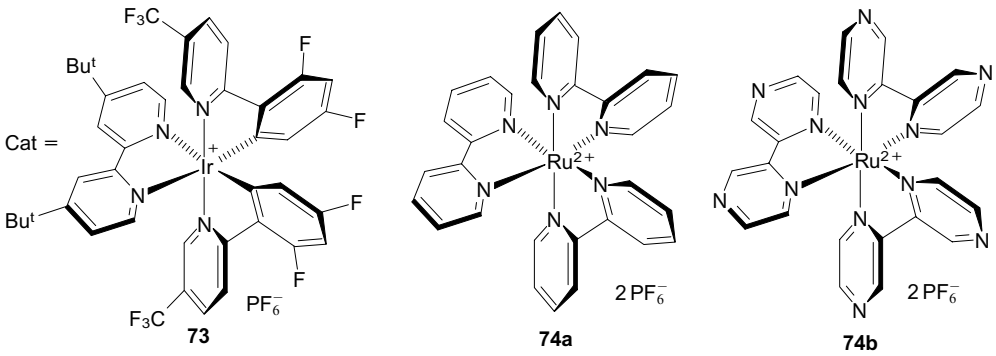


Scheme 23



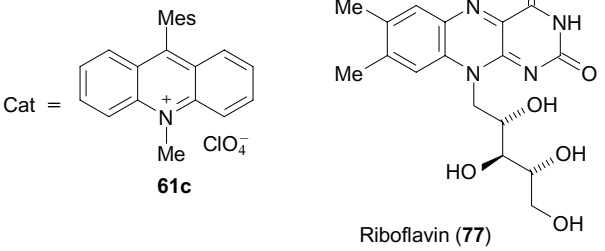
75 **76**

(*a*) Cat **73**, **74a**,**b** (1 mol.%), Selectfluor, LED (34 W), MeCN – H_2O (3 : 1), rt, 6 h

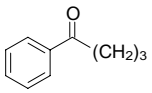
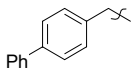
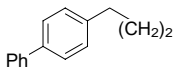
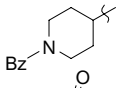
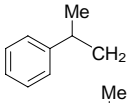
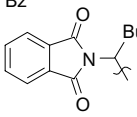
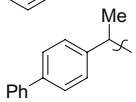
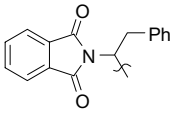
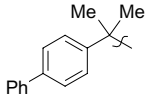
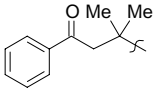
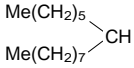
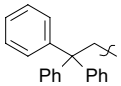
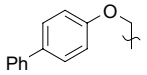
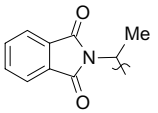
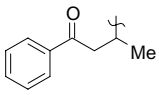
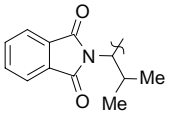
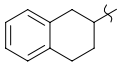
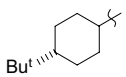


73 **74a** **74b**

(*b*) Cat **61c** or **77** (5 mol.%), Selectfluor, Cs_2CO_3, CFL (23 W), MeCN – H_2O (1 : 1), rt, 4 – 72 h

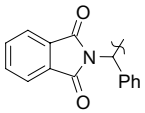
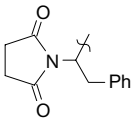
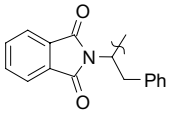
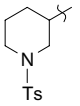
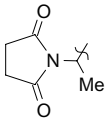
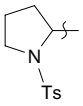
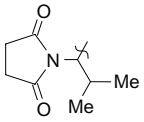
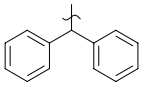
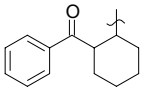
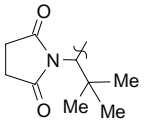
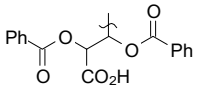


61c Riboflavin (**77**)

Compounds **75**, **76**	R	Conditions	Yield (%)	Compounds **75**, **76**	R	Conditions	Yield (%)
a		*a*	77	**m**		*a*	79
b		*a*	87	**n**		*a*	82
c		*a*	81	**o**		*a*	90
d		*a*	92	**p**		*a* *b*	90 96
e		*a*	85	**q**		*a* *b*	90 85
f		*a*	90	**r**		*b*	82
g	$[Me(CH_2)_4]_2CH$	*a*	83	**s**		*b*	55
h		*a*	82				
i		*a* *b*	99 73	**t**		*b*	62
j		*a*	96	**u**		*b*	98
k		*a*	71				
l		*a*	70				

Continued in the next page

Scheme 23 (continued)

Compounds **75**, **76**	R	Method	Yield, %	Compounds **75**, **76**	R	Method	Yield, %
v		*b*	98	**aa**		*b*	85
w		*b*	94	**ab**		*b*	71
x		*b*	87	**ac**		*b*	36
y		*b*	81	**ad**		*b*	45
				ae		*b*	53
z		*b*	76	**af**		*b*	51

Meanwhile, the use of iridium (**73**) and ruthenium (**74a**,**b**) photocatalysts for fluorination of aliphatic carboxylic acids **75a**–**g** with Selecfluor, which also proceeds through decarboxylation, makes it possible to substantially expand the range of substrates, resulting in the formation of structurally different alkyl and cycloalkyl fluorides **76a**–**g** in high yields (Scheme 23, conditions *a*).[67] It should be noted that neither the degree of replacement of the alkyl moiety R nor the presence of the heteroatom in the α or β position to the carboxyl group in starting acid **75** has significant effect on the efficiency of fluorination.

The mechanism of photofluorination proposed by Ventre *et al.*[67] involves the formation of alkyl or cycloalkyl radicals **A** and radical dication **1′** *via* the transformation of Selectfluor (**1**) (Scheme 24).

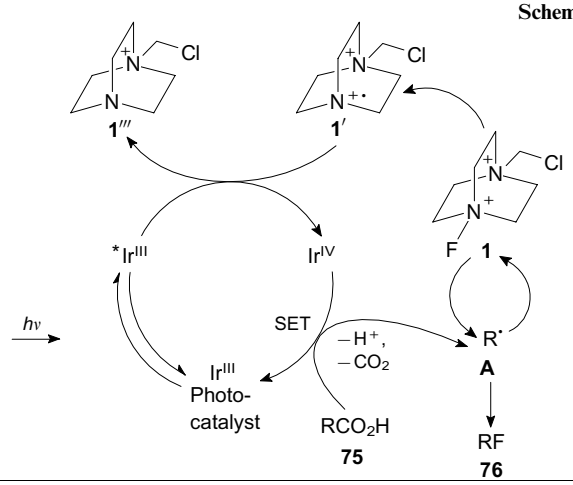
Not only transition metal compounds but also organic photooxidants, such as 9-mesityl-10-methylacridinum perchlorate (**61c**) or riboflavin (**77**), can be employed as photocatalysts for decarboxylative fluorination of aliphatic carboxylic acids **75i**,**r**,**s**, **75ad**–**af** and N-protected amino acids **75p**,**q**,**t**–**ac** with Selectfluor (**1**) (see Scheme 23, conditions *b*).[68]

The UV-induced photocatalytic transformation of 2,2-difluoroacetophenone **27g** adsorbed on a semiconductor (TiO_2) surface is also based on the $C(sp^3)-F$ bond transformation into $C(sp^3)-H$ (Scheme 25).[69]

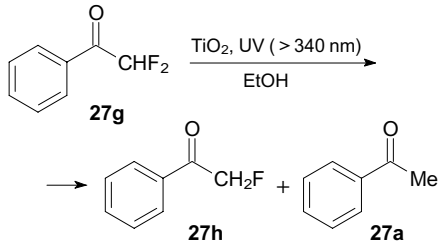
The proposed mechanism of the formation of monofluoride **27h** involves the following successive steps: reduction, protonation, F^- elimination and keto–enol rearrangement (Scheme 26).

Therefore, photocatalysis can be used to efficiently transform $C(sp^3)-H$, $C(sp^3)-C$ and $C(sp^3)-O$ bonds into the $C(sp^3)-F$ bond and allows the defluorination of fluoroalkyl derivatives, the selectivity of the reaction being often determined by stability of the resulting radical.

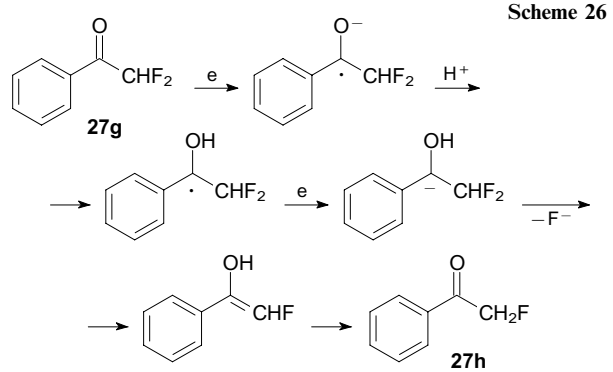
Scheme 24



Scheme 25



Scheme 26

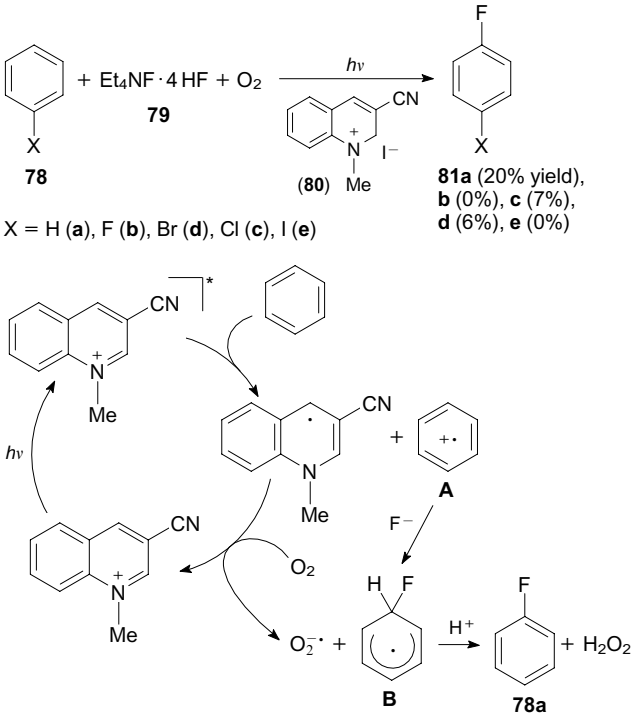


4. Formation and transformation of the F – C(sp²) bond

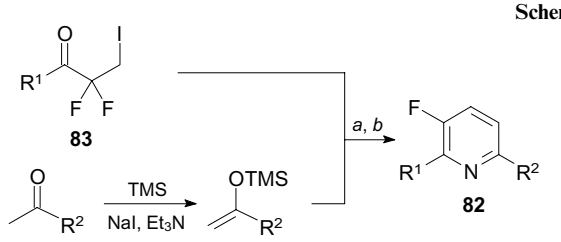
Data on the photocatalytic C(sp²) – H bond transformation into C(sp²) – F in aromatic compounds are limited to photocatalytic fluorination of benzene and its halogenated derivatives **78** with $Et_4NF \cdot 4HF$ (**79**) in the presence of 3-cyano-1-methylquinolinium iodide (**80**) as the photocatalyst. The reaction results in monofluorination giving fluorobenzenes **81** as the final products in low yield (Scheme 27).[70] Fluoro- and iodobenzenes do not undergo this reaction. The proposed mechanism involves the formation of arene radical cation **A**, which reacts with a fluoride anion to form radical **B**. The hydrogen abstraction from the latter by the $HO_2^{\bullet}$ radical generated *via* protonation of $O_2^{-\bullet}$ affords fluorobenzene **78a** and a hydrogen peroxide molecule.

The C(sp²) – F bond can be formed by means of multicomponent cyclization. Dilman and co-workers[71] developed a method for the synthesis of 3-fluoropyridines **82** based on the coupling of α,α-difluoro-β-iodoketones **83**

Scheme 27

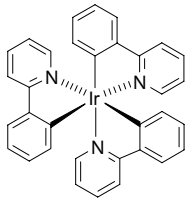


Scheme 28



(*a*) Ir(ppy)₃ (**84**) (0.3 мол.%), PPh_3,  (**85**), *hν* (blue LED), DMF, rt, 15 h;

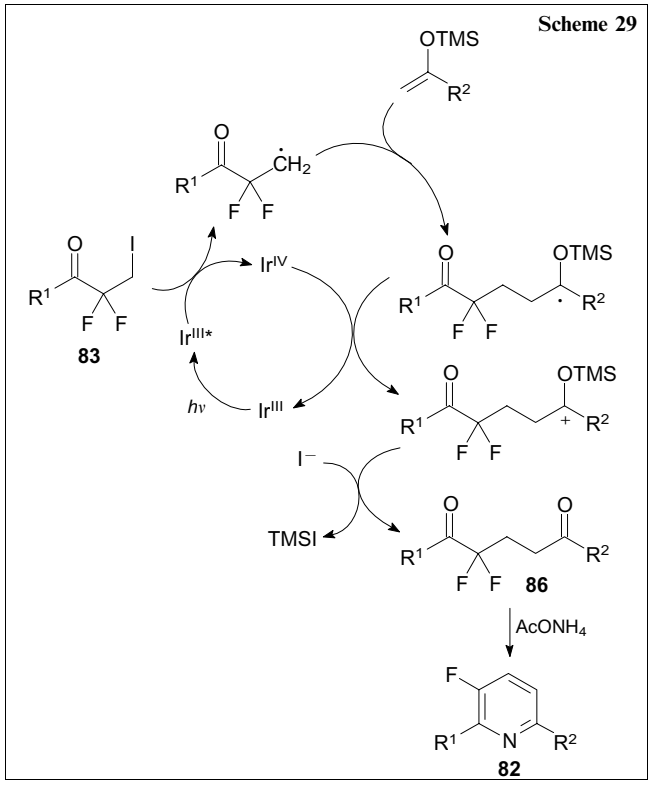
(*b*) NH_4OAc, DMF, 120 °C, 3 h; R^1 = Ph, 4-$MeOC_6H_4$, 4-ClC_6H_4, 2,4-$Me_2C_6H_3$, 2-Naph; R^2 = Bu^t, Ph, 4-NCC_6H_4, 4-ClC_6H_4, 4-$MeO_2CC_6H_4$, 4-FC_6H_4, 2-BrC_6H_4, 2,4-$Me_2C_6H_3$, 2-Py, 3-Py, 2-Th, PhCH=CH

84 = 

with silyl enol ethers in the presence of the complex Ir(ppy)₃ (**84**) as the photocatalyst (Scheme 28).[71]

The proposed mechanism of the photocatalytic cycle and cyclization is outlined in Scheme 29. Trimethyliodosilane that was eliminated during the reaction was trapped with propylene oxide (**85**) in order to prevent condensation of intermediate ketone **86**. The cyclization of the latter in the presence of a base at high temperature produced 3-fluoropyridines **82** in high yields.

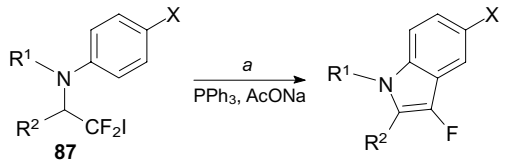
Scheme 29



An obvious advantage of this method is that it can be performed in a one-pot manner and tolerates a wide range of substituents in the starting ketone.

Photocatalytic cyclization of ICF_2-substituted *N*-arylamines **87** allows the synthesis of a wide range of 3-fluoroindoles **88** in yields > 80% (Scheme 30).[72]

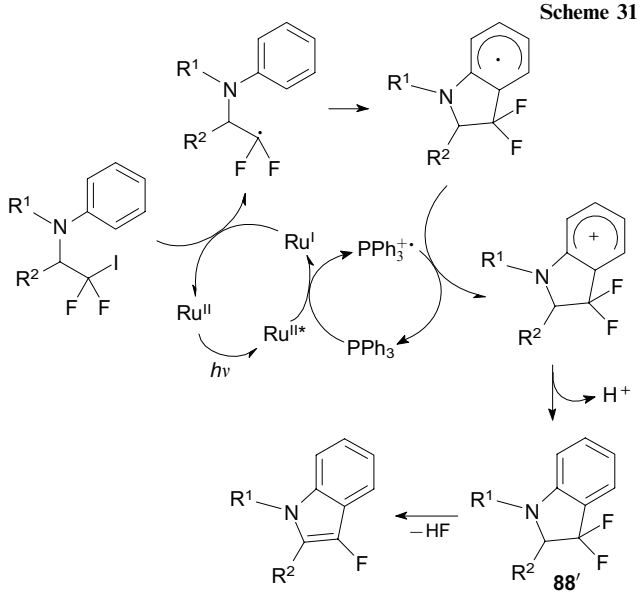
Scheme 30



(*a*) 1) $Ru(bpy)_3(BF_4)_2$ (0.5 mol.%), *hν* (blue LED), rt, 12 – 16 h; 2) SiO_2, rt, 4 – 16 h; X = H, R^1 = Me: R^2 = Ph, 4-ClC_6H_4, 4-$MeOC_6H_4$, 1-Naph; X = Br, R^1 = Pr^n: R^2 = Ph, 4-MeC_6H_4

The proposed mechanism involves the formation of difluoroindoline derivatives **88′** followed by dehydrofluorination (Scheme 31).

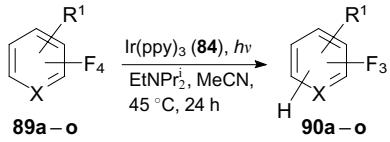
Scheme 31



The hydrodefluorination of polyfluoroaromatic and heteroaromatic compounds[44] is an alternative method for the synthesis of partially fluorinated derivatives applied in pharmaceutical and agrochemical industries.[73]

This photocatalytic reaction is usually performed in the presence of $Ir(ppy)_3$ (**84**) with a redox potential (V) of −2.20 V for Ir^{III}/Ir^{II}.[74] Perfluoroarenes and hetarenes have a low-lying lowest unoccupied orbital, due to which they can be photoactivated. Photocatalytic hydrodefluorination of perfluorinated derivatives of benzene, naphthalene and pyridine series **89a** – **o** can be applied to synthesize functionalized polyfluorinated mono- and polycyclic arenes **90a** – **o** (Scheme 32).[73] This reaction proceeds smoothly in high yields for perfluoroarenes containing a wide range of substituents. Meanwhile, substrates containing alcoholic, amino or thiol groups are less reactive. However, Senaweera

Scheme 32

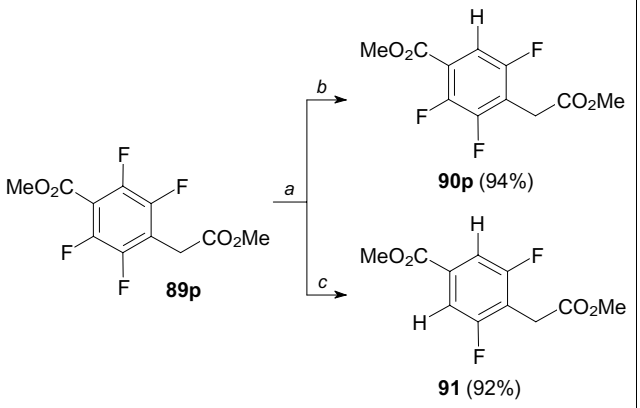


X = CF: R^1 = 4-F (**a**), 4-CN (**b**), 4-C(O)Me (**c**), 4-CO_2Me (**d**), 4-CO_2Bu^t (**e**), 4-CF_3 (**f**), 4-N(Ac)Cy (**g**), 4-PPh_2 (**h**), 4-SCO_2Et (**i**), 4-NHC(O)Me (**j**); X = N: R^1 = 4-F (**k**), 4-NHC(O)Me (**l**); X = CR^2: R^1 = R^2 = OC_6H_4Br-4 (**m**), R^1 = NH_2, R^2 = CO_2Me (**n**); R^1 = 4-NHAc, R^2 = 4-CF_3 (**o**)

et al.[73] functionalized these groups [preparation of ethers (**89m**), acylation (**89g**) and synthesis of thiocarbonates (**89i**), respectively] and achieved good yields (50% – 72%) with these substrates. The hydrodefluorination of polyfluorinated bi- and tricyclic arenes and hetarenes takes a long time for completion (72 h) and proceeds in 45% – 76% yields; $EtNPr^i_2$ was employed as the reducing agent. The use of $Ru(bpy)_3$ instead of $Ir(ppy)_3$ as the photocatalyst in the reaction with perfluoropyridine (**89k**) was shown to decrease the conversion.

Interestingly, mono- (compound **90p**) or dihydrodefluorination (compound **91**) products can be selectively synthesized by the reaction with tetrafluorinated methyl 4-(2-methoxy-2-oxoethyl)benzoate **89p** depending on the amount of $EtNPr^i_2$ (Scheme 33).[75]

Scheme 33



(*a*) $Ir(ppy)_3$ (**84**) (0.5 mol.%), *hν*, MeCN, 45 °C; (*b*) $EtNPr^i_2$ (1.1 equiv); (*c*) $EtNPr^i_2$ (6 equiv.)

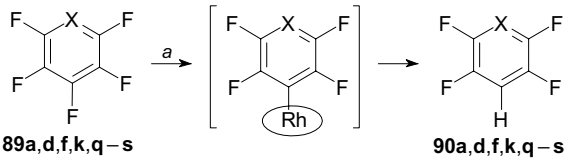
Photocatalytic hydrodefluorination of perfluoroarenes **89**, including hexafluorobenzene (**89a**), in the presence of the highly nucleophilic rhodium porphyrin complex $[(TSPP)Rh^I]^{5-}$ (**92**) produces penta- and tetrafluorinated derivatives **90a**,**d**,**f**,**q** – **s** and **90k** with virtually quantitative selectivity (91% – 99.5%) (Scheme 34).[76]

The C – F bond activation is highly efficient due to the Si – F and Rh – C bond formation, thereby making this process thermodynamically favourable (Scheme 35).

The photohydrodefluorination of monofluorinated compounds using metal complexes was described in the literature.

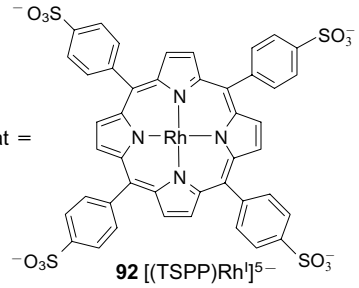
Thus, the photocatalytic cycle $*Ir(ppy)_3 - Ir^{II} - Ir^{III}$ involving Bu^tOK as the reducing agent (electron donor)

Scheme 34



(*a*) – Cat (**92**), Me_2EtSiH, MeOH, $(CH_2OH)_2$, *hv*, 60 °C, 36 h;

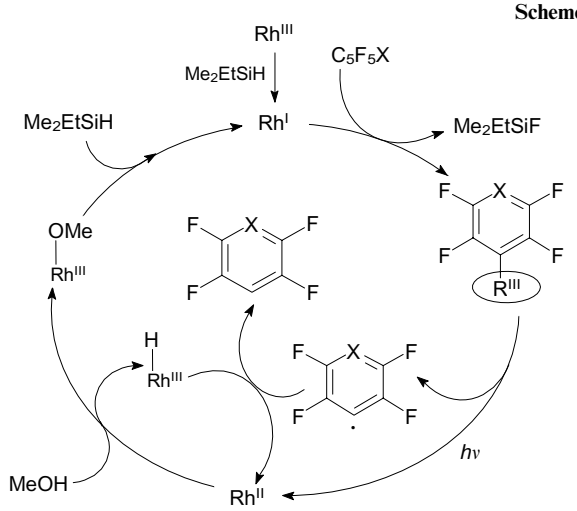
Cat =



92 $[(TSPP)Rh^{I}]^{5-}$

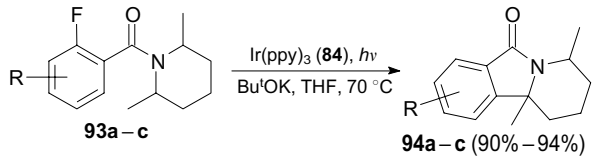
89, **90**: X = CR: R = F (**a**), CO_2Me (**d**), CF_3 (**f**), CHO (**q**), CO_2H (**r**), CO_2Et (**s**); X = N (**k**)

Scheme 35



allows the efficient defluorination of ketofluoroarenes **93a** – **c**. An interesting feature of this reaction is that defluorination is accompanied by intramolecular annulation to form tricyclic compounds **94a** – **c** (Scheme 36).[77]

Scheme 36



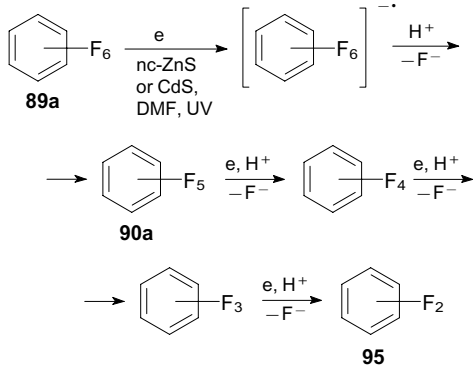
93: R = 4-Me (**a**), 4-MeO (**b**), 4-NMe_2 (**c**), *etc.*

Naumann *et al.*[78] developed a method for the transformation of *p*-fluorobenzoates into benzoates with hydrated electrons generated by irradiation of the photocatalyst $Ru(bpy)_3Cl_2$ (**68a**) with a light-emitting diode (green LED).

Photocatalytic hydrodefluorination of polyfluorobenzenes in the presence of ZnS and CdS nanocrystallites as the catalysts, unlike the metal complex-catalyzed reactions, proceed nonselectively and afford mixtures of fluorobenzenes, with a product containing one fluorine atom less than the substrate (product **90a**) predominating.[79] In all cases, at least 40% of the starting polyfluorobenzene remained unconsumed.

It is assumed that the photodefluorination proceeds *via* a radical-anion mechanism and yields difluorobenzene (**95**) as the final product (Scheme 37).

Scheme 37

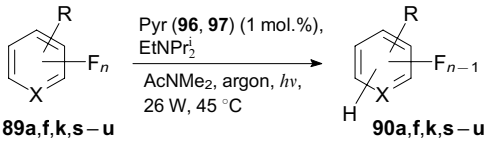


The employment of nc-CdS leads to an increase in the reaction time (6 h) and a decrease in the yield of the major product by ~20%.

Meanwhile, the use of Cu-, Ni- and Pb-doped zinc sulfide results in a significant increase in selectivity of photodefluorination of hexafluorobenzene and the predominant formation of pentafluorobenzene (**90a**).[80]

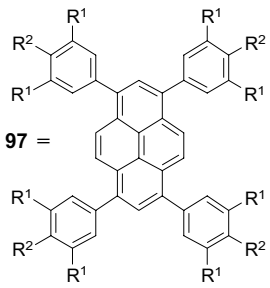
Methods for photocatalytic hydrodefluorination of polyfluoroarenes using metal-free photocatalysts were described. In particular, the hydrodefluorination of hexafluorobenzene (**89a**) and other perfluoroarenes **89f**,**k**,**s** – **u** was performed under mild conditions (45 °C, 12 h) with high selectivity using aryl-substituted pyrenes (Pyr) (**96**, **97**) (Scheme 38).[81] As in the case of the metal-containing catalyst $Ir(ppy)_3$ (**84**),[73] the hydrodefluorination of per-

Scheme 38



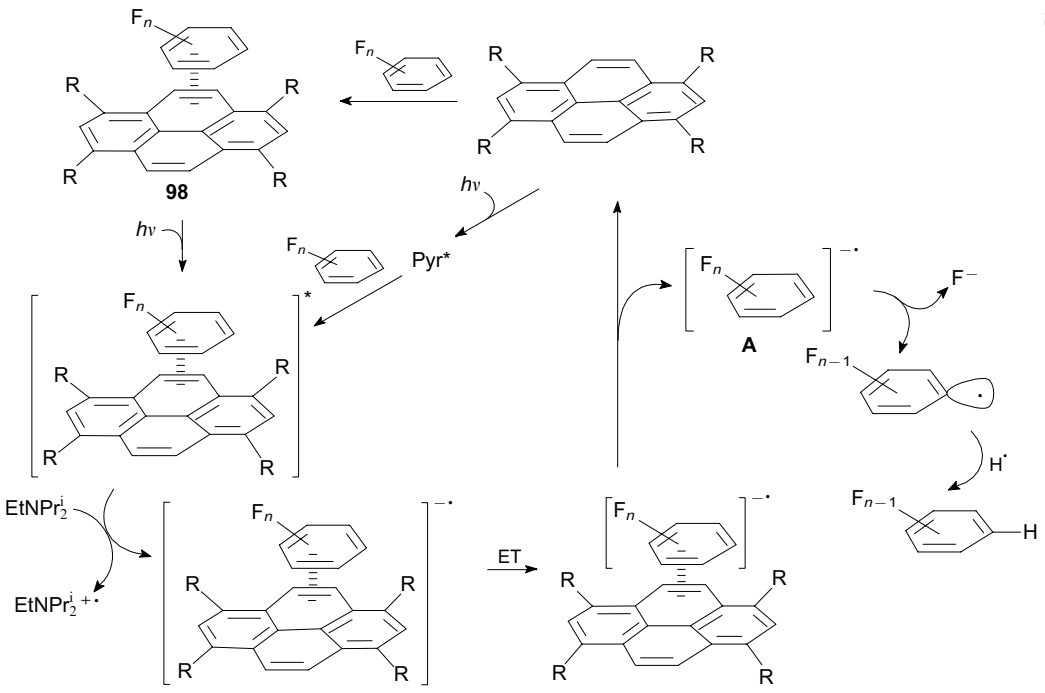
89: X = CF: R = F (**a**), 4-CF_3 (**f**), 4-CO_2Et (**s**), 4-MeC_6H_4 (**t**), 4-OPh (**u**); X = N, R = 4-F (**k**), *etc.*;

96, **97** =



96: R^1 = Me, R^2 = H (**a**);
97: R^1 = H, R^2 = C≡CBu^t (**b**)

Scheme 39



fluoronaphthalene proceeds in significantly lower yield (63%).

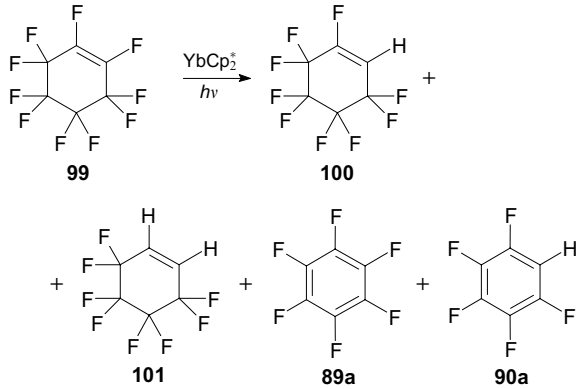
It was assumed that π-complex **98** is involved in the hydrodefluorination, thereby facilitating electron transfer even if ΔG_{ET} has unfavourable values (up to 0.63 eV) (Scheme 39).

High regioselectivity of defluorination of compounds **89f**,**s**–**u** was attributed to the presence of the highest unpaired electron density on the C–F bond in the *para* position of the resulting radical anion **A**.

Examples of photochemical hydrodefluorination of alkenes are rather rare. Let us mention the hydrodefluorination of perfluorocyclohexene (**99**) with $YbCp^*_2$ giving a mixture of nonafluorocyclohexene (**100**), octafluorocyclohexene (**101**), hexafluorobenzene (**89a**) and pentafluorobenzene (**90a**) (Scheme 40).[82]

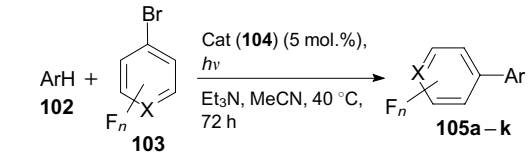
The photocatalytic dehalogenation of aromatic compounds can be accompanied by the $C(sp^2)-C(sp^2)$ bond formation. Thus, the direct arylation of arenes **102** with fluorinated aryl bromides **103** in the presence of the photocatalyst eosin (**104**) under mild conditions affords fluori-

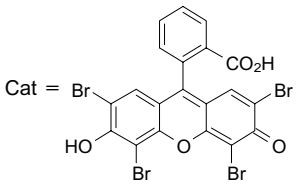
Scheme 40

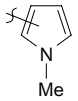


Cp* = $[C_5Me_5]^-$

Scheme 41



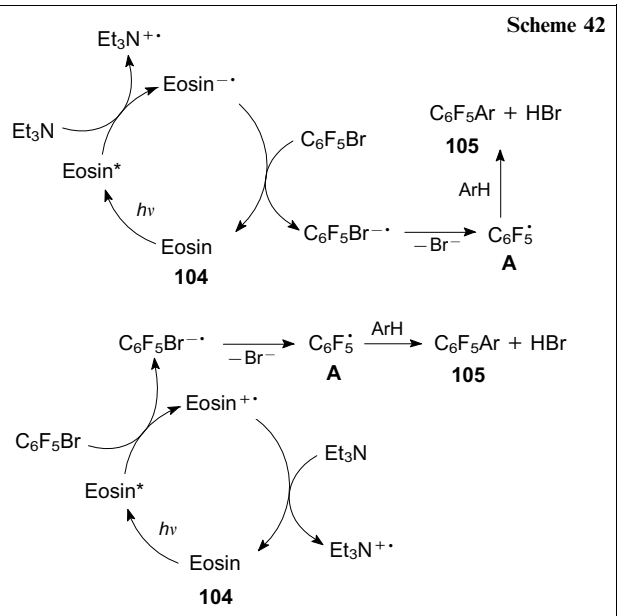


Compound **105**	X	Ar	*n*	Yield (%) (ratio of *o*-, *m*- and *p*-isomers)
a	CF	Ph	5	85
b	CF	C_6H_4Me	5	78
c	CF	$C_6H_4Pr^i$	5	85 (10 : 10 : 1)
d	CF	C_6H_4OMe	5	99 (2 : 1 : 10)
e	CF	C_6H_4F	5	62 (1 : 1 : 1)
f	CF	C_6H_4Cl	5	76 (1 : 4 : 4)
g	CF	$C_6H_4NO_2$	5	0
h	CF	Naph		87 (C(2) : C(3) = 1 : 10)
i	CF		4	57 (C(2) : C(3) = 5 : 2)
j	CH	Ph	4	82
k	CH	C_6H_4OMe	4	68 (3 : 2 : 12)

nated biaryls **105a**–**f**,**h**–**k** in good yields, except for nitro derivative **105g** (0%) (Scheme 41).[83]

Meyer *et al.*[83] considered two possible reaction mechanisms: the reductive (Scheme 42, upper part) and oxidative quenching cycles (Scheme 42, lower part). From the ther-

Scheme 42

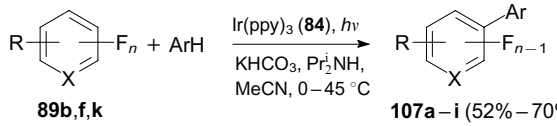


modynamic point of view, the reductive mechanism is more probable.

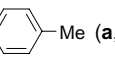
The key step of the reaction produces pentafluorophenyl radical **A**, which nonregioselectively reacts with aromatic substrate **102**. The radical character of the reaction was confirmed by trapping the resulting species with the radical scavenger based on (2,2,6,6-tetramethylpiperidin-1-yl)oxyl (TEMPO) (**106**), and the structures of the adducts were determined by liquid chromatography–mass spectrometry.

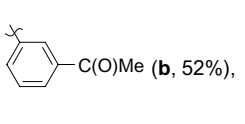
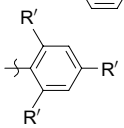
A photocatalytic method for the synthesis of biaryls **107** was developed based on the C–F bond transformation into C–C in polyfluorinated benzene and pyridine derivatives (**89f**,**k**,**v**) using the catalyst [Ir(ppy)$_3$] (**84**) (Scheme 43).[84]

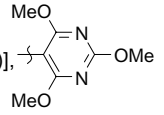
Scheme 43

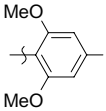


89b,**f**,**k** **107a–i** (52%–70%)

107: X = N, R = F, *n* = 4: Ar =  (**a**, 58% yield),

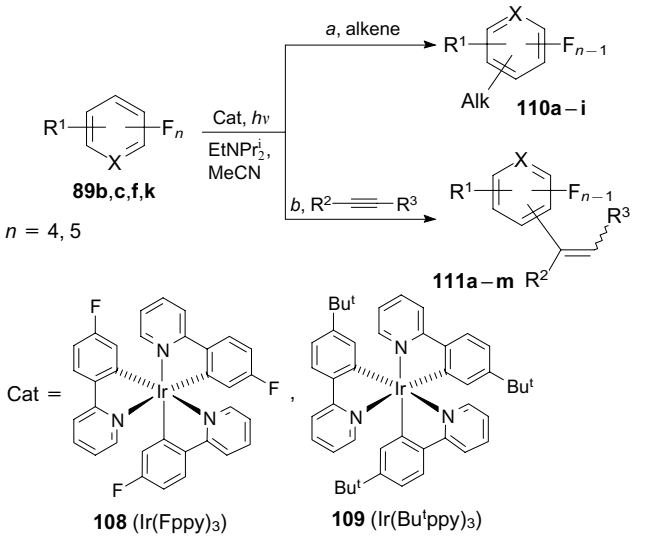
 (**b**, 52%),  [R′ = OMe (**c**, 70%),

Bu^t (**d**, 35%), Et (**e**, 55%)],  (**f**, 67%);

X = CF, Ar =  OMe : R = 4-CF$_3$ (**g**, 54%), 4-CN (**h**, 57%)

Iridium photocatalysts based on 2-phenylpyridine [Ir(ppy)$_3$ (**84**)] and its substituted derivatives [Ir(Fppy)$_3$ (**108**) and Ir(Bu^{t}ppy)$_3$ (**109**)] were employed to introduce alkyl, cycloalkyl and alkenyl groups into polyfluoroaromatic compounds **89** (Scheme 44).[85,86]

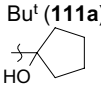
Scheme 44



(*a*) Ir(ppy)$_3$ (**84**) (0.25 mol.%), 45 °C

X	R^1	Alk	Yield (%)
N	F	4-Cy (**110a**)	79
N	F	4-  (**110b**)	61
N	F	4-(CH$_2$)$_6$OH (**110c**)	53
N	F	4-(CH$_2$)$_6$Cl (**110d**)	76
N	F	3-CH(CH$_2$OH)Pr^i (**110e**)	43
CF	CN	4-Cy (**110f**)	64
CF	CN	4-CH(Me)CH$_2$CO$_2$Me (**110g**)	54
CF	CF$_3$	4-CH(Me)CH$_2$CO$_2$Et (**110h**)	71
CF	C(O)Me	4-CH(Me)CH$_2$CO$_2$Et (**110i**)	50

(*b*) Cat (0.25 mol.%), 0 °C

Cat	X	R^1	R^2	R^3	Yield (%)	*Z*:*E*
Ir(ppy)$_3$ (**84**)	CF	3-CO$_2$Me	H	Bu^t (**111a**)	86	> 25 : 1
Ir(ppy)$_3$ (**84**)	CF	4-CO$_2$Me	H	 (**111b**)	63	> 25 : 1
Ir(ppy)$_3$ (**84**)	CF	4-CO$_2$Me	H	OEt (**111c**)	55	> 2.5 : 1
Ir(ppy)$_3$ (**84**)	CF	4-CO$_2$Me	CO$_2$Et	Et (**111d**)	53	> 25 : 1
Ir(Fppy)$_3$ (**108**)	N	F	H	Bu^t (**111e**)[a]	85	24 : 1
Ir(Fppy)$_3$ (**108**)	N	F	H	Pr^i (**111f**)[a]	74	> 25 : 1
Ir(Fppy)$_3$ (**108**)	N	F	H	Bu^n (**111g**)[a]	66	16.7 : 1
Ir(Fppy)$_3$ (**108**)	N	F	H	 (**111h**)[a]	63	> 25 : 1
Ir(Fppy)$_3$ (**108**)	CF	F	H	 (**111i**)	61	25 : 1
Ir(Fppy)$_3$ (**108**)	CF	4-CF$_3$	CH$_2$OH	CH$_2$OH (**111j**)	63	< 1 : 25
Ir(Bu^{t}ppy)$_3$ (**109**)	N	F	H	Bu^t (**111k**)[a]	77	1 : 25
Ir(Bu^{t}ppy)$_3$ (**109**)	N	F	H	Pr^i (**111l**)[a]	66	1 : 2
Ir(Bu^{t}ppy)$_3$ (**109**)	N	F	H	CH(OH)Et (**111m**)[a]	84	1 : 2.6
Ir(Bu^{t}ppy)$_3$ (**109**)	N	F	H	 (**111n**)[a]	71	1 : 7

[a] The alkenylation occurs at the *para* position.

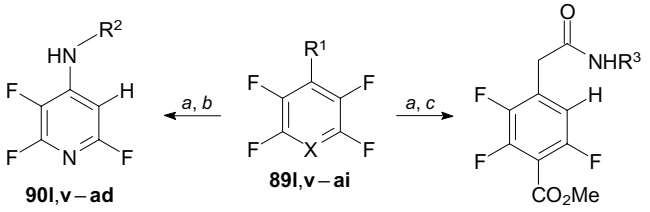
Photocatalytic defluorination of perfluoro(het)arenes **89b**,**c**,**f**,**k** with both alkenes and alkynes in the presence of iridium catalysts **108** and **109** proceeds stereoselectively to form alkyl- and alkenyl-substituted products **110a–i** and **111a–n**, respectively (see Scheme 44).[86]

It should be noted that the coordination of the iridium atom by three bidentate ligands gives catalysts **84**, **108** and **109**, which have a nearly spherical three-dimensional structure.

By studying the photocatalytic alkenylation of perfluoropyridine (**89k**) with *tert*-butylacetylene, the authors showed that the $E:Z$ isomer ratio in products **111e**,**k** is independent of the emissive energy of the iridium catalyst, but the relative amount of the Z isomer tends to decrease with increasing radius of the catalyst molecule [$Ir(ppy)_3$ < $Ir(Fppy)_3$ < $Ir(Bu^tppy)_3$].

This catalytic system allows the selective replacement of the C–F bond with C–H in the *ortho* position of perfluorinated derivatives of pyridine (**90l**,**v–ad**) and benzene **90ae–ai** (Scheme 45).[87]

Scheme 45

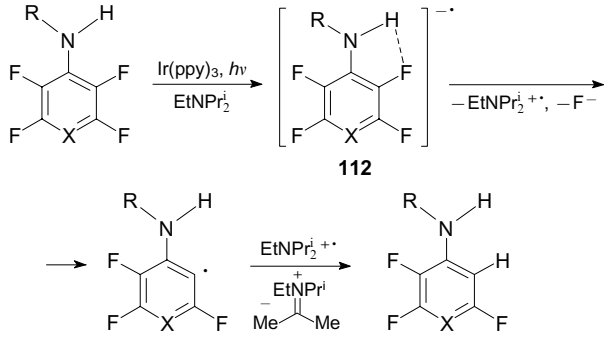


90l,**v–ad** **89l**,**v–ai** **90ae–ai**

(*a*) $Ir(ppy)_3$ (**84**), *hν*, $EtNPr^i_2$, MeCN;
(*b*) X = N, R^1 = HNR^2, 23 °C;
(*c*) X = CCO_2Me, R^1 = $CH_2C(O)NHR^3$, 45 °C

R^2	Yield (%)	R^3	Yield (%)
C(O)Me (**90l**)	98	Ph (**90ae**)	83
C(O)Et (**90v**)	97	C_6H_4F (**90af**)	85
C(O)Pr^i (**90w**)	93	C_6H_4Me (**90ag**)	94
$C(O)C_6H_4NMe_2$ (**90x**)	78	C_6H_4CN (**90ah**)	82
$C(O)C_6H_4OMe$ (**90y**)	85	CH_2CO_2Et (**90ai**)	81
$C(O)C_6H_4Me$ (**90z**)	86		
$C(O)C_6H_4F$ (**90aa**)	83		
$C(O)C_6H_4NO_2$ (**90ab**)	0		
Cy (**90ac**)	0		
Ph (**90ad**)	76		

Scheme 46



X = N, CCO_2Me

It is assumed that the hydrogen bonding in radical anion **112** between the *ortho*-F atom and the NH group not only ensures regioselectivity of the reaction but also increases its exothermicity (Scheme 46).

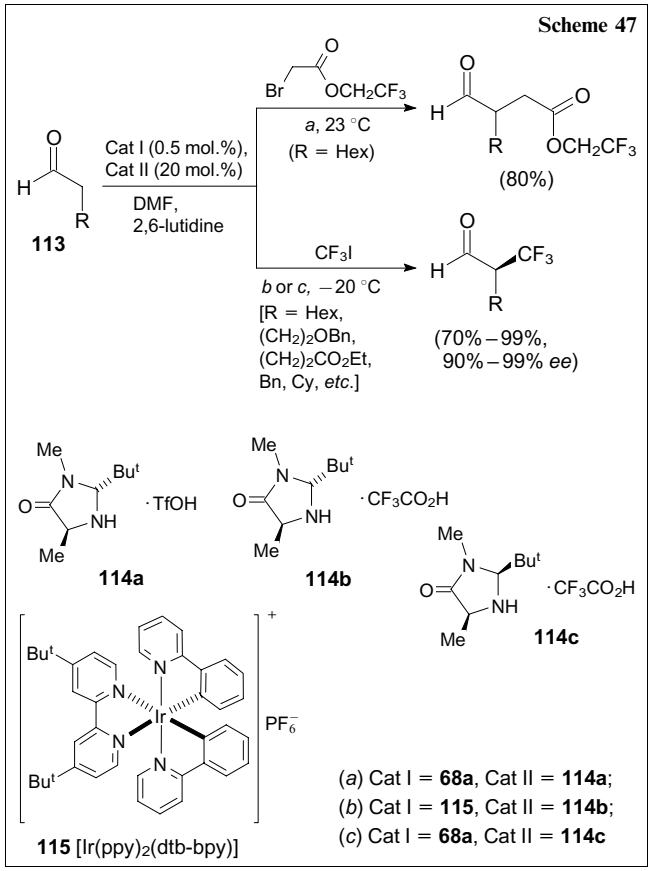
Hence, photocatalytic defluorination reactions of aromatic compounds have been studied in sufficient detail. By contrast, data on photocatalytic $C(sp^2)-F$ bond formation reactions are scarce.

5. Introduction of a trifluoromethyl group

Organic compounds containing fluoroalkyl groups are of great interest in medicinal chemistry due to high metabolic stability and lipophilicity.[88–90]

MacMillan and Nicewicz[91] were the first to perform photocatalytic enantioselective alkylation of aldehydes **113** by introducing the CF_3 group and using the $Ru(bpy)_3Cl_2$ (**68a**)–2-*tert*-butyl-3,5-dimethylimidazolidin-4-one trifluoromethanesulfonate (**114a**) catalyst system (Scheme 47,*a*).

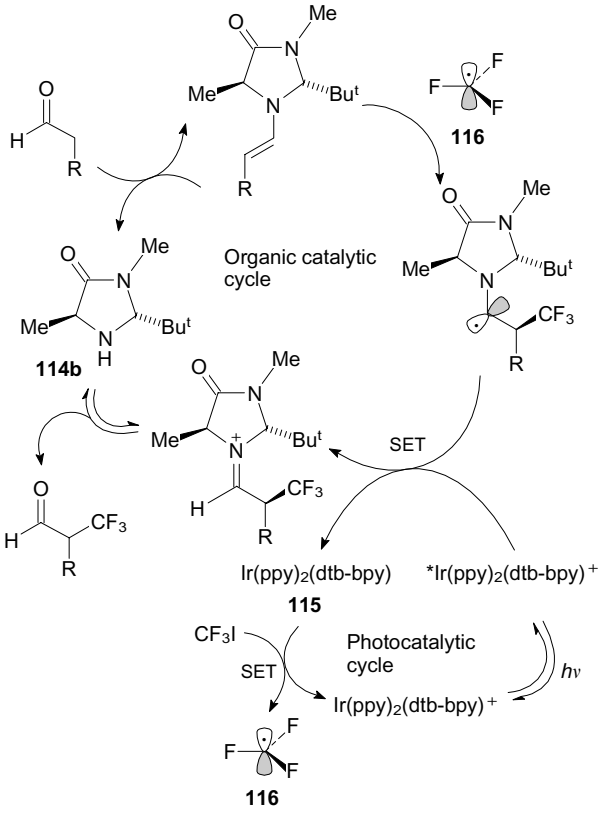
Scheme 47



Later, the enantioselective trifluoromethylation was performed using the iridium (**115**) or ruthenium (**68a**) photocatalyst and enantiomeric 2-*tert*-butyl-3,5-dimethylimidazolidin-4-one trifluoroacetates (**114b**,**c**) (see Scheme 47,*b*,*c*).[92]

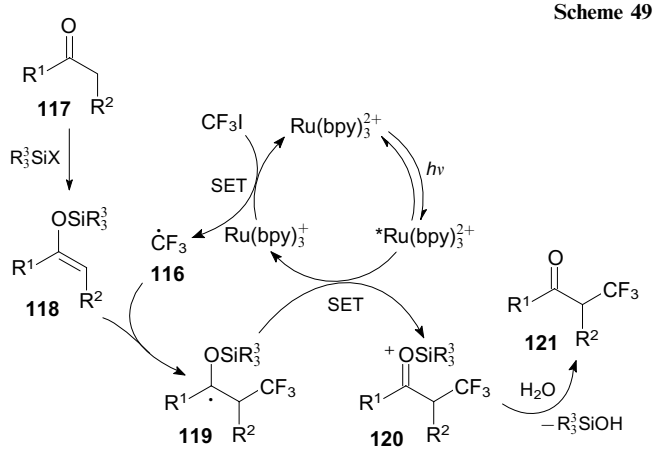
The highest yields and enantiomeric excess values were observed in the case of the combined application of *tert*-butyl-substituted iridium catalyst **115** and imidazolidin-4-one **114b**. The proposed mechanism of trifluoromethylation involves the following two cycles: a photocatalytic cycle in the presence of metal complex photocatalyst **115** and an organocatalytic cycle using imidazolidin-4-one **114b** (Scheme 48).

Scheme 48



A method was developed for the trifluoromethylation of carbonyl compounds, including amides and esters, using the photocatalyst $Ru(bpy)_3Cl_2$ (**68a**), R_3SiX and CF_3I as a source of the $^{\bullet}CF_3$ radical (**116**).[93] The proposed reaction mechanism is outlined in Scheme 49. In the first step, ketone **117** is transformed into Si enol **118** in the presence of R^3_3SiX. Then the visible light-initiated catalyst promotes the generation of the trifluoromethyl radical (**116**) from CF_3I followed by the reaction of this radical with enol **118** giving α-silyloxy radical **119**, which is transformed into silyloxocarbenium cation **120** *via* a SET mechanism. The latter cation is hydrolyzed to form α-trifluoromethyl-substituted ketones **121**.

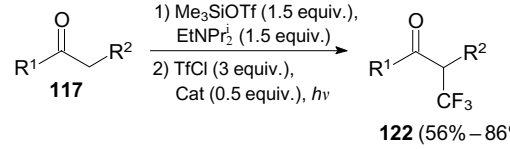
Scheme 49



R^1 = Ph, 4-$MeOC_6H_4$, 4-NCC_6H_4; EtO, Me_2N, 1-Ad, *etc.*; R^2 = H, Pr^n, Hex, *etc.*; R^3 = Me, Pr^i, Bu^t

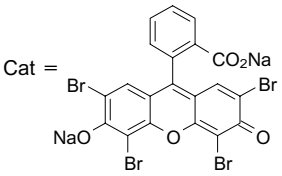
The trifluoromethylation of ketones **117** with trifluoromethanesulfonyl chloride TfCl was performed in the presence of eosin Y (eosin Y disodium salt **123**) as the photocatalyst (Scheme 50).[94]

Scheme 50



R^2 = H: R^1 = Ph, 4-FC_6H_4, 4-ClC_6H_4, 4-MeC_6H_4, 2-MeC_6H_4, 2-Py, 2-Naph; $R^1 - R^2 = (CH_2)_4$

Cat =



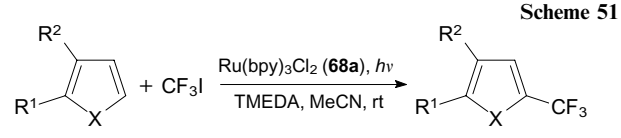
[**123** (eosin Y)]

The photocatalytic trifluoromethylation of heterocyclic compounds **124** and **125** using the catalyst $Ru(bpy)_3Cl_2$ (**68a**) and the reactant CF_3I allows the introduction of the CF_3 group into the heterocyclic moiety under mild conditions (Scheme 51).[95]

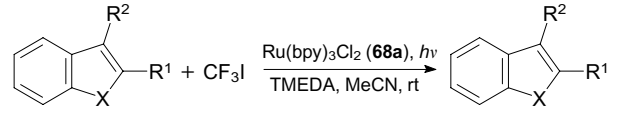
The reactions were assumed to involve trifluoromethyl (**116**) and heterocyclic (**128**) radicals (Scheme 52).

In order to elucidate the detailed mechanism of photocatalytic trifluoromethylation of heterocyclic compounds **124** and **125** with CF_3I, Su *et al.*[96] applied a microreactor technology to record UV-Vis spectra in flow. The quantum yields and rate constants of individual reaction steps were

Scheme 51

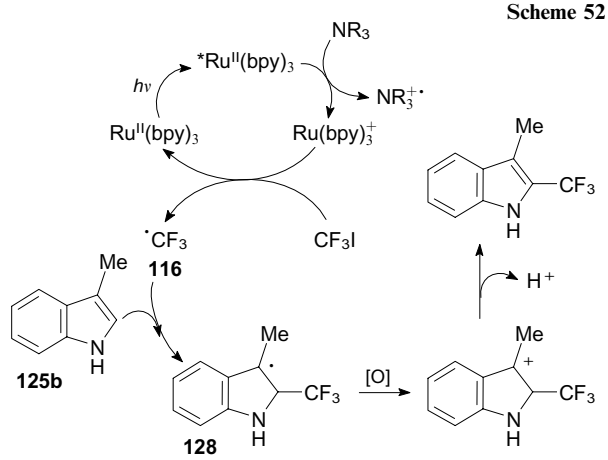


Compound **126**	X	R^1	R^2	Yield (%)
a	NH	CHO	H	71
b	NH	CO_2Me	H	80
c	NMe	H	H	95
d	O	Et	H	92
e	S	NH_2	CO_2Me	92

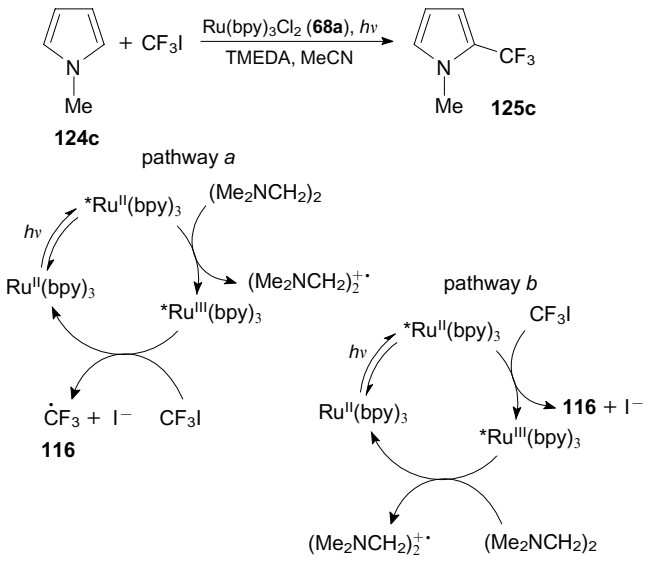


Compound **127**	X	R^1	R^2	Yield (%)
a	NH	CF_3	Me	90
b	NH	Me	CF_3	94
c	NH	CO_2Et	CF_3	81
d	NMe	Me	CF_3	94
e	NMe	CF_3	H	95

Scheme 52



Scheme 53



evaluated for the trifluoromethylation of *N*-methylpyrrole (**124c**), which provide evidence that the formation of the trifluoromethyl radical (**116**) proceeds by pathway *a* rather than pathway *b* (Scheme 53). This process cannot be assigned to radical chain reactions.

The trifluoromethyl group was introduced into aromatic and heteroaromatic products **129**–**131** using TfCl and the catalyst $Ru(phen)_3Cl_2$ (**132**) (Scheme 54).[97]

Trifluoromethanesulfonyl chloride is easily reduced with the catalyst to the radical anion $TfCl^{-\bullet}$, which is decomposed into the CF_3 radical (**116**), SO_2 and Cl^- (Scheme 55).

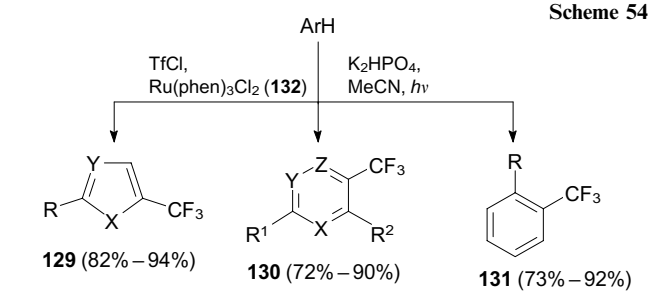
The employment of TfCl in the presence of iridium photocatalyst **115** allows the regioselective trifluoromethylation of exocyclic double bonds in saturated heterocycles **133** in high yields (Scheme 56).[98]

Electrophilic Umemoto reagent (Um) **134** is successfully employed as a CF_3 radical source in the presence of photocatalysts.

Thus, the photocatalytic hydroxyfluoromethylation of alkenes **135** with the Umemoto reagent (**134a**) in the presence of the catalyst $Ir(ppy)_3$ (**84**) proceeds in high yields with 100% regioselectivity (Scheme 57).[99]

The proposed mechanism of hydroxytrifluoromethylation (see Scheme 57,*a*) involves the formation of the CF_3 radical (**116**) and cation **136**, which reacts with water to form alcohol **137** (Scheme 58).

Scheme 54

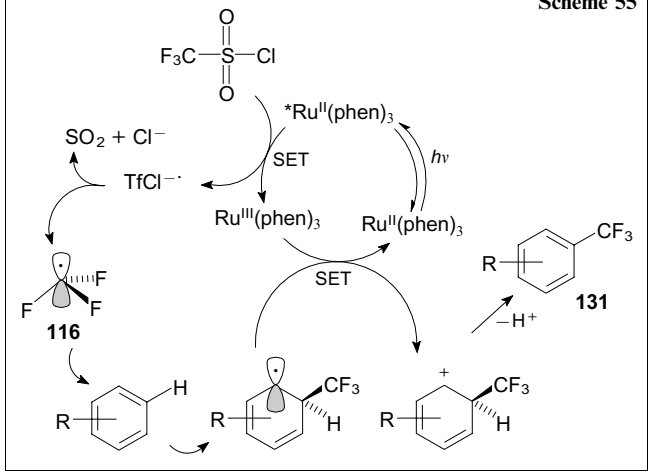


R = H, Y = H: X = NH, NMe; R = Me, Y = H: X = O, S, *etc.*

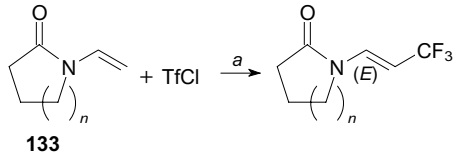
Y = Z = CH, X = N, R^1 = H, R^2 = MeO; Y = Z = CH, X = N, $R^1 = R^2$ = Me; Y = CH, X = Z = N, $R^1 = R^2$ = Me; Y = CH, X = N, Z = N, $R^1 = R^2$ = Cl, *etc.*

R = H, NHBoc, MeO, MeS, *etc.*

Scheme 55



Scheme 56



(*a*) $Ir(ppy)_2(dtb\text{-}bpy)PF_6$ (**115**), *hv*, MeCN, rt, 2 h; *n* = 1, 2

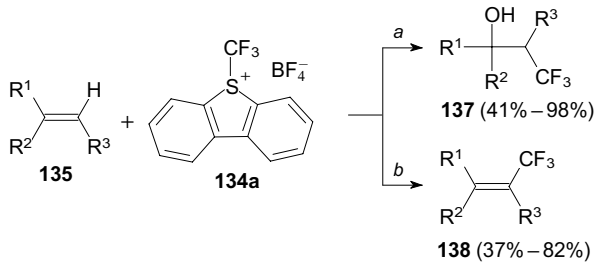
The exclusion of water from the reaction system and the use of ruthenium catalyst **68b** resulted in the formation of vinylic substitution products **138** (see Scheme 57,*b*).[100]

Oxotrifluoromethylation of alkynes **139** affords α-trifluoromethyl ketones **140** *via* rapid keto-enol tautomerization of the initially formed vinyl alcohol (Scheme 59).[101]

Photocatalytic oxotrifluoromethylation of 1,6-enynes **141** with CF_3SO_2Na (**142**) in the presence of 9,10-phenanthrenequinone (PQ, **33**) as the photocatalyst produces trifluoromethyl-substituted benzofurans, benzothiophenes and indoles **143** (Scheme 60).[102]

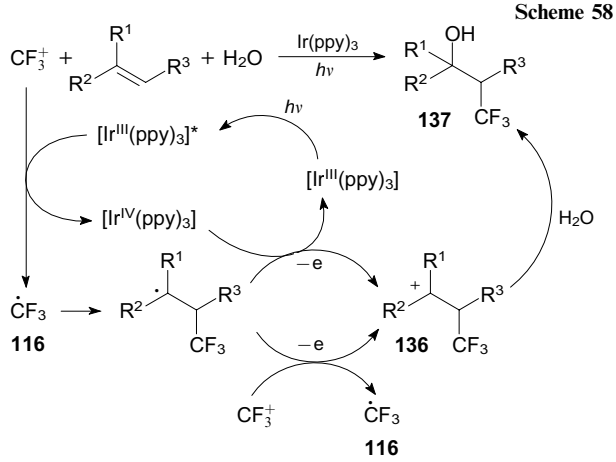
The proposed mechanism implies the use of trifluoromethyl (**116**) and vinyl (**144**) radicals and involves the

Scheme 57

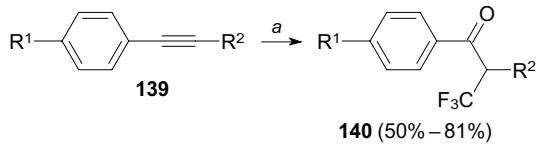


(*a*) Ir(ppy)$_3$ (**84**) (0.5 mol.%), *hν*, Me_2CO, H_2O, rt, 2 – 4 h;
$R^2 = R^3 = H$: R^1 = 4-XC_6H_4 (X = MeO, F, Cl, Br, AcO, F_3C);
R^1 = Ph, R^2 = H: R^3 = Me, Ph; R^1 = Ph, R^3 = H: R^2 = Me, Ph;
(*b*) [Ru(bpy)$_3$](PF_6)$_2$ (**68b**) (2 mol.%), *hν*, DMSO, rt, 2 h;
R^3 = H: $R^1 = R^2$ = Ph, 4-XC_6H_4 (X = MeO, Cl, Br);
$R^1 = R^2$ = Ph: R^3 = Me, Ph; R^1 = Ph: R^2 = 4-BocNHC$_6$H$_4$,
R^3 = H; R^2 = 4-$MeOC_6H_4$, R^3 = Me, Ph; R^2 = Ph,
R^3 = H: R^1 = 3-Py, Me(Ph)$CHCH_2$, 4-$O_2NC_6H_4$

Scheme 58

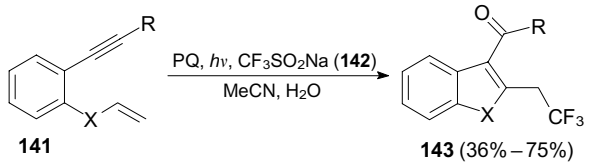


Scheme 59



(*a*) Ir(ppy)$_3$ (**84**) (2 mol.%), *hν*, Um (**134a**), Me_2CO, H_2O, rt, 12 h;
R^2 = Me: R^1 = H, MeO, OH, F, Cl, Br, MeC(O)NH, Me_2N;
R^1 = AcNH: R^2 = H, Bu^n, Cy, Ac, *etc.*

Scheme 60



X = NBoc, O, S; R = Ph, C_6H_4X (X = 4-Cl, 4-OMe, 4-OH, 3-Cl, 3-Me, 2-Br, 2-CF_3), 2-Naph, 3-Th, *etc.*

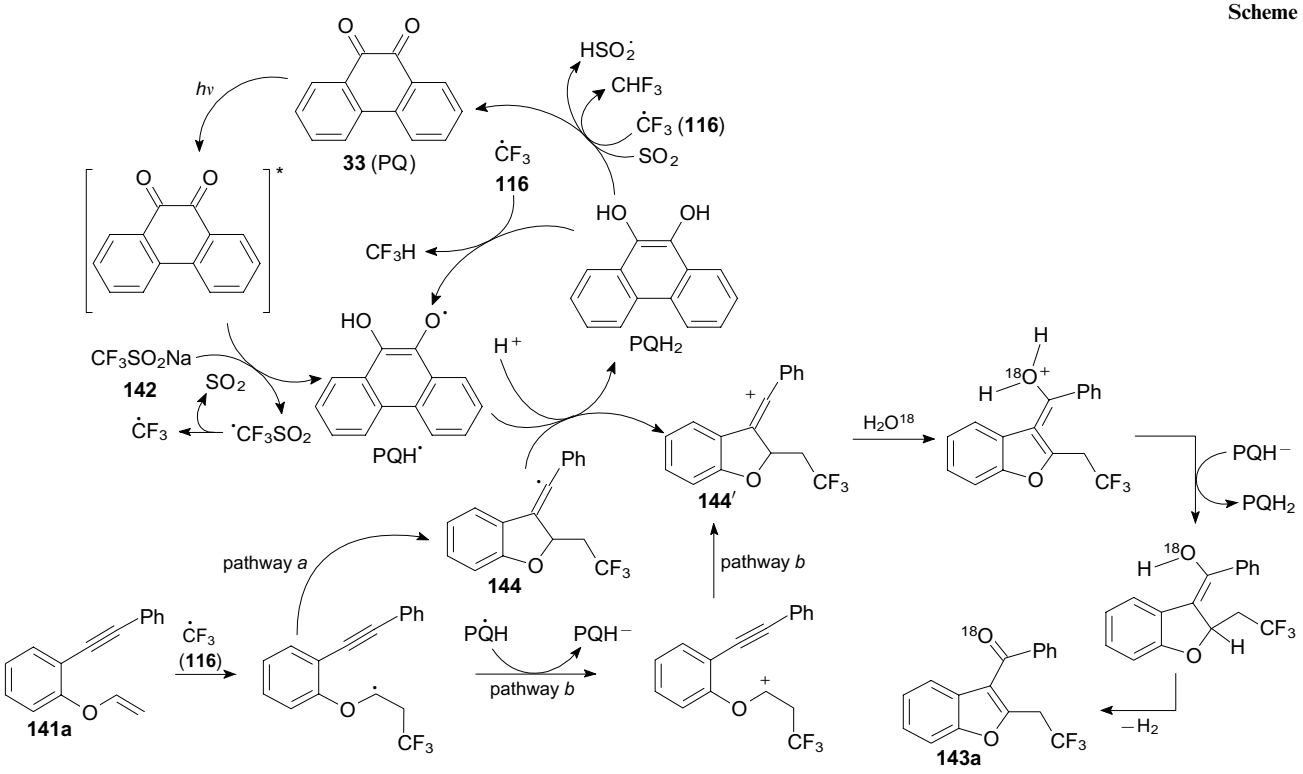
formation of vinylic carbocation **144′** through the *exo-dig*- (pathway *a*) or cationic (pathway *b*) cyclization (Scheme 61).

This mechanism was confirmed by trapping the trifluoromethyl radical (**116**) with the 2-methyl-2-nitrosopropane dimer and the O^{18} labelling of the benzylic position of product **143a** (see Scheme 61).

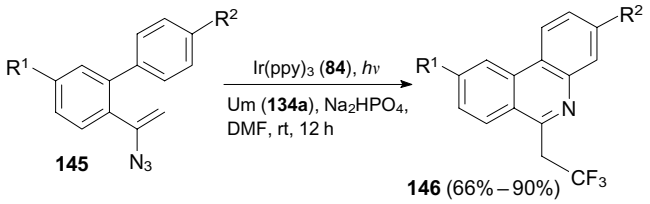
An efficient method for the synthesis of 6-trifluoroethylphenanthridines **146** was developed based on trifluoromethylation of biphenylvinyl azides **145** using the Um (**134a**) – Ir(ppy)$_3$ (**84**) system (Scheme 62).[103]

The photocatalytic trifluoromethylation of α-(1-hydroxycycloalkyl)-substituted styrenes **147** with Umemoto reagent **134b** proceeds *via* ring expansion to form cycloalkanones **148** – **150** (Scheme 63).[104]

Scheme 61

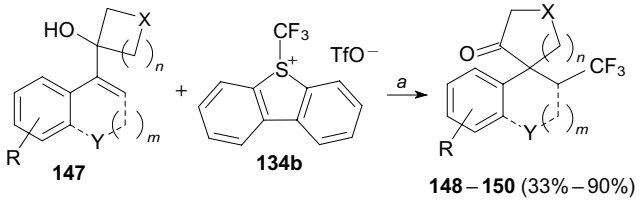


Scheme 62



R^1 = H: R^2 = H, CF_3, MeO, Bu^t, Cl; R^2 = H: R^1 = Me, F, *etc.*

Scheme 63



(*a*) $[Ru(bpy)]_3(PF_6)_2$ (**68b**) (1 mol.%), *hν*, TMSOTf, DMF, rt, 8 h;
148: X = O, Y is absent, *n* = 1, *m* = 0: R = H (**a**, 27% yield); F (*b*, 29%);
149: X = CH_2, Y is absent, *n* = 1, *m* = 0; R = H (**a**, 74%), 4-F (**b**, 73%), 4-Cl (**c**, 60%), 4-Me (**d**, 78%), 4-Ph (**e**, 82%), 4-OMe (**f**, 90%), 2-Me (**g**, 39%), 3-Me (**h**, 51%);
150: X = CH_2, Y = CH_2, *n* = 1, *m* = 1; R = H (**a**, 52%), 4-OMe (**b**, 47%); Y = 0, *n* = 1, *m* = 1; R = H (**c**, 41%)

The ring expansion involves the 1,2-alkyl migration in cation **A** as the key step (Scheme 64).

2-Aryl-2-(2,2,2-trifluoroethyl)cyclopentanones **149a**–**d**,**h**,**i** were also independently synthesized by Woo and Kim,[105] who showed that the time of this reaction can be decreased to 15 min by using the $Ru(phen)_3Cl_2$ (**132**) – Um (**134a**) catalyst system in acetone (Scheme 65).

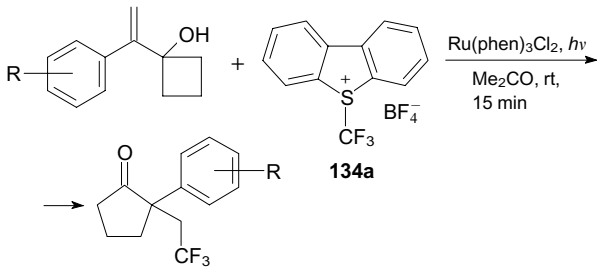
A photocatalytic procedure was developed for the direct vicinal halotrifluoromethylation of styrenes and alkenes **135** with Umemoto reagent **134a** using the catalyst $Ru(bpy)_3](PF_6)_2$ (**68b**) and the reactants TMSHal (Hal = Cl, Br) or CsHal (Hal = Br, I) (Scheme 66).[106]

The main steps of the reaction responsible for selectivity are as follows: the reduction of Umemoto reagent **134a** resulting in generation of the trifluoromethyl radical (**116**), which adds to alkene to form benzyl-type radical **A**, the oxidation of the radical **A** to cation **B** and the reaction of the latter with a halogen source (Scheme 67).

The Umemoto reagent was employed in the photocatalytic synthesis of trifluoromethyl-substituted heterocyclic compounds **153** (Scheme 68).[107]

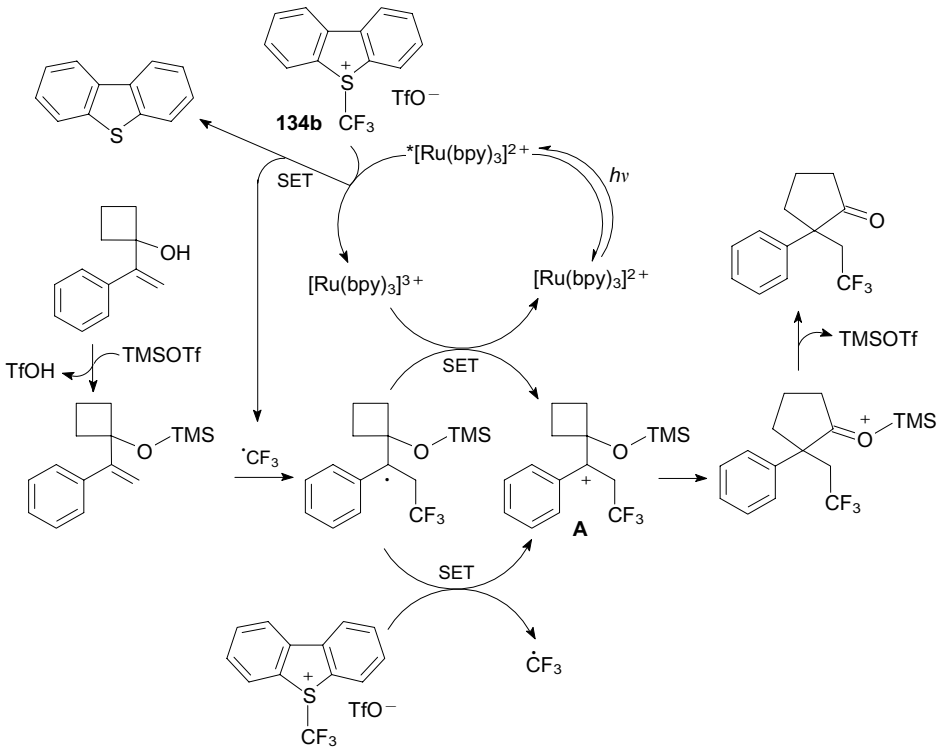
Togni reagent **154** can be used as a trifluoromethyl radical source in photocatalytic trifluoromethylation. Thus, the Togni reagent (**154**) – $Ir(ppy)_3$ (**84**) system was

Scheme 65



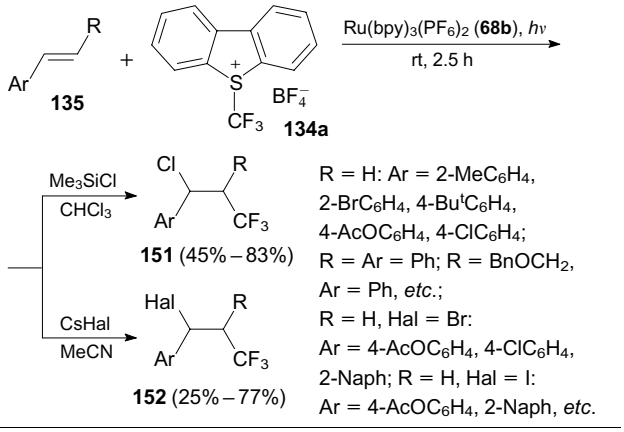
R = H (**a**, 77%), 3-Me (**h**, 73%), 3-F (**i**, 66%), 4-Me (**d**, 73%), 4-F (**b**, 70%), 4-Cl (**c**, 70%), *etc.*

Scheme 64

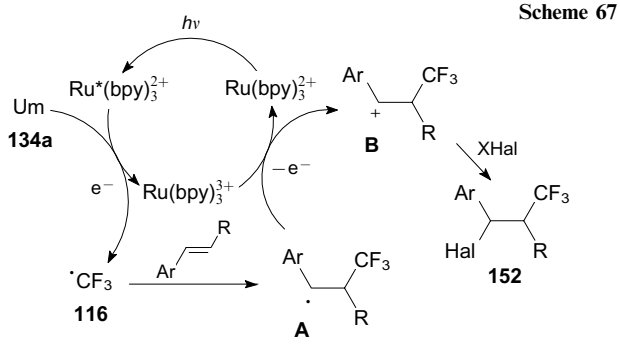


TMS = $SiMe_3$

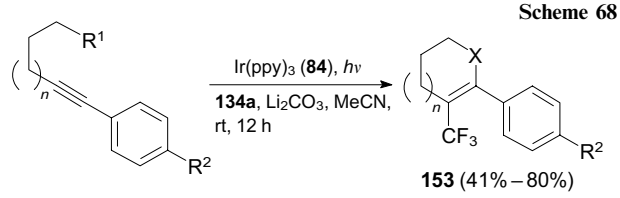
Scheme 66



Scheme 67

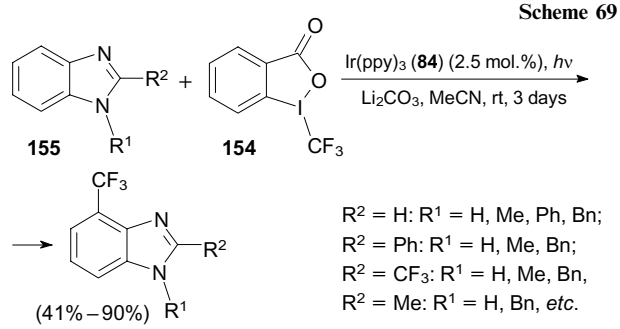


Scheme 68



R^1 = OH: R^2 = H, OMe, Cl, Br, NHAc, NHTs, NHBoc;
R^1 = NHTs: R^2 = H, OMe, Cl, Br, NHAc, NHTs, NHBoc, *etc.*;
X = O, NTs, NBoc; *n* = 1 – 3

Scheme 69

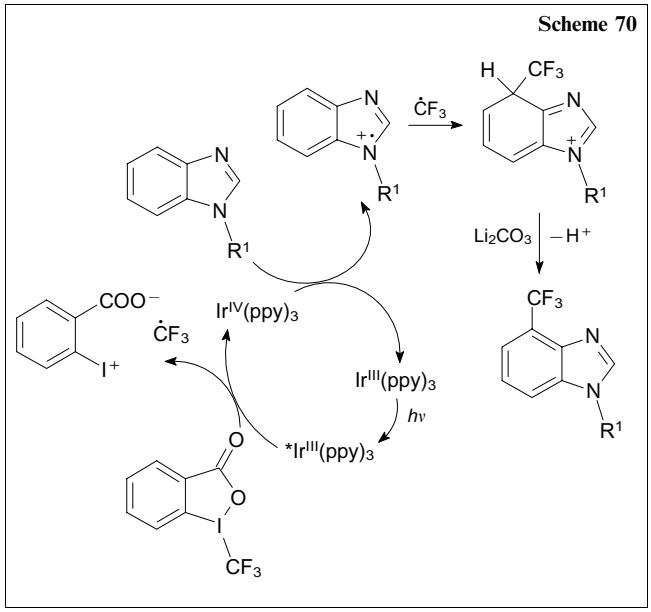


employed to introduce a CF_3 group at the C(4) position of benzimidazoles **155** (Scheme 69).[108]

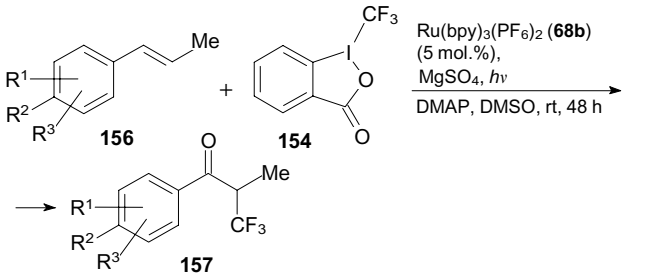
The proposed mechanism of this reaction is shown in Scheme 70.

Photocatalytic trifluoromethylation of 1-aryl-2-methyl-substituted alkenes **156** with Togni reagent **154** allows the synthesis of α-trifluoromethyl ketones **157**. It should be noted that this method is applicable only to electron-rich alkenes, the corresponding products being formed in low to

Scheme 70



Scheme 71



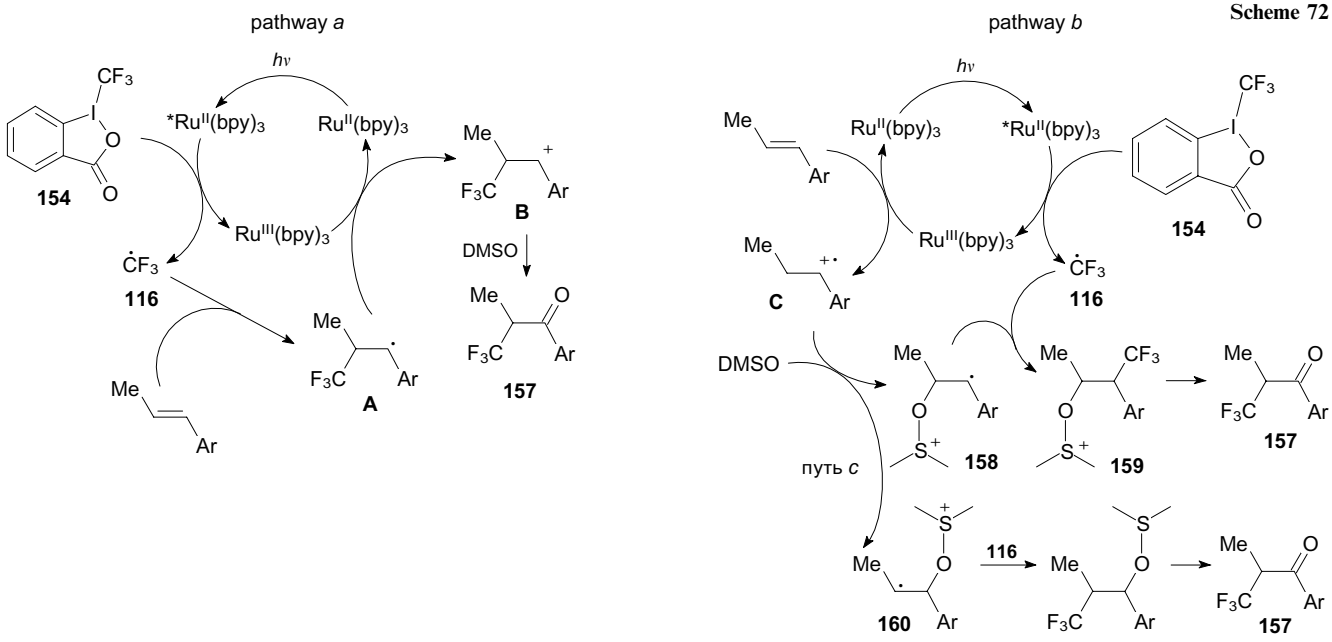
R^1	R^2	R^3	Yield (%)
H	OMe	H	40
H	NO_2	H	0
H	OMe	3-OMe	23
2-OMe	H	H	17
2-OMe	H	6-OMe	27
2-OMe	OMe	H	8
3-Br	OMe	H	29
2-OMe	OMe	5-OMe	20
3-OMe	OMe	5-OMe	31

moderate yields (8% – 40%). Electron-deficient alkenes ($R^1 = R^3 = H$, $R^2 = NO_2$) do not undergo this reaction (Scheme 71).[109]

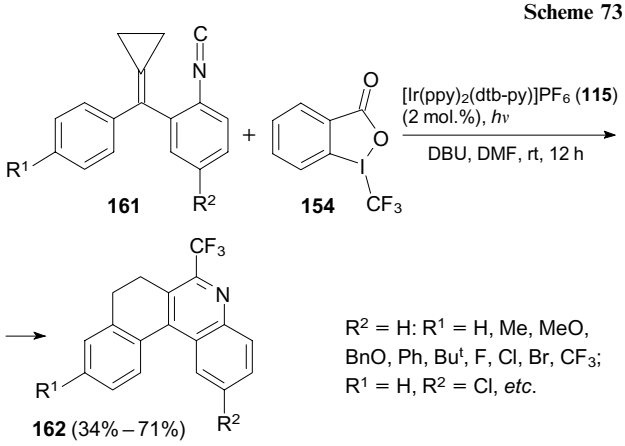
Li *et al.*[109] proposed two possible reaction mechanisms. One of them involves the oxidation of radical **A** with the complex $Ru^{III}(bpy)_3$ to carbocation **B** (pathway *a*). In an alternative mechanism, the initial stabilization of radical cation **C** with a DMSO molecule (intermediate **158**) is followed by the reaction with the CF_3 radical (pathway *b*) (Scheme 72). Upon the addition of $H_2{}^{18}O$ to the solvent, product **157** did not contain ^{18}O. Consequently, DMSO is the most likely source of oxygen in the product. Meanwhile, the proposed mechanism *via* pathway *b* implies the migration of methyl and aryl groups during the transformation of intermediate **159** into the reaction product, which seems doubtful.

The more probable mechanism involves the attack of radical cation **C** at the C – Me moiety by a DMSO molecule (see Scheme 72, intermediate **160**, pathway *c*).

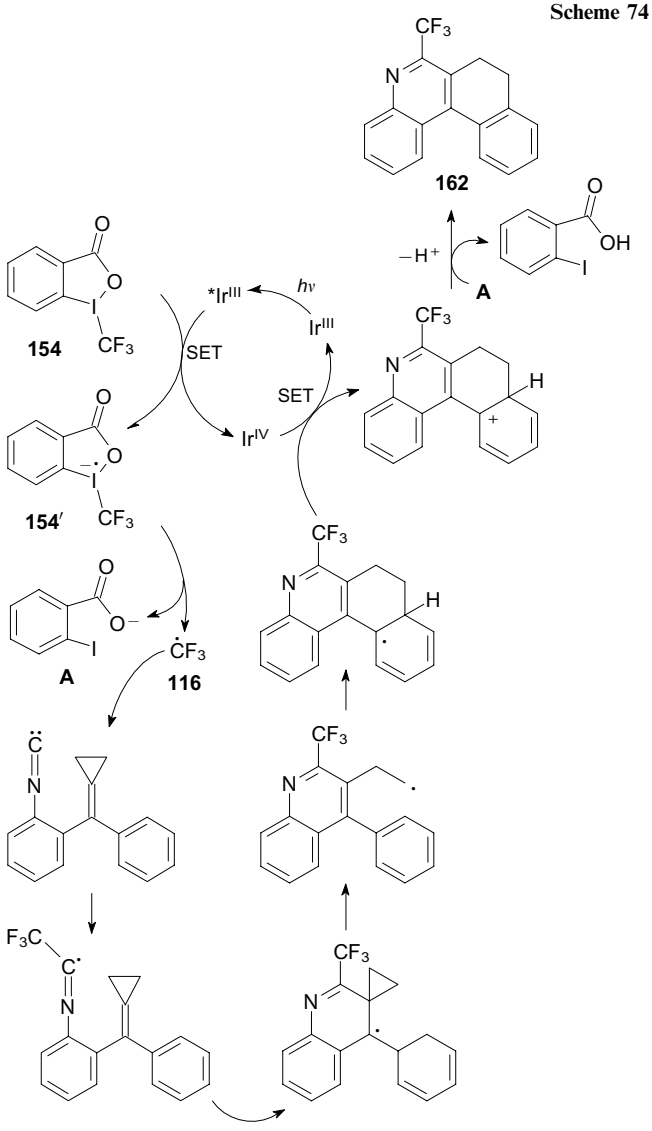
Scheme 72



Scheme 73



Scheme 74



Photocatalytic trifluoromethylation of isonitrile-substituted methylenecyclopropanes **161** allows the synthesis of 6-(trifluoromethyl)-7,8-dihydrobenzo[*k*]phenanthridines **162** under mild conditions in good yields (Scheme 73).[110]

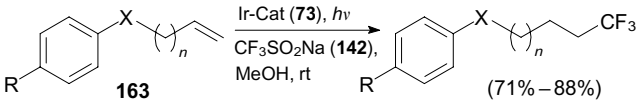
The proposed mechanism involves the reaction of trifluoromethyl radical **116**, which is generated from the radical anion of Togni reagent **154′**, with an isonitrile moiety followed by cyclization and cyclopropane ring opening (Scheme 74).

Zhu *et al.*[111] described the use of CF_3SO_2Na (**142**) as a trifluoromethyl radical source in the photocatalytic hydrofluoroalkylation of terminal alkenes **163** (Scheme 75). The highest yields of the trifluoromethylation products were achieved in the presence of iridium catalyst **73**, whereas the employment of the ruthenium catalyst $Ru(bpy)_3Cl_2$ (**68a**), as well as of other fluorinating agents (CF_3CO_2Na, CF_3CO_2H, $TMSCF_3$) in this reaction was not successful.

The possible reaction mechanism is shown in Scheme 76.

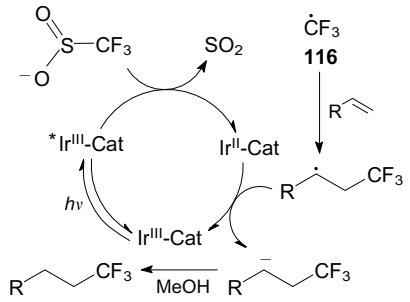
Photocatalytic trifluoromethylation of alkenes **164** with CF_3I in the presence of the ruthenium catalyst $Ru(bpy)_3Cl_2$ (**68a**) and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) pro-

Scheme 75

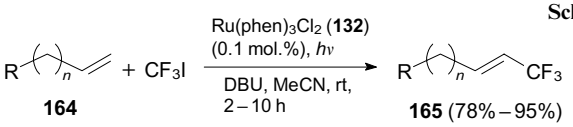


X = O, *n* = 4: R = H (77% yield), OMe (82%), Br (74%), CHO (78%), Me (82%); X = S, *n* = 2, R = Me (65%); X = CH_2, *n* = 1, R = H (85%); X is absent, *n* = 0, R = H (0%);

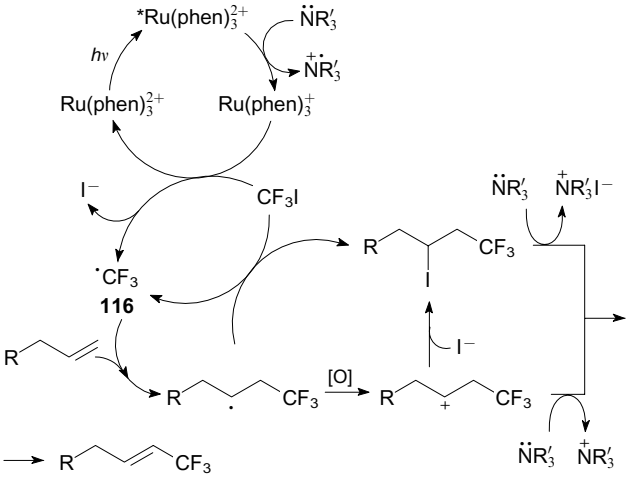
Scheme 76



Scheme 77



n = 1: R = $O(CH_2)_4OH$, $NHC(O)C_7H_{15}$-n;
n = 2: R = Ph; *n* = 4: R = OH, OTMS, OSO_2Ph, $OC(O)NMe_2$, $OC(O)Ph$, $OC(O)C_7H_{15}$-n; *n* = 8: R = CHO, C(O)Me;
n = 9: R = Me



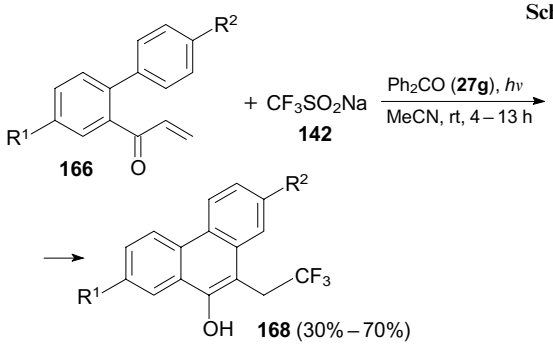
NR'_3 = DBU

vides a convenient route to functionalized trifluoromethylated alkenes **165** having an *E* configuration under mild conditions (Scheme 77).

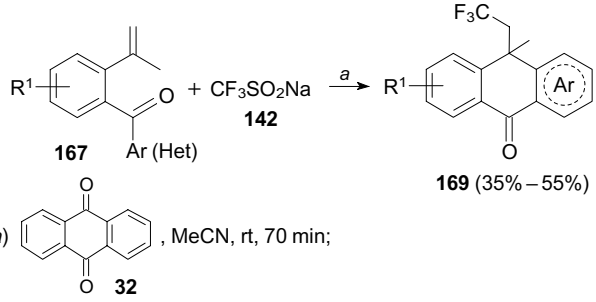
The best results as regards regio- and stereoselectivity and product yields were achieved with terminal alkenes. The reaction with internal unsaturated compounds gave a mixture of *E* and *Z* isomers in lower yields.[112]

The difunctionalization of alkenes resulting in the $C(sp^3)-CF_3$ and $C(sp^2)-C(sp^2)$ bond formation was performed using CF_3SO_2Na (**142**) in the presence of benzophenone (**27g**) or anthraquinone (**32**) as the photocatalyst.[113] In this work, α,β- (**166**) and γ,δ-unsaturated ketones (**167**) were used as substrates, which were subjected to tandem radical cyclization giving 2,2,2-trifluoroethyl-substituted phenanthren-9-ols **168** and anthrones **169**, respectively (Scheme 78). In both cases, the yields of the cyclic products were on average 30% – 50%; the presence of a strong electron-withdrawing substituent in alkenes promotes an increase in the yield of the product (**168h**, 70%). The nature of the substituent in the (het)aryl group has no significant effect on the yield of the final product.

Scheme 78



R^2 = H: R^1 = H (**a**, 45%), OMe (**b**, 47%), Cl (**c**, 30%), F (**d**, 44%);
R^1 = H: R^2 = Me (**e**, 30%), Bu^t (**f**, 38%), OMe (**g**, 47%), F (**h**, 70%);
R^1 = OMe, R^2 = F (**k**, 50%)



(*a*) , MeCN, rt, 70 min;

R^1 = H: Ar = 3-Cl-4-FC_6H_3 (**a**, 47%), 2-ClC_6H_4 (**b**, 59%), 1-Naph (**c**, 43%), Ph (**d**, 51%), 4-Py (**e**, 46%), 2-Th (**f**, 39%);
R^1 = 4-OMe, R^2 = 4-FC_6H_4 (**g**, 44%), *etc.*

The proposed reaction mechanism involves the addition of the trifluoromethyl radical (**116**) to the double bond in alkene **166** followed by the attack of the resulting radical **170** on the adjacent aromatic ring (Scheme 79).

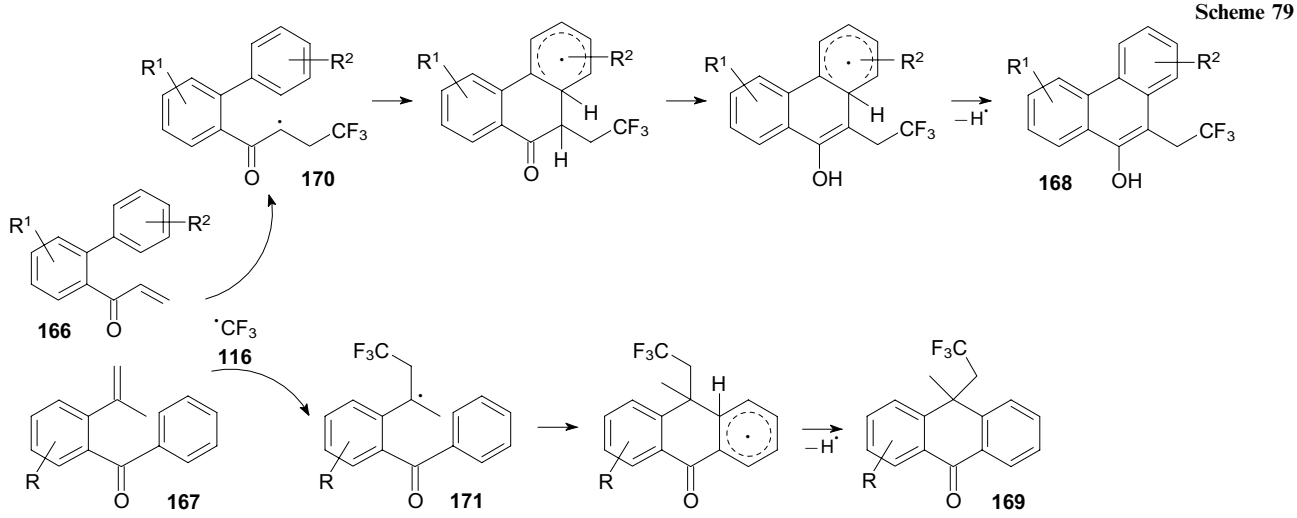
Similarly, radical **171**, generated through the addition of the CF_3 radical (**116**) to alkene **167**, is transformed into product **169**.

The formation of trifluoroethyl derivatives of phenanthridines **172** from *N*-arylacetamides **173** proceeds by a similar mechanism involving cyclization steps (Scheme 80).[114]

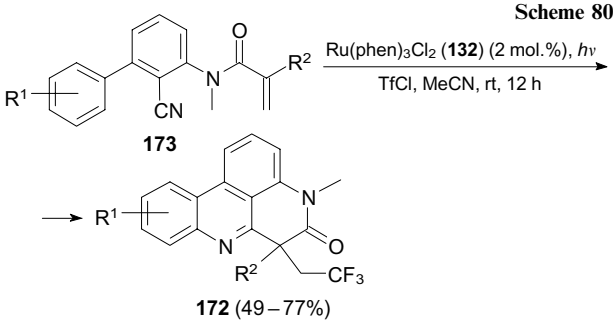
The employment of 2,2,2-trifluoroethyl iodide (**174**) and cobalt photocatalyst **175** in the reaction with styrenes **135** allows the synthesis of allyltrifluoromethanes **176** in moderate to high yields (Scheme 81).[115]

A study of the influence of the nature of metal complex catalysts (**84**, **177** – **180**) on the selectivity of trifluoroethylation of styrenes showed that dimerization is the main reaction pathway regardless of the ligand structure (Scheme 82, product **C**).[116] However, the use of the heterogeneous catalysts UiO-67-Ir$(ppy)_2$ (**179**) and UiO-67-Ir$(ppy^F)_2$ (**180**), which were prepared by the inser-

Scheme 79

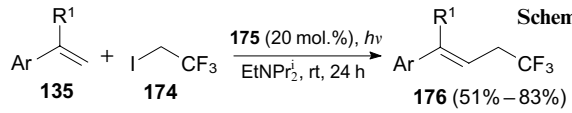


Scheme 80



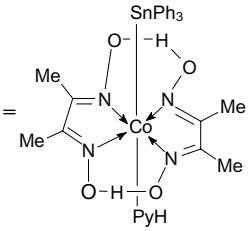
173: R^1 = R^2 = H; R^2 = Me: R^1 = H, 4-F, 4-Cl, 4-Br, 4-CN, 4-Et, 4-Bu^t, 4-Ph, 4-OMe, 3-Me, *etc*.

Scheme 81

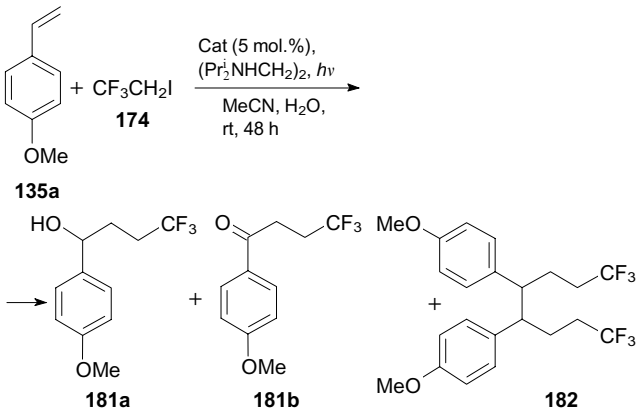


R^1 = H: Ar = 4-$R^2C_6H_4$ (R^2 = Bu^t, MeO, AcO, Me_2N, HO, MeS), 2-Naph; R^1 = Ar = Ph, *etc*.;

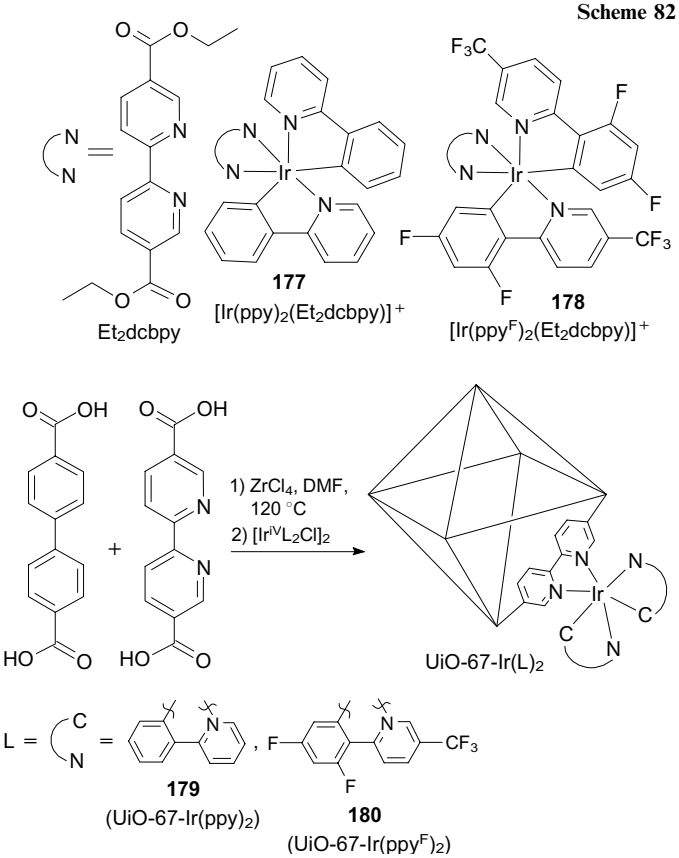
175 =



Scheme 82



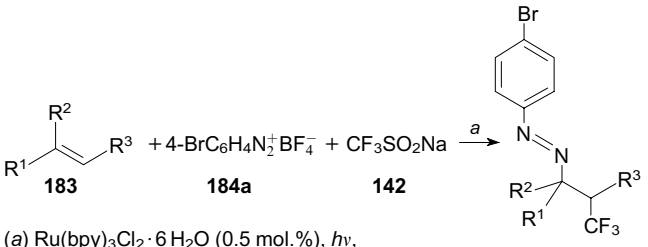
Cat	Yield (%)		
	181a	**181b**	**182**
Ir(ppy)$_3$ (**84**)	10	9	80
[Ir(ppy)$_2$](Et$_2$dcbpy)Cl (**177**)	20	7	72
[Ir(ppy^F)$_2$](Et$_2$dcbpy)Cl (**178**)	32	8	60
UiO-67-Ir(ppy)$_2$ (**179**)	60	11	28
UiO-67-Ir(ppy^F)$_2$ (**180**)	76	18	2



tion of complexes **177** and **178** into the Zr^{IV}-metal-organic framework (UiO-67), made it possible to significantly improve the selectivity of the synthesis of trifluoroethylated styrenes.

The photocatalytic trifluoromethylation of alkenes **183** with the participation of diazonium salts **184** and CF_3SO_2Na (**142**) affords fluorinated azo compounds **185** (Scheme 83).[117] The reactions were assumed to involve trifluoromethyl and phenyl radicals.

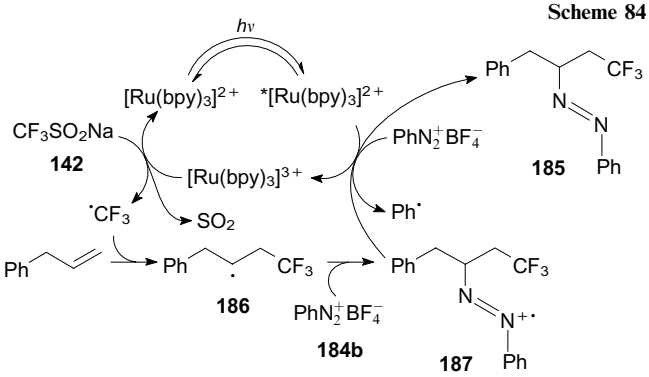
Scheme 83



(*a*) $Ru(bpy)_3Cl_2 \cdot 6H_2O$ (0.5 mol.%), *hν*, MeCN, 40 min; $R^2 = R^3 = H$: R^1 = Bn, $Ph(CH_2)_2$, 4-$BrC_6H_4CH_2$, $PhO(CH_2)_3$, $AcOCH_2$, $TMSCH_2$, Bu, Cy; $R^3 = H$, R^2 = Me, $R^1 = Ph(CH_2)_2$; $R^1 = H$, $R^2 = R^3$ = Et, *etc.*

The possible reaction mechanism includes the trapping of CF_3-containing radical **186** with diazonium salt **184b** to form radical cation **187** and the reduction of the latter with the species $[Ru(bpy)_3]^{2+}$ giving the final product **185** (Scheme 84).

Scheme 84



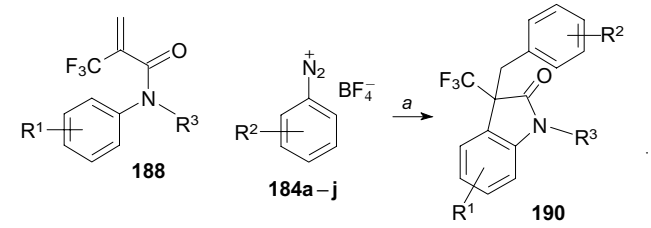
The photocatalytic transformation of acrylamides **188** in the presence of aryl diazonium salts **184a–j** and erythrosine B (**189**) as an organic photocatalyst was applied to prepare 3-trifluoro-2,3-dihydroindol-2-ones **190** (Scheme 85).[118]

4,4′-Dimethoxybenzophenone (**191**) is an efficient photocatalyst for trifluoromethylation of unsaturated N,O-heterocycles [pyrrolinediones **192** and 2,5-furandione (**193**) with CF_3SO_2Na (**142**)] (Scheme 86).[119] The reactions proceed through diarylmethyl (**194**) and cycloalkyl (**195**) radicals (Scheme 87).

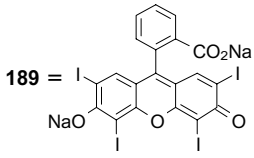
The photocatalytic reaction of *N*-(het)aryl-*N*-hydroxylamides **196** with perfluoroalkyl iodides **197** in the presence of ruthenium catalyst **68b** provides the most common approach to the synthesis of perfluoroalkoxy-substituted arenes and hetarenes **198** (Scheme 88).[120]

The reaction is accompanied by the N–C migration of the OR_f group (Scheme 89).

Scheme 85

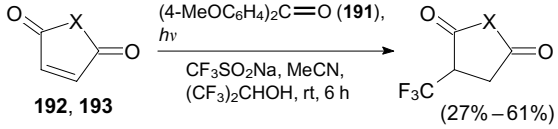


(*a*) **189** (5 mol.%), *hν*, MeOH, –50 °C, 4–6 h;
184: R = 4-Br (**a**), H (**b**), 4-Me (**c**), 4-MeO (**d**), 4-F (**e**), 4-Cl (**f**), 3-Cl (**g**), 2-Cl (**h**), 2-CN (**i**), 2-F (**j**);



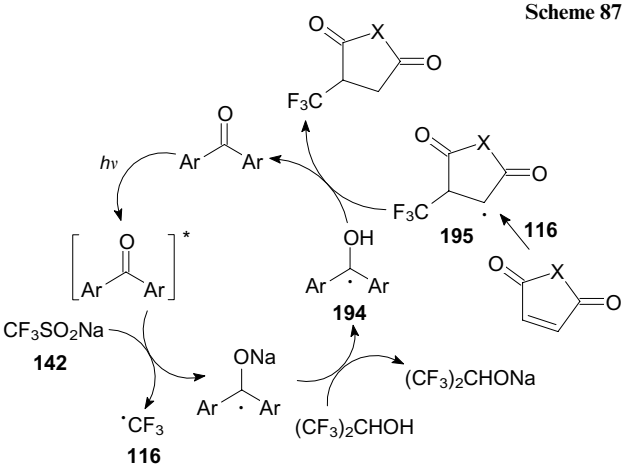
$R^1 = H$, R^3 = Me: $R^2 = H$ (41%), 4-Me (83%), 4-MeO (38%), 4-F (70%), 4-Cl (73%), 4-Br (80%), 3-Cl (34%), 2-Cl (35%), 2-NC (0%); $R^1 = H$, R^3 = Et: R^2 = 2-F (26%), 4-F (67%); R^1 = 5-Cl, R^3 = Me, R^2 = 4-Cl (57%), *etc.*

Scheme 86

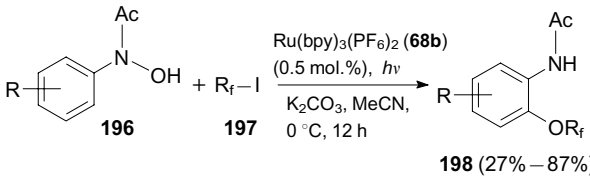


X = MeN, Bu^nN, BnN, PhN, O, 2-MeC_6H_4N, 2-$F_3CC_6H_4N$, 2-$MeOC_6H_4N$, 4-ClC_6H_4N, 3-BrC_6H_4N, *etc.*

Scheme 87

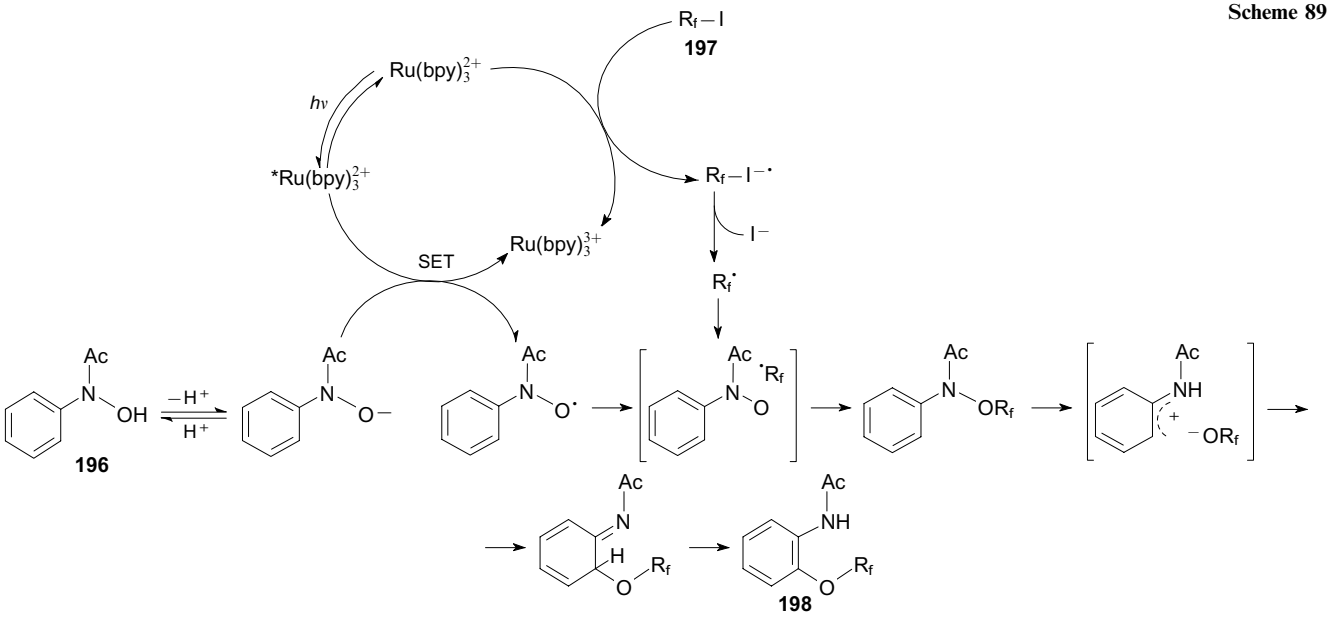


Scheme 88



$R_f = CF_3$: R = H, 4-Bu^t, 4-Br; R = 4-Bu^t: $R_f = CF(CF_3)C_2F_5$, $(CF_2)_5CF_3$, $(CF_2)_2Cl$, $(CF_2)_2Br$

Scheme 89

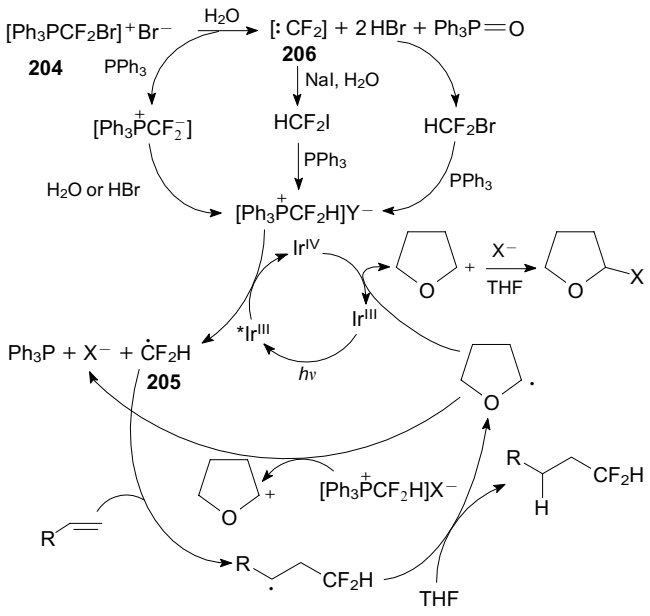


6. Introduction of CF_2X groups

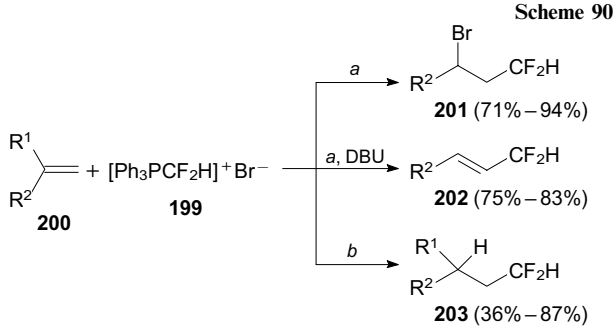
Among various fluorine-containing alkyl groups, the difluoromethyl group is an important structural unit. The introduction of this moiety into a molecule generally leads to an increase in the binding ability and lipophilicity of the drug. Besides, this group is isosteric and isopolar to such groups as OH and SH.[121–123] It was shown that (difluoromethyl)triphenylphosphonium bromide (**199**) can be used as a $^{\bullet}CF_2H$ radical source.[124] The reaction of terminal alkenes **200** with this reagent in the presence of the catalyst $Ir(ppy)_3$ (**84**) affords bromodifluoromethylation products **201** in high yields (Scheme 90,*a*). In the presence of DBU, the reaction proceeds *via* dehydrobromination to form difluoromethyl-substituted alkenes **202** predominantly in the *E* configuration. The use of the catalyst $Ir(ppy)_3$ (**84**) in the presence of the $NaI-Ph_3P-KHCO_3-H_2O$ system allows the selective difluoromethylation (product **203**), while the formation of bromodifluoromethylated by-products **201** is suppressed (see Scheme 90,*b*).[125]

The photocatalytic hydrodifluoromethylation of alkenes with (bromodifluoromethyl)triphenylphosphonium bromide (**204**) presumably gives, apart from the $^{\bullet}CF_2H$ radical (**205**), difluorocarbene (**206**) (Scheme 91).[125]

Scheme 91



Scheme 90



(*a*) $Ir(ppy)_3$ (**84**), $CuBr_2$, DMF, *hν*, rt, 10 h; R^1 = H: R^2 = $(CH_2)_2Ph$, $(CH_2)_3OC_6H_4CO_2Et$-4, $(CH_2)_2OC(O)Ph$, $(CH_2)_8CO_2H$, ONaph, *etc.*; (*b*) $Ir(ppy)_3$ (**84**), Ph_3P, NaI, $KHCO_3$, H_2O, THF, *hν*, rt, 10 h; R^1 = H: R^2 = $(CH_2)_2Ph$, $(CH_2)_6Br$, $(CH_2)_8OH$, $(CH_2)_8CHO$, $(CH_2)_8CO_2H$, $(CH_2)_2OBz$, $CH_2P(O)Ph_2$, C_6H_4OMe-4

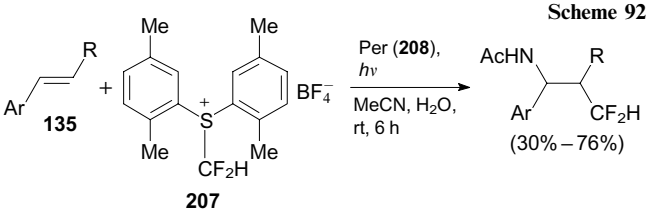
Noto *et al.*[126] developed a method for the regioselective aminodifluoromethylation of terminal and internal alkenes **135** containing aromatic substituents based on the combined use of *S*-difluoromethyl-*S*-di(*p*-xylyl)sulfonium tetrafluoroborate (**207**) and perylene (**208**) as the photocatalyst (Scheme 92).[126]

The C–N bond is formed *via* the Ritter reaction (Scheme 93).

Iridium photocatalyst **84** and bromides $BrCF_2R$ (**209**) were employed to introduce a CF_2R group [R = H, CO_2Et, $C(O)NEt_2$, CF_2Br, *etc.*] into uracils and pyridinones **210**, as well as into coumarins and quinolinones **211** (Scheme 94).[127]

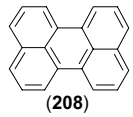
This reaction presumably proceeds through difluoromethyl (**212**) and cycloalkyl (**213**) radicals as the key intermediates (Scheme 95).

Scheme 92



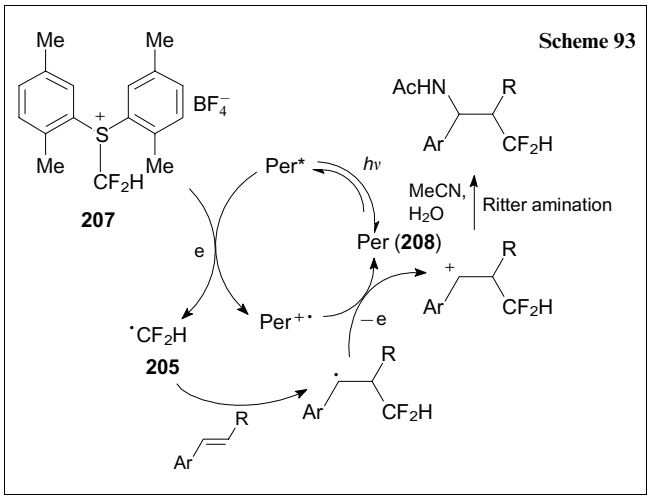
R = H: Ar = Ph, 4-MeC_6H_4, 4-FC_6H_4, 4-ClC_6H_4, 4-BrC_6H_4, 4-AcOC_6H_4, 3-OHCC_6H_4, Mes; R = Me, Ar = Ph; R = Ar = Ph , *etc.*;

Per =

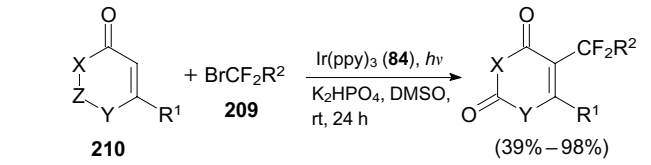


(**208**)

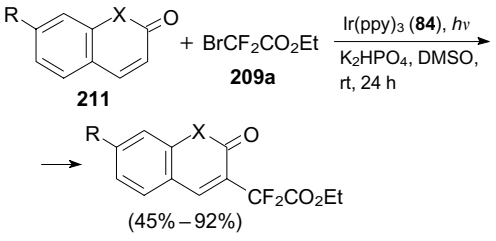
Scheme 93



Scheme 94



X = Y = NH, Z = CH: R^1 = H, Me, CF_3, R^2 = CO_2Et; X = Y = NMe, Z = C(O): R^1 = H, R^2 = CO_2Et, CF_2Br, C(O)NEt_2 , *etc.*



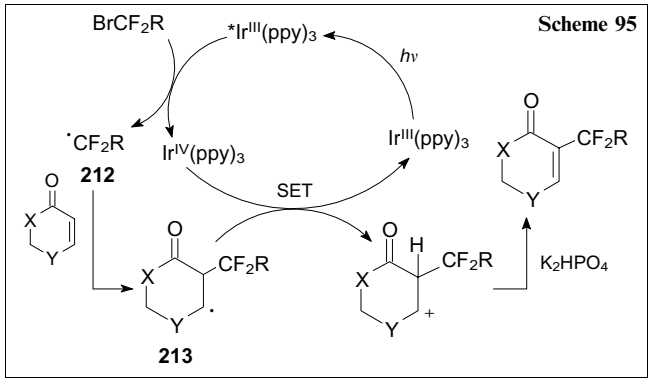
X = NH: R = H, Br; X = NMe, R = H; X = O: R = H, Me, OMe, OH, NEt_2, *etc.*

Yin *et al.*[128] developed a photocatalytic method for the selective introduction of a CF_2CO_2Et group into imidazo[1,2-*a*]pyridines (Scheme 96).

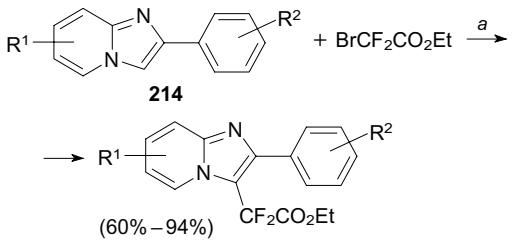
An efficient procedure for the enantioselective difluoro- and perfluoroalkylation of β-ketoesters **215** was developed based on cooperative photocatalysis and asymmetric Lewis acid catalysis (Scheme 97).[129]

The participation of the $^{\cdot}CF_2CO_2Et$ radical (**212a**) in this reaction was confirmed using the radical scavenger

Scheme 95

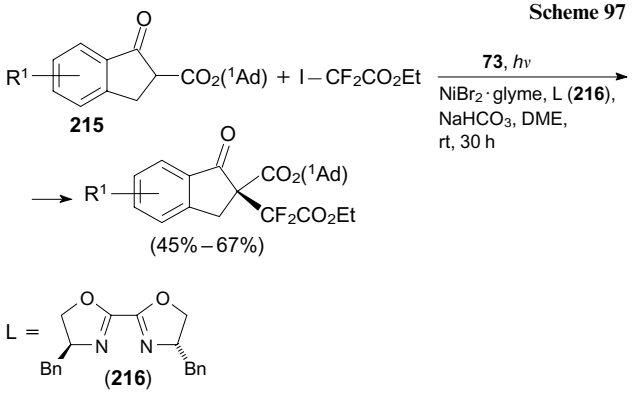


Scheme 96

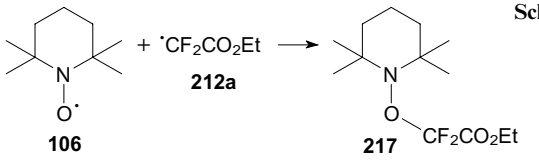


(*a*) Ir(ppy)$_3$ (**84**), *hv*, K_2CO_3, DMSO, rt, 24 h;
R^1 = H: R^2 = 4-Me, 4-Cl, 4-Br, 4-F, 4-CF_3, 4-CN, 3-Me, 3-MeO, 3-Br;
R^2 = H: R^1 = 7-Me, 8-Me, 6-Cl, 8-Cl, *etc.*

Scheme 97



Scheme 98



(TEMPO, **106**), and the structure of adduct **217** was determined by NMR spectroscopy (Scheme 98).[129]

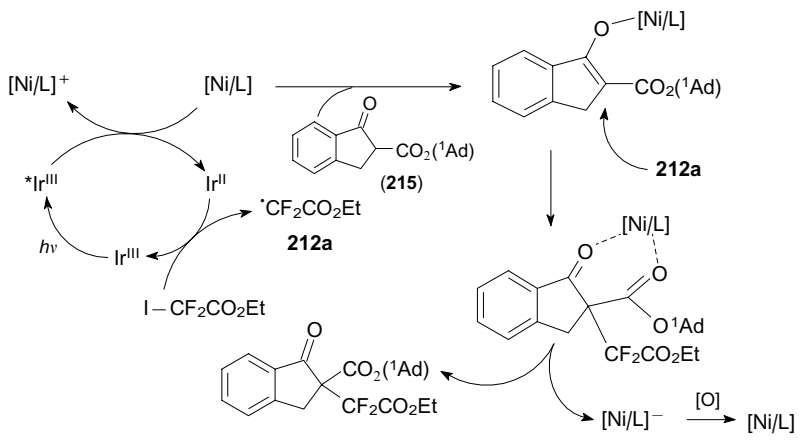
The proposed reaction mechanism is shown in Scheme 99.

gem-Difluorinated phosphonium salts **218** were employed in the photocatalytic synthesis of β-difluorohydroxyalkyl-substituted benzenes **219** (Scheme 100).[130]

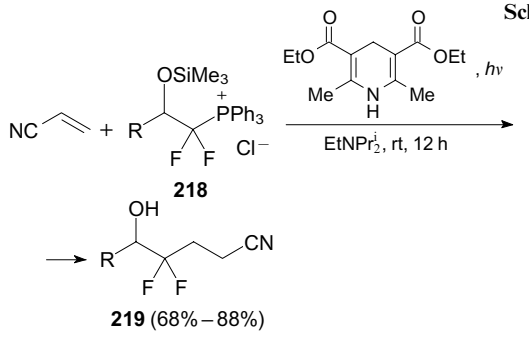
The possible mechanism involves the formation of alkyl radicals **220**, **221** and Hantzsch ester radical cation **222** (Scheme 101).

gem-Difluorohomoallyl alcohols **223** were synthesized by the photocatalytic replacement of iodine in β-iododi-

Scheme 99

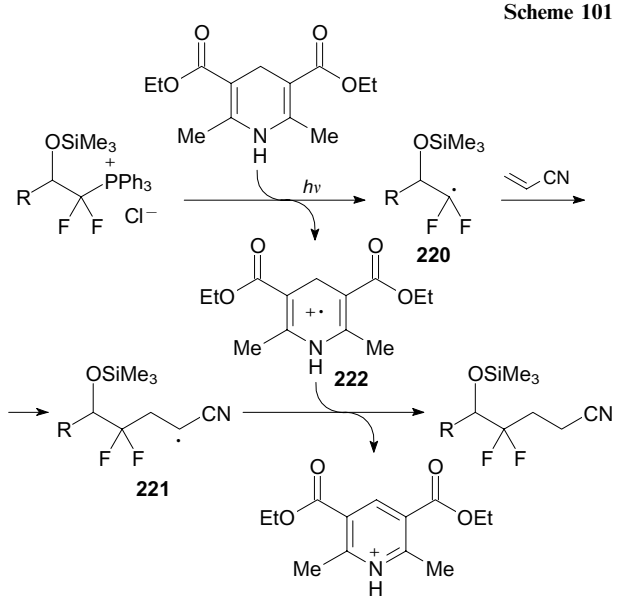


Scheme 100

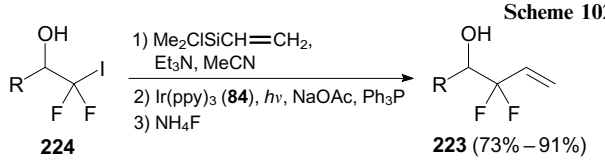


R = 4-XC_6H_4 (X = H, OMe, CO_2Me, CN, Cl, $PhCH_2$)

Scheme 101

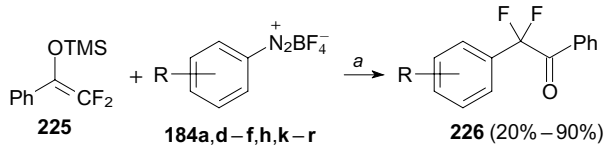


Scheme 102



R = Ph, 4-$MeOC_6H_4$, 4-NCC_6H_4, 4-$MeO_2CC_6H_4$, 4-ClC_6H_4, 4-PhC_6H_4 , *etc.*;

Scheme 103



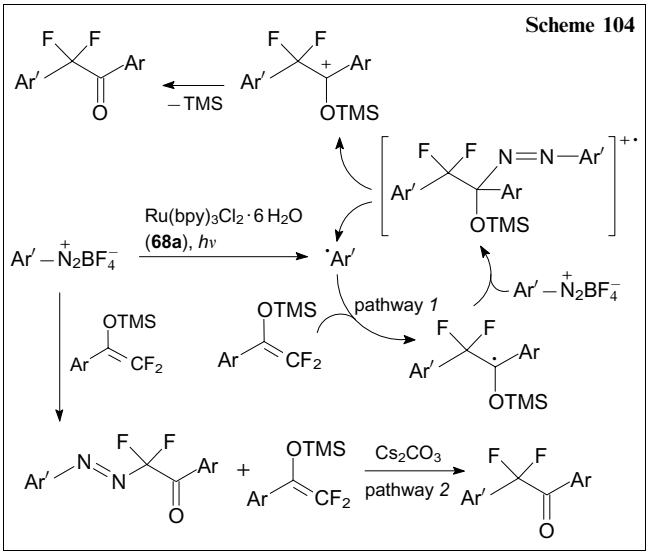
(*a*) $Ru(bpy)_3Cl_2 \cdot 6H_2O$ (**68a**), *hν*, Cs_2CO_3, MeCN, rt, 2 h;
184: R = 4-Br (**a**), 4-OMe (**d**), 4-F (**e**), 4-Cl (**f**), 2-Cl (**h**), 4-I (**k**), 4-NO_2 (**l**), 4-CF_3 (**m**), 4-CO_2Et (**n**), 4-CN (**o**), 3-NO_2 (**p**), 3-CF_3 (**q**), 2-NO_2 (**r**)

fluoromethyl-substituted alcohols **224** by the vinyl moiety (Scheme 102).[131]

The visible light-initiated reaction of α-aryl-β,β-difluoroenol silyl ether (**225**) with aryldiazonium tetrafluoroborates **184a**,**d**–**f**,**h**,**k**–**r** in the presence of ruthenium catalyst **68a** affords difluoroketones **226** rather than diazo compounds as the major products (Scheme 103).[132] In most cases, the reaction proceeds in high yields; however, the presence of an electron-withdrawing substituent in the *ortho* position of the starting diazo compound leads to a significant decrease in the product yield [**184r** (20%), **184h** (40%)].

The reactions are inhibited by the addition of TEMPO (**106**), which attests to the participation of radicals in the photocatalysis and indicates that the reaction proceeds

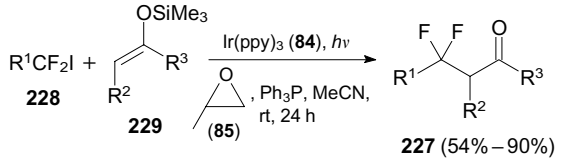
Scheme 104



predominantly by pathway *1* rather than pathway *2* (Scheme 104).

A selective procedure for the synthesis of β,β-difluoroketones **227** is based on the cleavage of α,α-difluorinated iodides **229** (Scheme 105).[133] The proposed mechanism involves the visible-light-induced reduction of iodide R^1CF_2I (**228**) with the catalyst $Ir(ppy)_3$ (**84**) as the key step, which is confirmed by a comparison of the reduction potential of this iodide and the potential for the $*Ir^{III}/Ir^{IV}$ pair (−1.11 and −1.73 V, respectively).

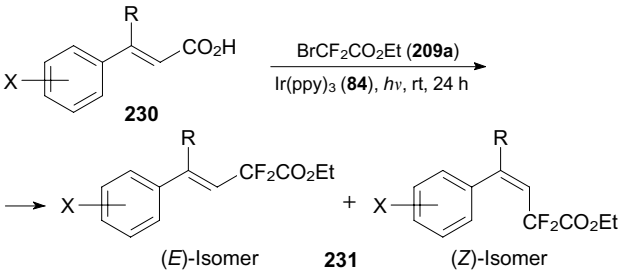
Scheme 105



R^1 = Bn, R^2 = H: R^3 = Ph, 4-$MeOC_6H_4$, 4-IC_6H_4, 2-Naph, 2-Th; R^1 = Ph(Me)CH, R^2 = H: R^3 = 4-$MeOC_6H_4$, furan-2-yl; R^1 = 4-$MeO_2CC_6H_4CH_2$, R^2 = H: R^3 = 4-ClC_6H_4, Bu^t, *etc.*

The photocatalytic reaction of cinnamic acid derivatives (**230**) with $BrCF_2CO_2Et$ (**209a**) in the presence of iridium catalyst **84** proceeds *via* decarboxylation giving difluoromethylstyrenes **231** (Scheme 106).[134]

Scheme 106



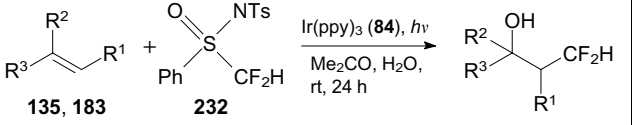
R	X	Isomer ratio (*E* : *Z*) **231**	
		batch conditions	continuous-flow reactions
H	2-Me	6 : 94	92 : 8
H	2-MeO	9 : 91	87 : 13
H	2-F	14 : 86	91 : 9
H	2-Cl	8 : 92	90 : 10
Me	H	10 : 90	90 : 10
Me	4-Br	18 : 92	90 : 10

The use of a continuous-flow system with a controlled reaction time allows the synthesis of predominantly the *E* isomer. Meanwhile, the reaction in batch affords the *Z* isomer as the major product. The reaction with arylpropiolic acids proceeds in a similar manner.

The photocatalyst $Ir(ppy)_3$ (**84**) was also used for hydroxydifluoromethylation of alkenes **135** and **183** with $PhS(O)CF_2H(NTs)$ (**232**) (Scheme 107).[135]

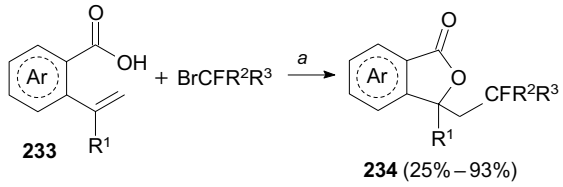
The photocatalytic cascade difluoroalkylation of alkenes **233** followed by intramolecular cyclization provides

Scheme 107



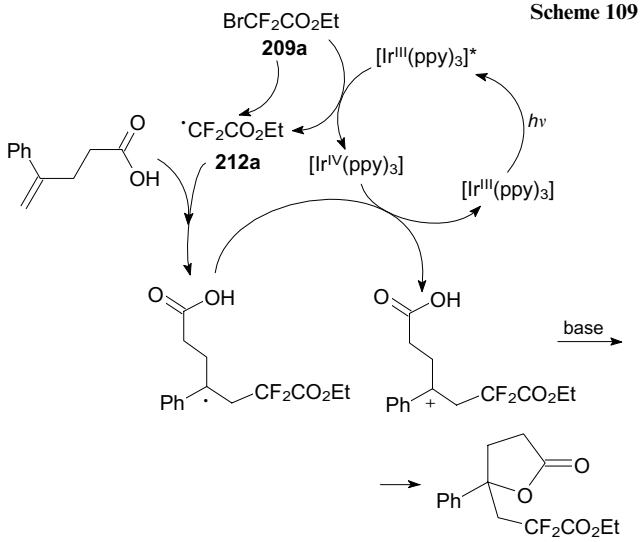
R^1 = R^2 = H, R^3 = 4-XC_6H_4 (X = H, Me, MeO, Bu^t, Br, Cl, F); R^2 = H, R^3 = Ph, R^1 = Me, CH_2OH, Ph; R^1 = H; R^2 = Me, R^3 = Ph; R^1 = H, R^2 = R^3 = Cy; R^1 = R^2 = Me, R^3 = Ph

Scheme 108



(*a*) [Ir(ppy)$_3$] (**84**), *hν*, HCO_2Na, CH_2Cl_2, rt, 24 h; Ar = C_6H_4, R^2 = F, R^3 = CO_2Et: R^1 = H, Me, Ph, 4-MeC_6H_4, 4-ClC_6H_4; Ar is absent, R^2 = F, R^3 = CO_2Et: R^1 = Ph, 4-PhC_6H_4, 4-ClC_6H_4, 4-$MeOC_6H_4$, 4-FC_6H_4, 4-MeC_6H_4; Ar is absent, R^1 = Ph, R^2 = F: R^3 = F, P(O)$(OEt)_2$, furyl carbonyl, C(O)C_6H_4OMe-4, morpholinocarbonyl, C(O)NH – cyclo-C_7H_{13}; R^2 = H, R^3 = CO_2Et

Scheme 109



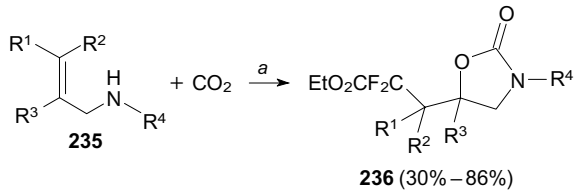
a route to oxygen heterocycles **234** in moderate to high yields (Scheme 108).[136]

The radical character of the reaction (Scheme 109) was confirmed by its suppression upon the addition of the radical scavenger TEMPO (**106**).

The selective photocatalytic difluoroalkylation of alkenes **235** with the participation of CO_2 and ruthenium catalyst **68a** is an efficient and environmentally friendly route to oxazolidin-2-ones **236** (Scheme 110).[137]

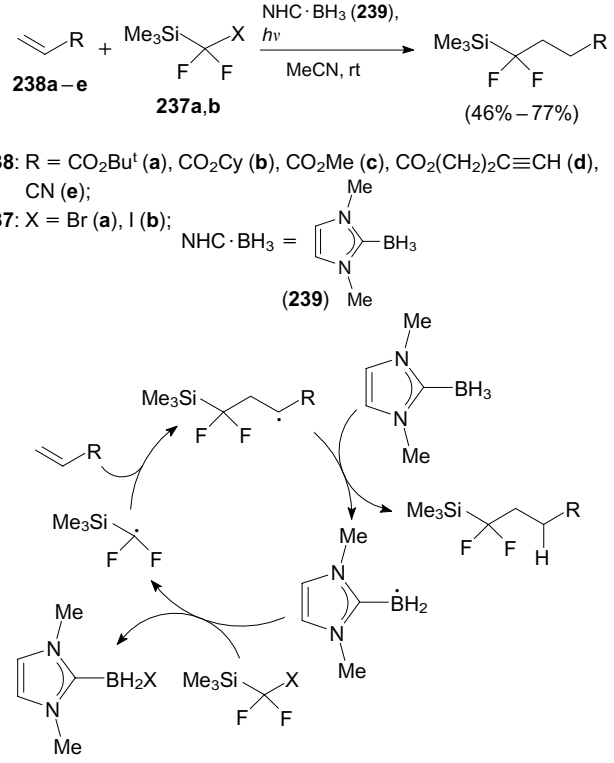
The reaction of bromo- or iododifluoromethylsilanes **237** with electron-deficient alkenes **238** in the presence of heterocyclic carbenoids **239** was performed under visible light irradiation by a radical chain mechanism (Scheme 111).[138]

Scheme 110



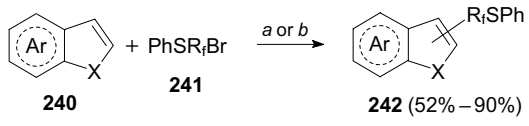
(*a*) $Ru(bpy)_2Cl_2 \cdot 6H_2O$ (**68a**), *hν*, $BrCF_2CO_2Et$ (**209a**), DABCO, DMF, rt, 10 h; $R^1 = R^2 = H$: R^3 = Ph, 3-MeC_6H_4, 3-ClC_6H_4, 4-MeC_6H_4, 4-ClC_6H_4; R^1 = Me, R^2 = H, R^3 = Ph; R^4 = Bn

Scheme 111



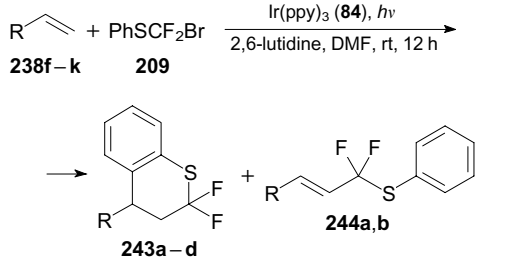
238: R = CO_2Bu^t (**a**), CO_2Cy (**b**), CO_2Me (**c**), $CO_2(CH_2)_2C{\equiv}CH$ (**d**), CN (**e**);
237: X = Br (**a**), I (**b**);
NHC·BH_3 = (**239**)

Scheme 112



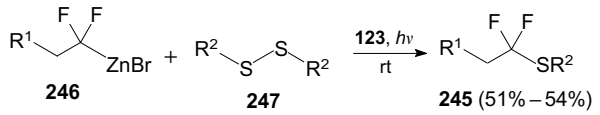
(*a*) $Ir(ppy)_3$ (**84**), 2,6-lutidine, DMF, *hν*, rt, 12 h, $R_f = CF_2$;
(*b*) $[Ru(phen)_3]Cl_2$ (**132**), TMEDA, MeCN, *hν*, 24 ч, $R_f = (CH_2)_n$, n = 2, 4; Ar = C_6H_4: X = NH, NMe; $R_f = (CF_2)_n$, n = 1, 2, 4, X = O, S, $R_f = CF_2$; Ar is absent, X = NMe, $R_f = (CF_2)_n$, n = 1, 2, 4, R^1 = H, *etc*.

Scheme 113



243: R = n-C_8H_{17} (**a**, 75%), $Ph(CH_2)_2$ (**b**, 76%), $PhCO_2(CH_2)_4$ (**c**, 80%), 4-$ClC_6H_4C(O)NHCH_2$ (**d**, 70%);
244: R = 4-$MeOC_6H_4$ (**a**, 81%), $Ph_2C{=}CH$ (**b**, 90%)

Scheme 114



$R^2 = Et_2NC(S)$: R^1 = Ph, 4-$MeO_2CC_6H_4$; $R^1 = R^2$ = Ph

Arylthiofluoroalkylation of unactivated heteroaromatic compounds and alkenes **240** with readily available phenylthiofluoroalkyl bromides **241** in the presence of Ir or Ru organometallic photocatalysts **84** and **132** allows the simultaneous introduction of a sulfur atom and a fluoroalkyl group into molecule **240** under mild conditions (Scheme 112).[139] It should be noted that different combinations of a photocatalyst, a base and a solvent enable one to prepare compounds **242** in high yields regardless of the reactivity of the arylthiofluoroalkyl radical.

The thiofluoroalkylation of alkenes **238f–k** affords either heterocyclic (**243**) or acyclic alkenyl products (**244**) (Scheme 113).[139] The reactions of aryl- and diphenylethylene-substituted alkenes **238j**,**k** yield acyclic compounds **244a**,**b** as the major reaction products, while the reactions of aliphatic alkenes **238f–i** performed under the same conditions give cyclization products **243a–d**.

Another approach to the photocatalytic synthesis of difluoromethyl-containing organosulfur compounds **245** is based on the reaction of *gem*-difluorinated organozinc compounds **246** with disulfides **247** as electrophilic agents (Scheme 114).[140]

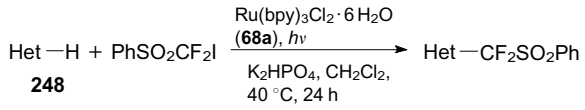
A new method was developed for the introduction of the $PhSO_2CF_2$ group into nitrogen, oxygen and sulfur heterocycles **248** in the presence of ruthenium photocatalyst **68a** (Scheme 115).[141]

Pyrrole derivatives (**248a–e**) and furan derivatives (**248f–h**) were regioselectively difluoromethylated in position 2 of the heterocycle. The lowest regioselectivity of the reaction was observed for thiophene and its derivatives **248i–l**. Su *et al.*[141] failed to detect the adduct of the CF_2SO_2Ph radical and the radical scavenger TEMPO (**106**). They employed radical clocks to trap this radical (Scheme 116, lower equation). The reaction of $PhSO_2CF_2I$ with allyl ether **249** gave cyclic product **250**, which attests to the participation of the $PhSO_2CF_2$ radical in the reaction.

S-Perfluoroalkyl sulfilimino iminium salts **251** were proposed as sources of R_f radicals ($R_f = CF_3$, C_4F_9, CF_2Br, $CFCl_2$) in the photocatalytic alkoxyperfluoroalkylation of alkenes **135** and **183** (Scheme 117).[142] The radical character of the reaction (Scheme 118) is confirmed by its inhibition in the presence of TEMPO (**106**) or O_2.

Photocatalytic ethoxycarbonyldifluoromethylation of alkenols **147** with ethyl bromodifluoroacetate (**209a**) affords difluoroalkyl-substituted cyclic ketones **252** *via* difluoroal-

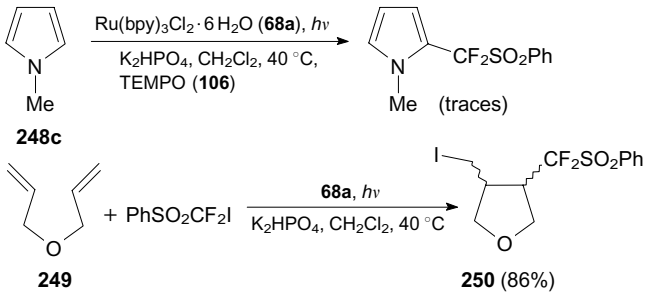
Scheme 115



248 =  [X = NH: R = H (**a**), 2-CO_2Et (**b**); X = NMe: R = H (**c**), 2-CH_2CO_2Me (**d**), 2-C(O)Me (**e**); X = O: R = H (**f**), 2-Et (**g**), 2-OMe (**h**); X = S: R = H (**i**), 2-Me (**j**), 2-Ph (**k**), 3-OMe (**l**)];

 [X = NH, R = Me (**m**); X = NMe: R = Me (**n**), n-C_5H_{11} (**o**), Pr^i (**p**), Ph (**q**)]

Scheme 116

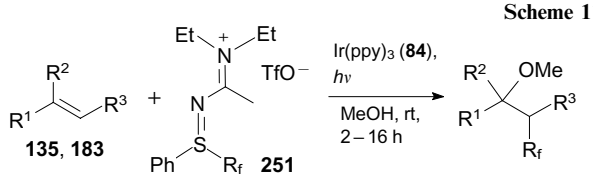


kylation and 1,2-alkyl migration (Scheme 119).[143] Upon the addition of TEMPO (**106**), reaction products were not detected, which is indicative of the participation of radicals in the key steps of the reaction.

Photocatalytic carbodifluoroalkylation of secondary and tertiary homopropargyl alcohols **253** in the presence of iridium catalyst **84** proceeds *via* 1,4-aryl migration (Scheme 120).[144]

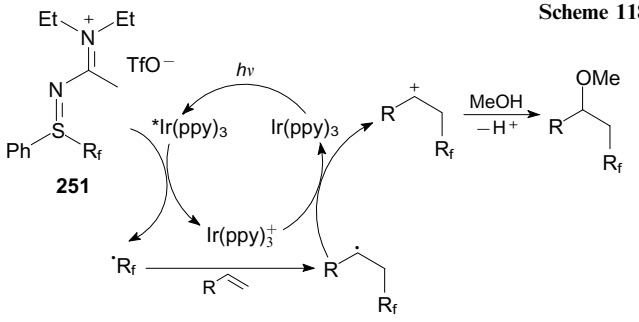
In a similar reaction, 1,3-diarylpropynones **254** undergo radical cyclization to form 3-aryl-2-ethoxycarbonyldifluoromethylindenones **255** (Scheme 121).[145]

Scheme 117

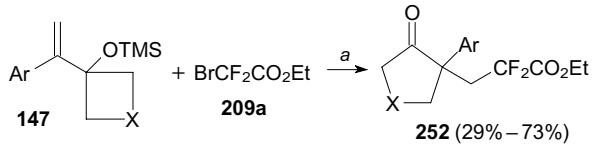


R^1 = 4-Bu^{t}C$_6$H$_4$, R^2 = R^3 = H: R_f = C_4F_9 (72%), CF_2Br (77%), $CFCl_2$ (66%); R^1 = 3-MeC$_6$H$_4$, R^2 = R^3 = H: R_f = C_4F_9 (68%), CF_2Br (65%); R^1 = 4-MeOC$_6$H$_4$, R^2 = R^3 = H: R_f = C_4F_9 (77%), CF_2Br (76%), $CFCl_2$ (65%); R^1 = 4-ClC$_6$H$_4$, R^2 = R^3 = H: R_f = CF_2Br (67%), $CFCl_2$ (64%); R^1 = Ph, R^2 = H, R^3 = Ph, R_f = $CFCl_2$ (58%); R^1 = AcMeN, R^2 = R^3 = H, R_f = C_4F_9 (83%), *etc.*

Scheme 118

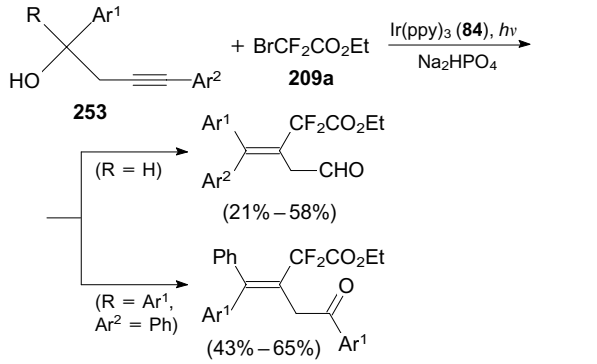


Scheme 119



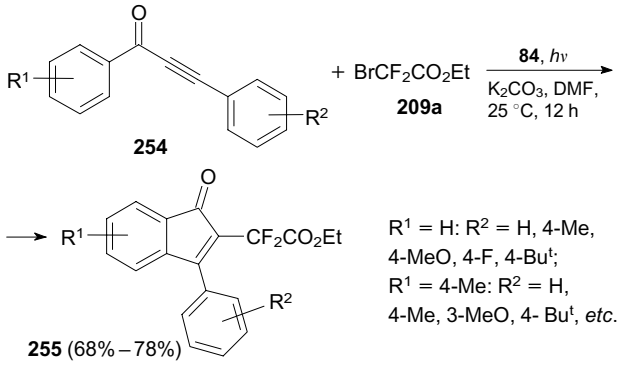
(*a*) Ir(ppy)$_3$ (**84**), *hv*, K_2CO_3, DMF, rt, 3 h;
X = CH_2: Ar = Ph, 4-MeC$_6$H$_4$, 4-FC$_6$H$_4$, 3-FC$_6$H$_4$, 4-ClC$_6$H$_4$, 3-MeC$_6$H$_4$; X = O: Ar = Ph, *etc.*

Scheme 120



Ar^2 = Ph: Ar^1 = $R^1C_6H_4$ (R^1 = 4-Me, 4-MeO, 4-Br, 3-Me);
Ar^1 = Ph: Ar^2 = $R^2C_6H_4$ (R^2 = 4-F, 4-Br);
Ar^1 = 4-BrC$_6$H$_4$, Ar^2 = Ph; R = Ar^1 = Ph, 4-MeC$_6$H$_4$, 4-MeOC$_6$H$_4$, 4-FC$_6$H$_4$, *etc.*

Scheme 121

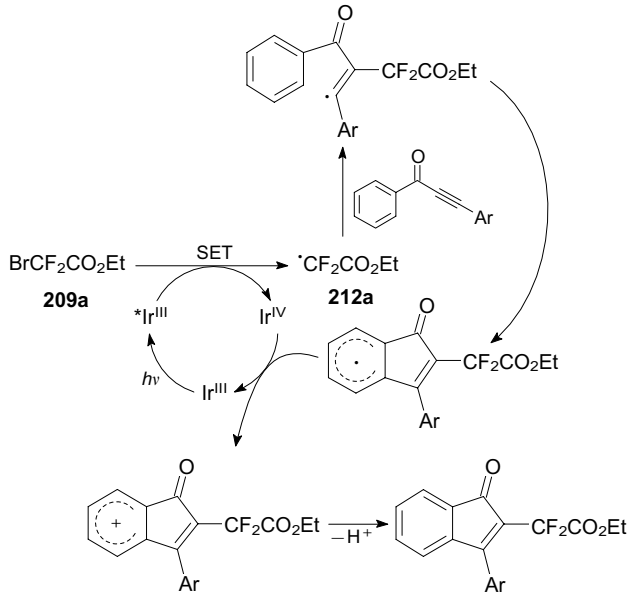


R^1 = H: R^2 = H, 4-Me, 4-MeO, 4-F, 4-Bu^t;
R^1 = 4-Me: R^2 = H, 4-Me, 3-MeO, 4- Bu^t, *etc.*

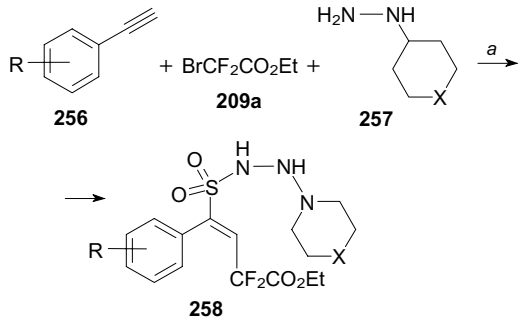
The mechanism of this reaction is shown in Scheme 122.

Photocatalytic vicinal difluoroalkylation and aminosulfonylation of alkynes **256** with ethyl 2-bromo-2,2-difluoroacetate (**209a**) in the presence of hydrazine derivatives **257**, a complex of 1,4-diazabicyclo[2.2.2]octane with SO_2 and 9-mesityl-10-methylacridinium perchlorate (Mes-Acr$^+$) (**61c**) as the photocatalyst proceeds with high stereoselectivity (Scheme 123).[146]

Scheme 122



Scheme 123

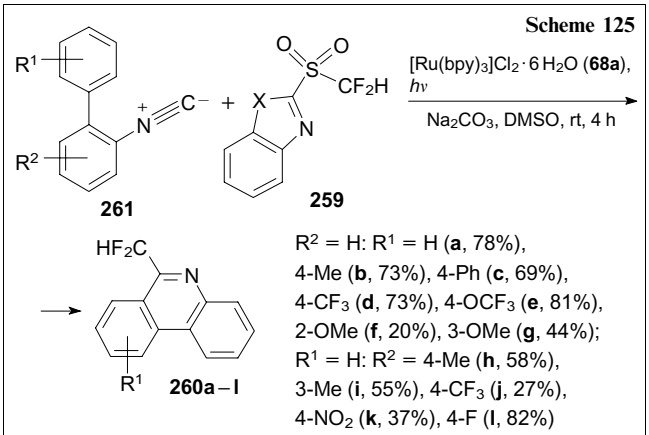


(*a*) **61c**, *hν*, DABCO · $(SO_2)_2$, DMF, rt, 12 h;
X = O: R = H (71%), 2-Me (77%), 4-Me (88%), 4-MeO (80%), 4-Ph (82%), 4-Cl (45%), 4-Br (68%); X = CH_2: R = 4-MeO (55%), 4-NH_2 (82%), *etc*.

The reaction is inhibited by the addition of TEMPO (**106**). The probable mechanism of the formation of product **258** is shown in Scheme 124.

Fluorinated sulfones **259** were used as a source of the CF_2H radical (**205**) in the photocatalytic synthesis of fluoroalkyl-substituted phenanthridines **260** (Scheme 125).[147] For a wide range of substituents in isonitriles **261**, the yields of the reaction products were higher than 58%, the lowest yields being observed in the presence of strong electron acceptors [**260j** (27%), **260k** (37%)] or the MeO group in the *ortho* position of the free aromatic ring of the starting isonitrile [**260f** (20%)].

Scheme 125



R^2 = H: R^1 = H (**a**, 78%), 4-Me (**b**, 73%), 4-Ph (**c**, 69%), 4-CF_3 (**d**, 73%), 4-OCF_3 (**e**, 81%), 2-OMe (**f**, 20%), 3-OMe (**g**, 44%); R^1 = H: R^2 = 4-Me (**h**, 58%), 3-Me (**i**, 55%), 4-CF_3 (**j**, 27%), 4-NO_2 (**k**, 37%), 4-F (**l**, 82%)

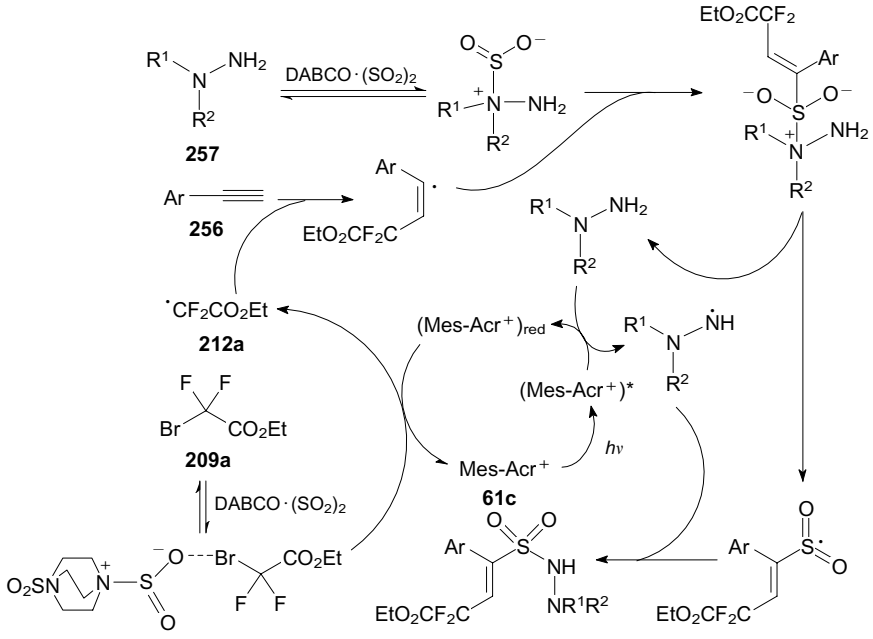
A method for the synthesis of 3,3-difluoro-2-oxoindoles **263** was developed based on the photocatalytic difluoromethylation – amidation of anilines **262** (Scheme 126).[148]

The photocatalyst Ir(ppy)$_3$ (**84**) is presumably involved in the formation of the CF_2CO_2Et radical (**212a**) and arenonium ion **264** (Scheme 127).

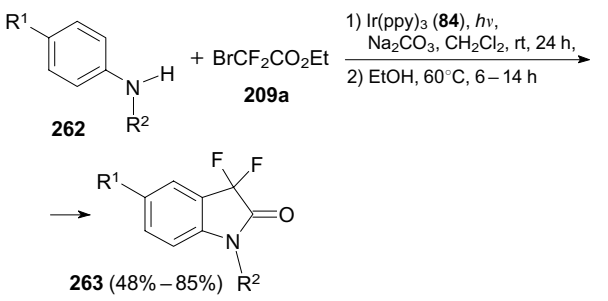
A similar mechanism was proposed for the reaction of substituted benzenes **78** with $BrCF_2CO_2Et$ (**209a**) in the presence of photocatalyst **84** and the base Bu^{t}OK giving ethyl 2-aryl-2,2-difluoroacetates **265** (Scheme 128).[149]

The reaction is very sensitive to the bulkiness of the substituent in the aromatic ring, which is apparently attrib-

Scheme 124

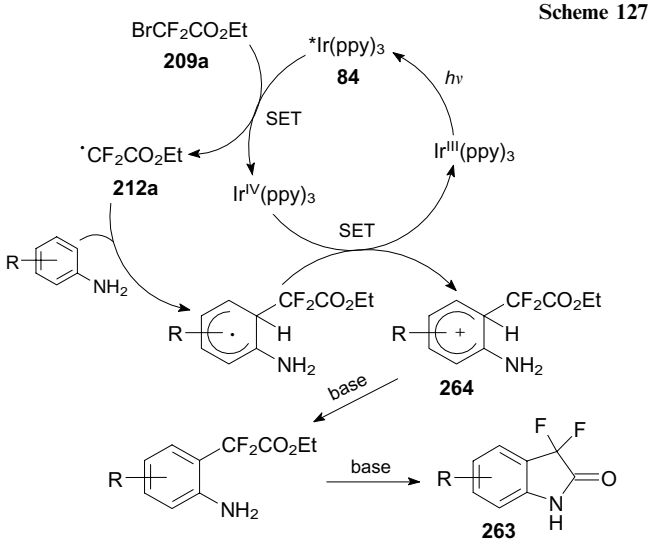


Scheme 126



R^2 = H: R^1 = Me (72%), Cl (73%), Br (66%), I (70%), Pr^i (78%), EtO (48%), CF_3 (55%); R^2 = Me: R^1 = Me (85%), F (79%), *etc*.

Scheme 127



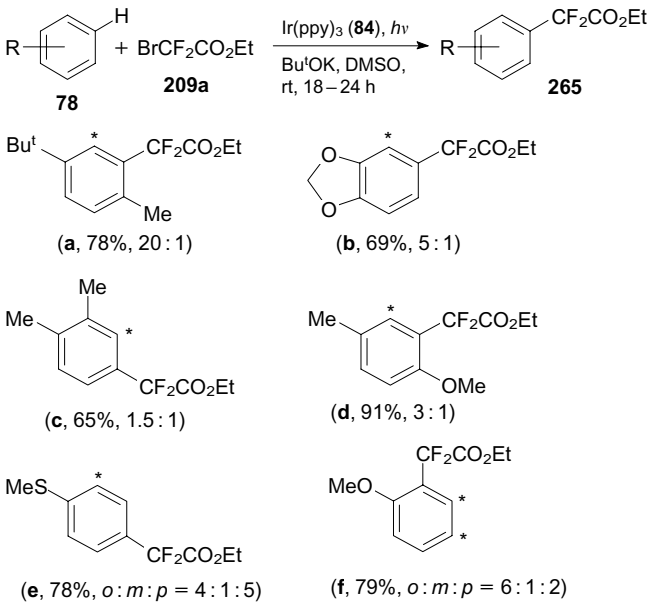
uted to steric hindrance to the insertion of the CF_2CO_2Et radical (**212a**). The reactions with monosubstituted benzenes containing electron-donating substituents afford predominantly *ortho* and *para* isomers.

A method for the photocatalytic synthesis of difluoroalkyl-substituted isoquinolinones **266** was developed based on the cascade radical cyclization of isonitriles **267** (Scheme 129).[150] The authors employed the Cu^I-catalyzed cyclization in the CuBr – bis(pinacolato)diboron [$(Bpin)_2$] system (100 °C, 8 h) as an alternative approach to the synthesis of quinolines, thus making it possible to prepare products in comparable yields.

The pathway of photocatalytic difluoromethylation of N-substituted 1-(2-allyloxyphenyl-3-amino)prop-2-en-1-ones **268** and **269**, which allows the synthesis of functionalized CF_2-substituted benzoxepines **270** and **271**, depends on the number of substituents at the amino group (Scheme 130).[151] It was assumed that in the presence of two methyl groups at the nitrogen atom (compound **269**), the resulting imino cation **272** is hydrolyzed (Scheme 131, pathway *a*), while in the presence of an NRH group, the reaction proceeds *via* deprotonation followed by tautomerization (pathway *b*).

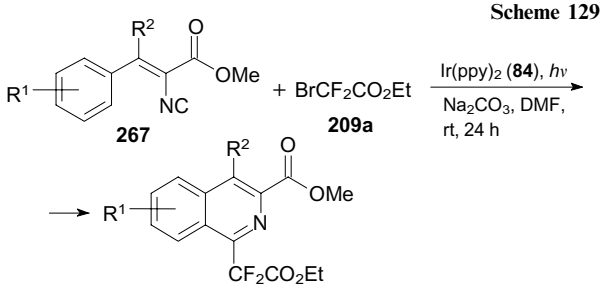
The Smiles rearrangement of sulfonates **273** initiated by the photocatalyst $Ru(bpy)_3Cl_2 \cdot 6H_2O$ (**68a**) was used to introduce the CF_2CH_2OH group into the aromatic ring,

Scheme 128



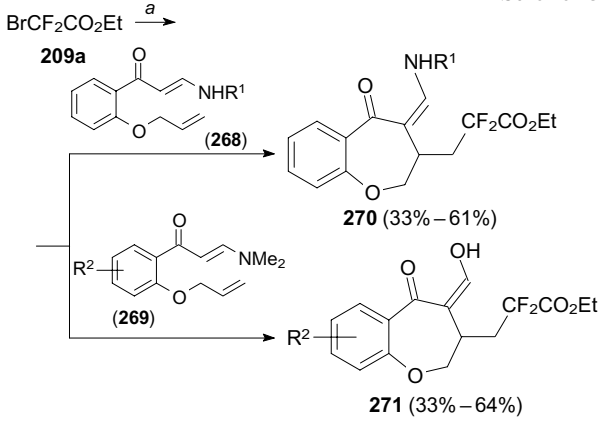
The position of the substituent in the minor regioisomers is marked with an asterisk

Scheme 129



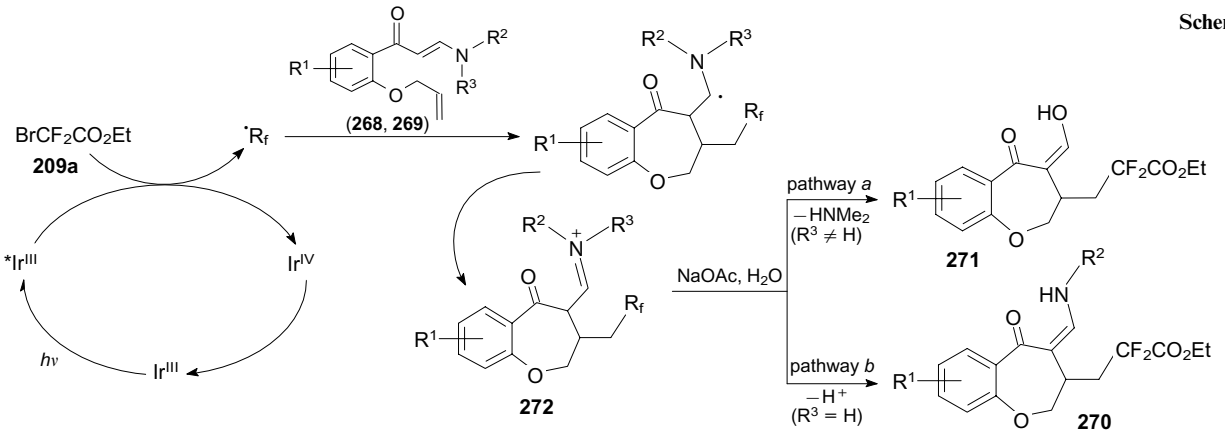
R^1 = H, R^2 = Ph; R^2 = H: R^1 = 4-Cl, 2-Br; R^1 = 4-Me: R^2 = Me, 4-F, 4-Cl, 4-Br, *etc*.

Scheme 130



(*a*) **123**, *hv*, NaOAc, $CH_2Cl_2 - H_2O$, rt, 48 h;
R^1 = H, Bu^n, cyclo-C_3H_5, Cy, Bn и др.; R^2 = 4-Me, 4-MeO, 4-F, 4-Cl, 4-Br, 5-Me, 5-F, 5-Br, *etc*.

Scheme 131



thereby allowing the synthesis of (het)aryl-substituted difluoroalkanols **274** (Scheme 132).[152]

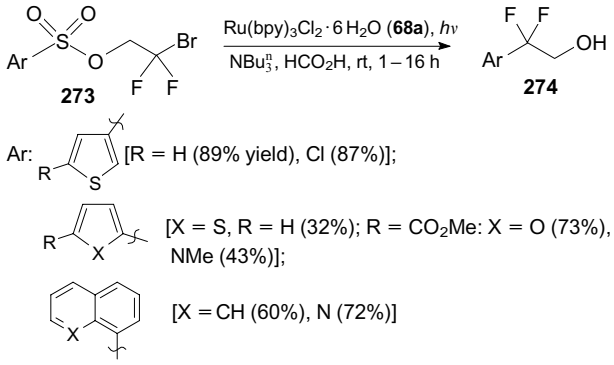
The proposed mechanism involves the radicals $ArCF_2CH_2OSO_2^{\bullet}$ (**275**), $Bu_2^nN-\dot{C}H-Pr^n$ (**276**) and the radical cation $[NBu_3^n][HCO_2H]^{+\bullet}$ (**277**) (Scheme 133).

A method was proposed for the direct introduction of the $CF_2P(O)(OEt)_2$ group into arenes and hetarenes in the presence of iridium photocatalyst **84**, allowing the synthesis of (het)aryldifluoromethyl phosphonates **278** in good yields (Scheme 134,*a*).[153] The reaction presumably proceeds with the participation of the $CF_2P(O)(OEt)_2$ radical.

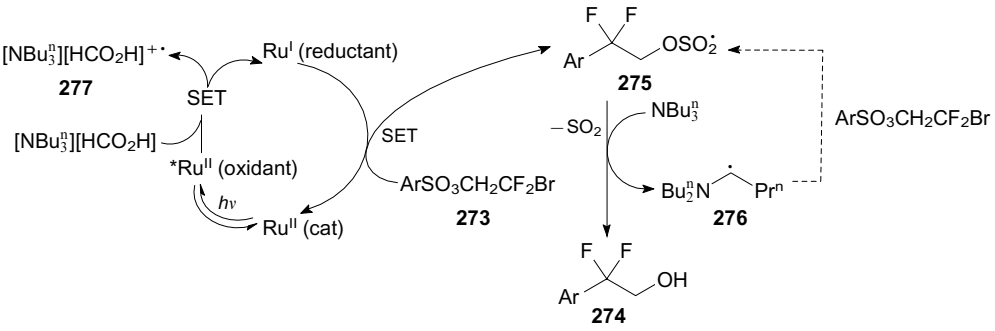
Photocatalyst **84** also exhibits high efficiency in the hydrophosphonodifluoromethylation of mono- and disubstituted alkenes, providing a route to functionalized alkyl- and alkylaryl-substituted difluoromethylenephosphonates **279** (see Scheme 134,*b*).[154]

Unlike other $C(sp^3)-Hal$ bonds (Hal = I, Br, Cl), the $C(sp^3)-F$ bond is chemically inert, which hinders the selective monodefluorination of compounds $ArCF_3$. Chen *et al.*[155] reported the first example of the photocatalytic $C(sp^3)-F$ bond scission in trifluoromethylarenes **280** and their transformation to difluoromethylarenes **281**. The

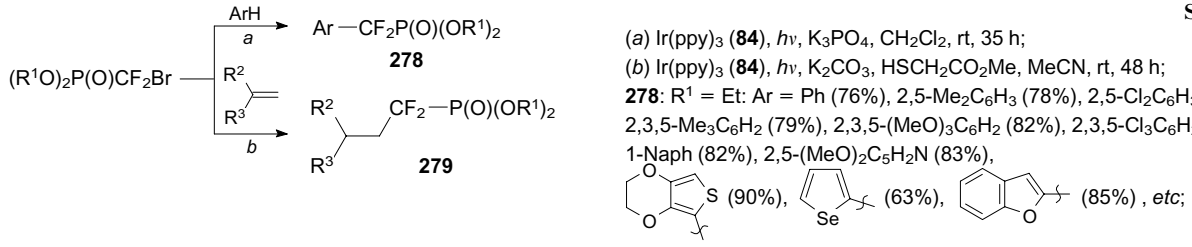
Scheme 132

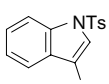
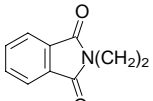


Scheme 133

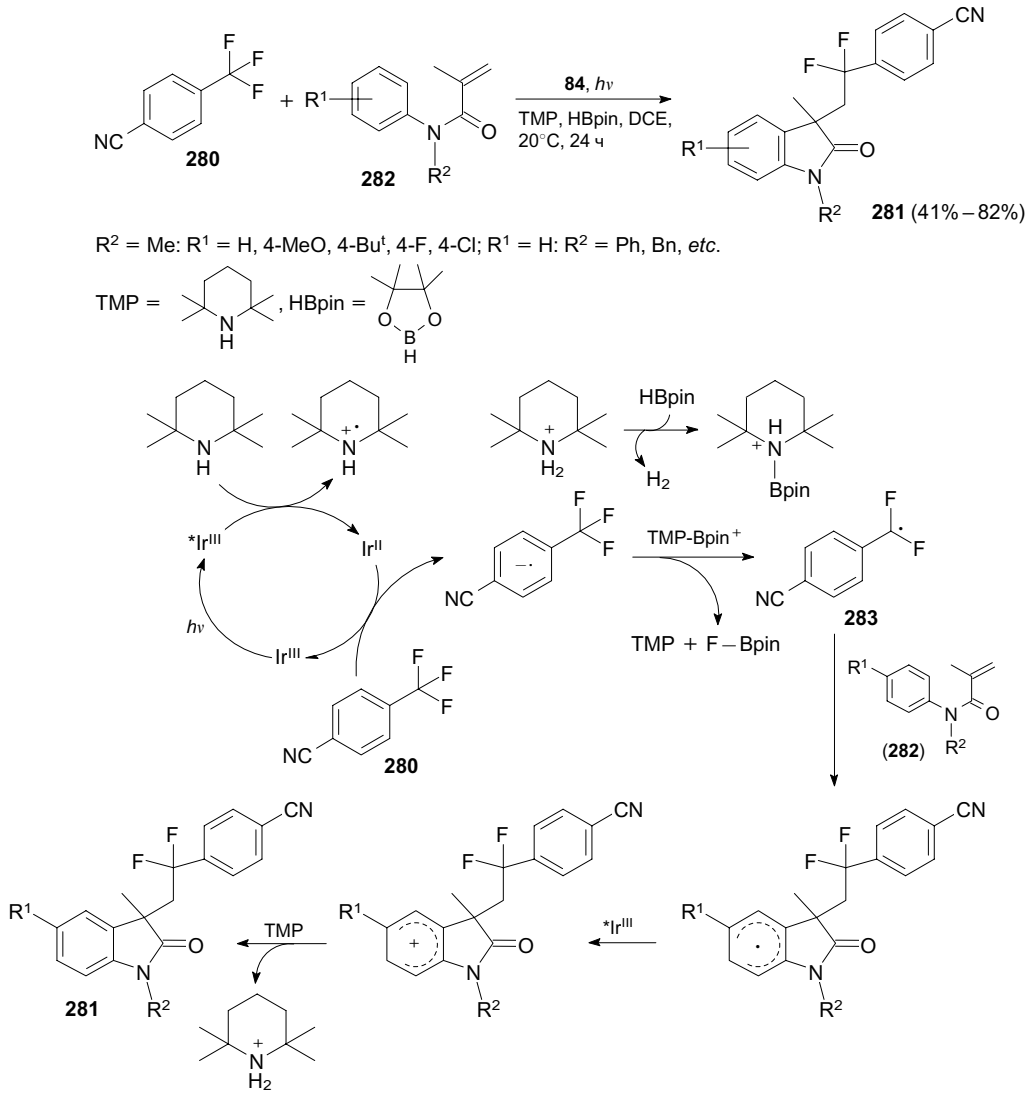


Scheme 134



279: R^1 = Et, R^2 = H: R^3 = $NaphO(CH_2)_2$ (51%), $Ar'O_2C(CH_2)_3$ [Ar′ = Ph (60%), 4-MeC_6H_4 (72%)], $TMSCH_2$ (72%), Cy (25%); R^1 = Et, R^2 = Me, R^3 = 4-$MeOC_6H_4CH_2$ (73%); R′ = Et, R^2 = Et, R^3 =  (73%); R^1 = Me, Et, Pr^i; R^2 = Me; R^3 = 

Scheme 135



authors assumed that the photocatalytic cleavage of this bond affords aryldifluoromethyl radical **283**, which selectively reacts with the double bond in *N*-arylmethacrylamide **282** (Scheme 135).

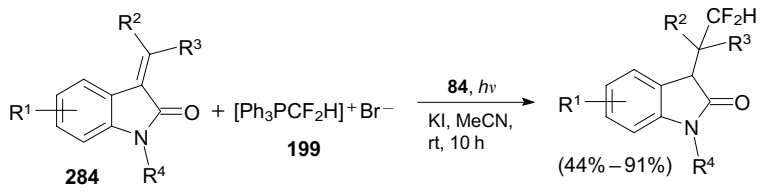
Related indolin-2-ones containing the CF_2HCR_2 group in position 3 were synthesized by the visible light-induced reaction of 3-alkylideneindolin-2-ones **284** with difluoromethyltriphenylphosphonium bromide (**199**) in the presence of photocatalyst **84** (Scheme 136).[156]

The key step of the reaction presumably involves the addition of the difluoromethyl radical at the double bond.

The three-component photocatalytic difluoroalkylarylation of 4-methoxystyrene (**135a**) with $BrCF_2CO_2Et$ (**209a**) and indoles **248** affords indole derivatives **285** in 46% – 90% yields (Scheme 137).[157] The authors suggested that the reaction proceeds through the generation of the $^{\bullet}CF_2CO_2Et$ radical (**212a**), which reacts with methoxy-substituted styrene **135a** to form radical **286**; the subsequent oxidation of the latter gives benzyl-type cation **286′** followed by its reaction with indole derivatives (see Scheme 137).

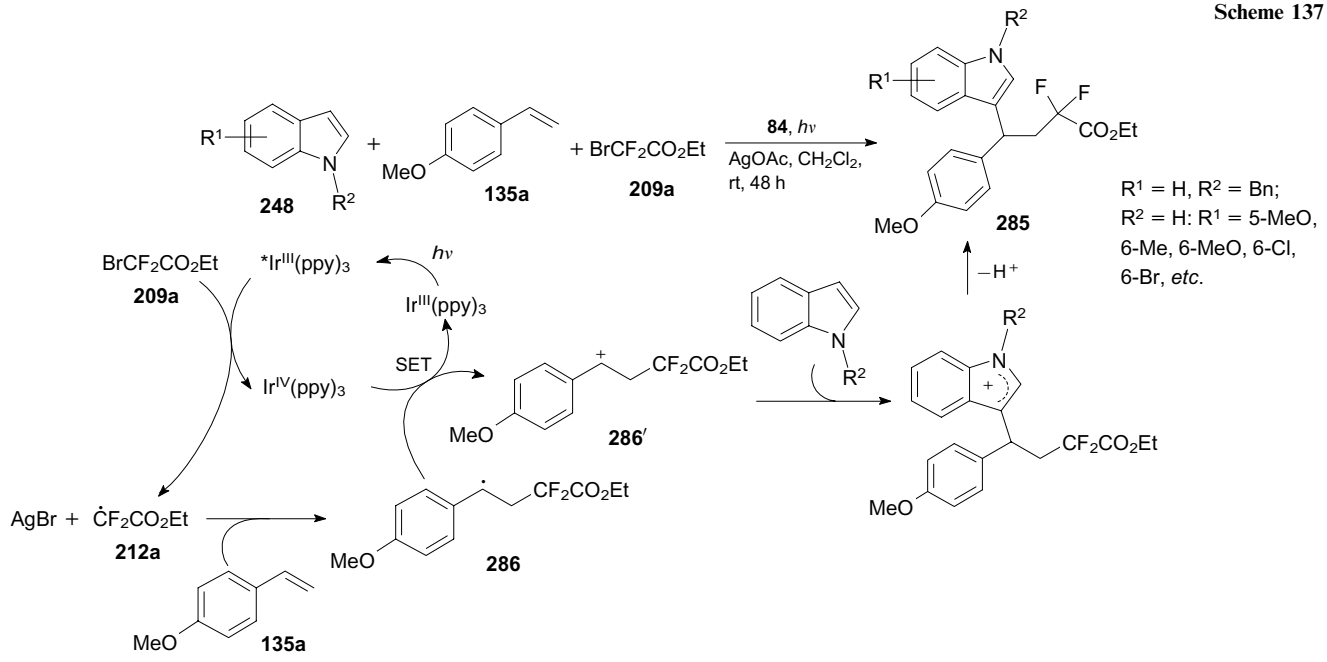
The three-component difluoroalkylation of substituted benzaldehydes **287** with *N*-aminomorpholine (**289**) and $BrCF_2CO_2Et$ (**209a**) in the presence of 1,2,3,5-tetrakis(carbazolo)-4,6-dicyanobenzene (CzIPN) (**288**) as the photocatalyst produces α,α-difluoroketone hydrazones **290** in 51% – 93% yields (Scheme 138).[158]

Scheme 136

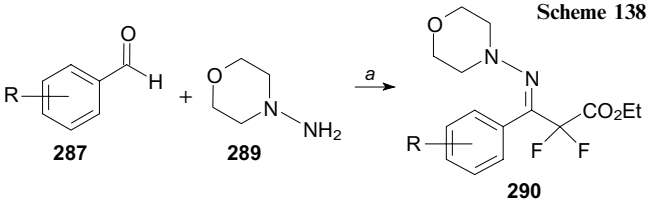


R2 = R3 = Me, R4 = H: R1 = H, 5-Me, 5-OMe, 5-Ac, 5-CF_3, 5-F, 5-Cl, 5-Br; R1 = R4 = H, R2 = R3 = Me; R1 = R4 = H, R2 = Et, R3 = Me, *etc.*

Scheme 137

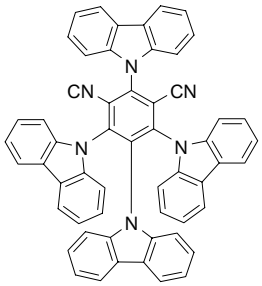


Scheme 138



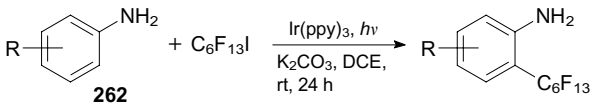
(*a*) $BrCF_2CO_2Et$ (**209a**), CzIPN, *hν*, Na_2HPO_4, DMF, rt, 12 h;
R = H, 4-Me, 4-OMe, 4-F, 4-Cl, 4-Br, 4-CN, 3-Me, 3-F, 3-Cl, 3-Br, 3-CN, *etc*;

CzIPN =



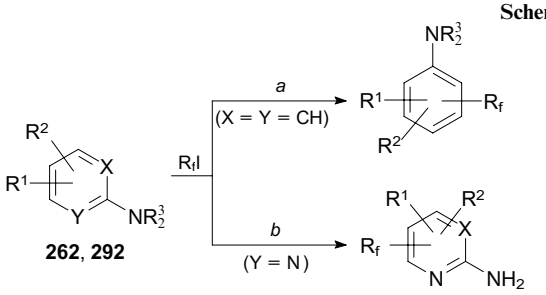
(**288**)

Scheme 139

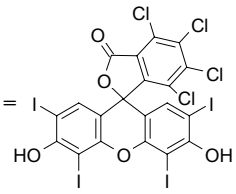


R = 4-Me (77%), 4-Pr^i (72%), 4-CF_3 (91%), 4-OEt (72%), 4-F (76%), 4-Cl (90%), 4-Br (83%), 4-I (91%), 4-CN (43%), *etc*.

Scheme 140



(*a*) RB, *hν*, Cs_2CO_3, MeCN, rt; RB =



291 (Rose Bengal)

$R^1 = R^2 = R^3 = H$: $R_f = C_4F_9$ (98%, isomers *p* : *o* = 70 : 30), C_8F_{17} (80%, isomers *p* : *o* = 60 : 40), C_4F_8I (65%, isomers *p* : *o* = 65 : 35), $R^1 = R^2 = H$, $R^3 = Me$: R_f = 4-C_4F_9 (96%), $R^1 = R^3 = H$, R_f = 4-C_4F_9: R^2 = 2-OMe (95%), 2-Me (93%), 2-Br (45%); R_f = 5-C_4F_9, R^2 = 2-NO_2 (5%), 4-OMe (94%), 4-Me (81%), 4-NO_2 (0%);
(*b*) RB, DMF or Cs_2CO_3, MeCN or DMF, *hν*, 20 h;
X = CH, $R^1 = R^2 = H$: R_f = 5-C_4F_9 (34%), 3-C_4F_9 (25%);
X = CH, $R^2 = H$: R^1 = 3-NH_2, R_f = 4-C_4F_9 (12%); R^1 = 5-Me, R_f = 4-C_4F_9 (47%); X = N, R^1 = 4-NH_2, R_f = 5-C_4F_9: R^2 = 6-NH_2 (48%), 6-OH (64%), *etc*.

7. Synthesis of compounds with perfluoroalkyl groups C_nF_m ($n > 1$, $m > 3$)

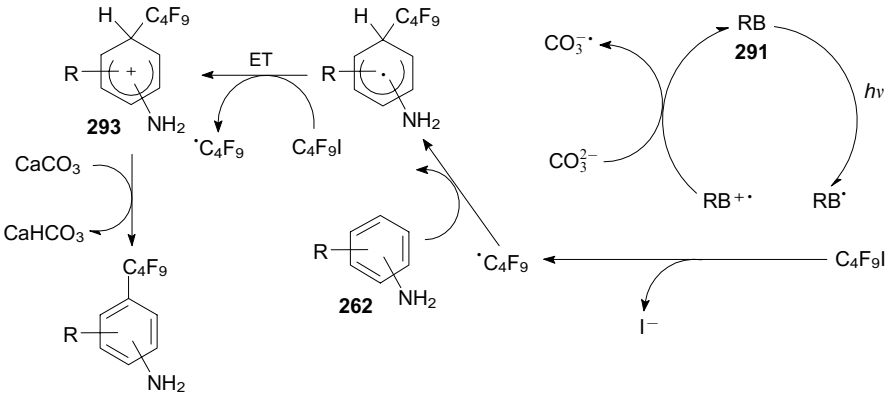
He *et al.*[159] developed a visible light-mediated mild and operationally simple method for perfluoroalkylation of anilines **262** with $C_6F_{13}I$ in the presence of iridium catalyst **84** (Scheme 139).[159]

Rose Bengal (RB) (**291**) is also an efficient photocatalyst for the introduction of perfluoroalkyl groups into anilines **262**, pyridines and pyrimidines **292** (Scheme 140).[160, 161]

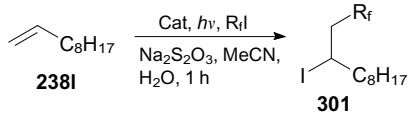
The observed acceleration of perfluorobutylation upon introduction of electron-donating groups into the aromatic ring of aniline was attributed to the participation of cationic σ-complex **293** in the reaction (Scheme 141).[160]

Organic dyes **123**, **189**, **294**–**297** were employed as photocatalysts for iodoperfluoroalkylation of alkenes (Scheme 142).[162] The yield of the reaction product substantially depends on the nature of the catalyst, the structure of

Scheme 141

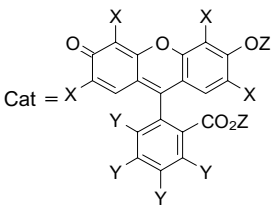


Scheme 142

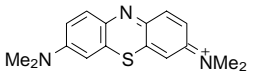


238l **301**

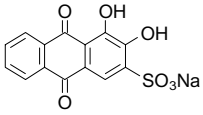
R_f = iso-C_3F_7, C_4F_9, C_6F_{13};



X = Br, Y = H, Z = Na (**123**, eosin Y);
X = I, Y = H, Z = Na (**189**, erythrosine B);
X = Y = Z = H (**294**, fluorescein);
X = Br, Y = Cl, Z = Na (**295**, phloxine B)



296 (methylene blue)



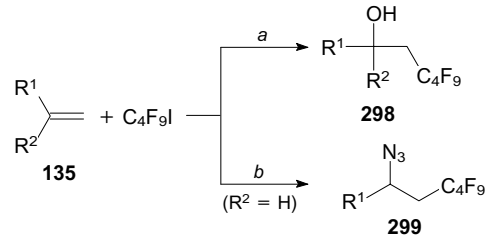
297 (alizarin red)

the substrate and the type of a light-emitting diode (LED) lamp. In the absence of water and $Na_2S_2O_3$, the reaction does not proceed. The yield of the product decreases with decreasing wavelength of emission light of the LED lamp [blue (λ = 470 nm) < green (525 nm) < red (660 nm)] and in the series of the photocatalysts: erythrosine B, eosin Y > fluorescein, methylene blue > alizarin red.

After the addition of the perfluoroalkyl radical to alkene **238l**, the reaction may proceed by the following three mechanisms: radical chain (*1*), cationic (*2*) and radical (*3*) (Scheme 143). Experiments with the addition of TEMPO (**106**) after short-term irradiation, as well as the absence of a product containing the hydroxy group attest to pathway *1*, while mechanisms *2* and *3* are less probable.

Photocatalytic hydroxyfluoroalkylation of alkenes **135** with perfluorobutyl iodide in the presence of ruthenium catalyst **68a** giving fluorobutyl-substituted alkanols **298** was accomplished in the $H_2O-MeCN-Bu^n_3N$ system with high regioselectivity (Scheme 144,*a*).[163] The reaction presumably involves oxygen (Scheme 145).

Scheme 144



135 **298** **299**

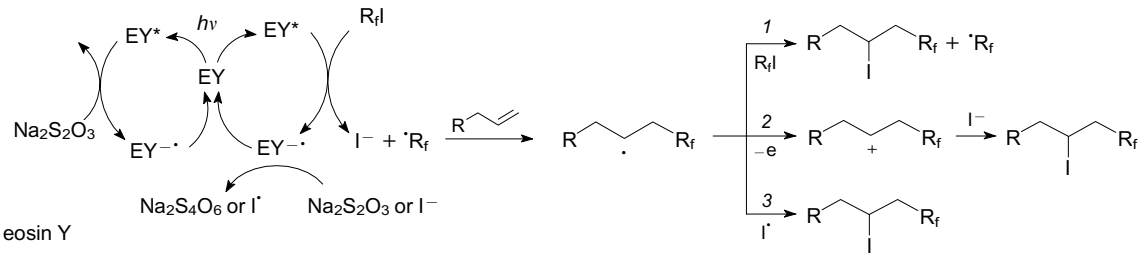
(*a*) $Ru(bpy)_2Cl_2 \cdot 6H_2O$ (**68a**), blue LED, Bu^n_3N, $MeCN-H_2O$, rt;
R^1 = H: R^2 = 2-Naph (68%), 2-MeC_6H_4 (59%), 3-MeC_6H_4 (78%), $Me(CH_2)_7$ (39%), 4-RC_6H_4 (R = H (64%)), Me (75%), Cl (45%), $Ph(CH_2)_2$ (43%)); R^1 = Me: R^2 = $Ph(CH_2)_2$ (56%), Ph (73%);
(*b*) $Ru(bpy)_3Cl_2 \cdot 6H_2O$ (**68a**), blue LED, NaN_3, $BnEt_3NBr$, NaI, DMF – dioxane, 30 °C, 12 h;
R^1 = 2-Naph (68%), $Ph(CH_2)_2$ (41%), $Me(CH_2)_n$ [*n* = 7 (36%), 9 (43%)]; 4-RC_6H_4 [R = Me (80%), Bu^t (67%), 4-Cl (71%), 4-Br (53%), 4-CN (37%)], *etc.*

A related reaction in the presence of NaN_3 affords azidofluoroalkyl derivatives **299** (see Scheme 144,*b*).[164]

The perfluorobutylation of coumarins **211** using the salts $K_2C_2O_4$ or $Cu(OAc)_2$ in the presence of anthraquinone-2-sulfonic acid (ANQ-2-SO_3H, **300**) as the photocatalyst presumably proceeds through the formation of perfluorobutyl radical **301** (Scheme 146).[165]

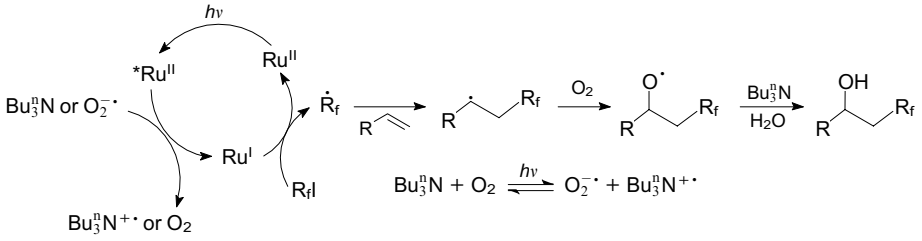
The visible light-induced reaction of *o*-diisocyanoarenes **302** with perfluoroalkyl iodides **197** in the presence of

Scheme 143

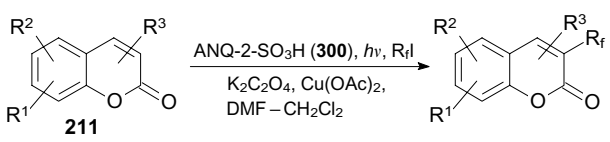


EY = eosin Y

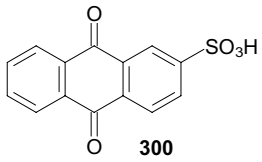
Scheme 145

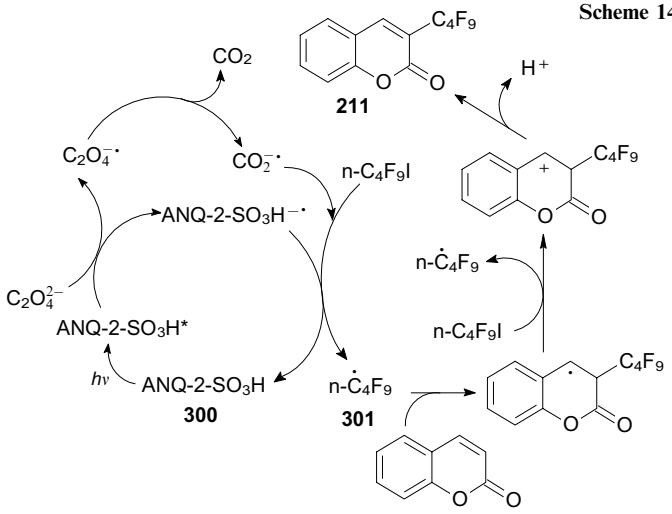


Scheme 146

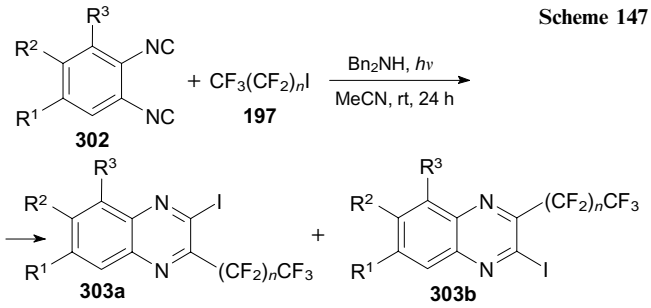


$R_f = C_4F_9$: $R^1 = R^2 = R^3 = H$ (77%); R^1 = 7-OMe, $R^2 = R^3 = H$ (68%); R^1 = 7-OH, $R^2 = H$, R^3 = 4-Me (99%); R^1 = 7-C(O)Me, R^2 = 6-C(O)Me, R^3 = 4-Me (60%); R^1 = 7-OMe, R^2 = 5-OMe, R^3 = 4-Me: $R_f = C_4F_9$ (67%), CF_3 (26%)





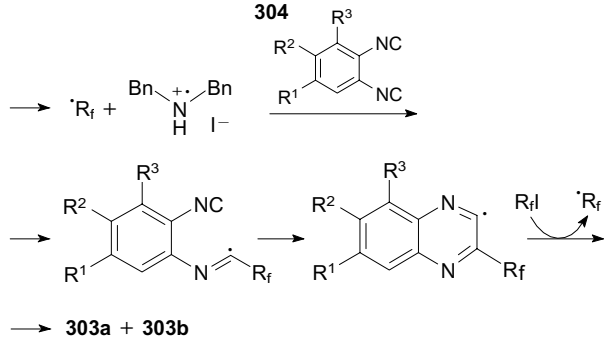
Scheme 147



R^1	R^2	R^3	n	Yield (%)	
				303a	**303b**
Me	Me	H	0	82	–
Me	Me	H	2	50	–
Me	Me	H	3	69	–
Me	Me	H	5	61	–
Me	Me	H	6	68	–
Me	Me	H	7	65	–
OMe	OMe	H	7	66	–
OMe	H	H	7	40	32
H	H	OMe	7	28	33
H	H	H	7	50	–
H	H	H	0	76	–
OMe	OMe	H	0	73	–

amines gives 2-fluoroalkyl-3-iodoquinoxalines **303** (Scheme 147).[166] The reaction proceeds through intermediate complex **304** as a double radical insertion (Scheme 148).

Scheme 148

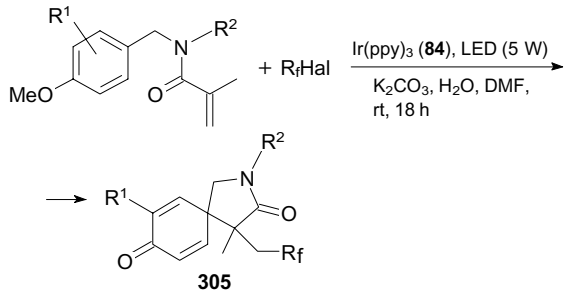


The radical cyclization is also a key step in the photocatalytic synthesis of perfluoroalkylated azaspirocyclic cyclohexadienones **305** (Scheme 149).[167]

The photocatalytic reaction of nitrones **306** with perfluoroalkyl iodides **197** in the presence of ascorbic acid (AA), collidine and iridium catalyst **115** produces fluorinated hydroxylamines **307** in up to quantitative yields (Scheme 150).[168] The lowest yields (40% – 67%) were observed in the case of CF_3 substituents.

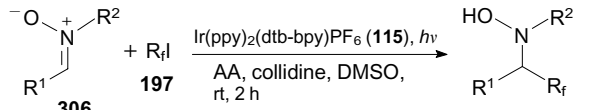
Therefore, numerous compounds can be used as perfluoroakyl radical sources in photocatalytic fluoroalkylation reactions: CF_3I, CF_3SO_2Cl, CF_3SO_2Na, $[Ph_3PCF_2H]^+Br^-$, Togni reagent, Umemoto reagent, *etc*.

Scheme 149



Hal = I, Br; $R_f = C_4F_9$, R^1 = H: $R^2 = Bu^t$ (55%), Bu^n (61%), Pr^i (62%); $R_f = C_4F_9$; $R^2 = Bu^t$: R^1 = Br (64%, enantiomer ratio 1.2 : 1), Cl (67%, enantiomer ratio 1 : 1.4); R^1 = H, $R^2 = Bu^t$: R_f = n-C_8F_{17} (62%), $C_{10}F_{21}$ (65%), CH_2CF_3 (72%), CF_3 (72%)

Scheme 150



R^1 = Ph, R^2 = Me, $R_f = CF_3(CF_2)_n$ (n = 0, 2, 3);
R^1 = Ph, R^2 = Bn: $R_f = CF_3$, $PhCH_2CF_2$;
R^1 = 2-Py, R_2 = Me: $R_f = CF_3$, $CF_3(CF_2)_2$, *etc.*

8. Photocatalytic thiofluoroalkylation

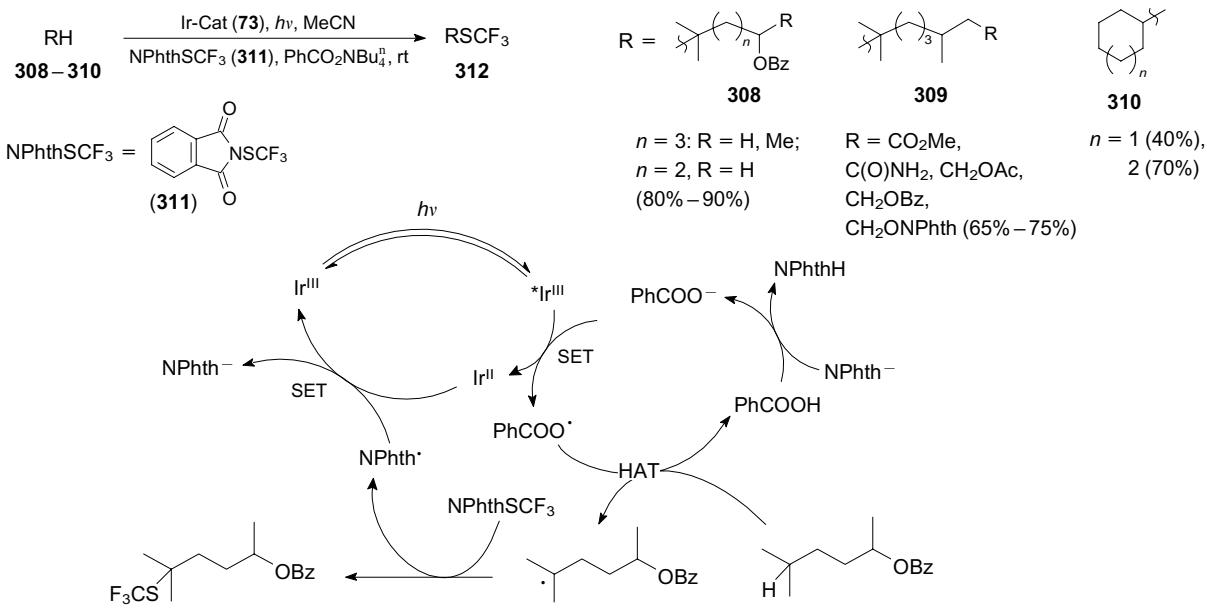
The application of photocatalysis for the introduction of functional CF_3X groups (X = S, CH_2S) into different substrates is an important issue considering environmental and economic factors. Mukherjee *et al.*[169] showed that compounds **308** – **310** with an unactivated C(sp^3) – H bond can undergo thiotrifluoromethylation in the presence of iridium photocatalyst **73** and trifluoromethylthiophthalimide (**311**), thereby providing a route to a wide range of trifluorothiomethyl derivatives **312** (Scheme 151).

Thiotrifluoromethylation of arylalkenes **135** with 1-(trifluoromethylthio)pyrrolidine-2,5-dione (**313**) in the presence of iridium photocatalyst **314** affords hydroxytrifluoromethylthio derivatives **315** (Scheme 152).[170] The reaction mechanism presumably proceeds through the formation of the trifluoromethylthio radical, which reacts with alkene followed by oxidation to the arylalkyl carbocation.

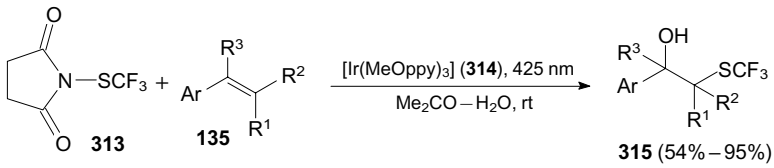
The employment of trifluoromethylthiosaccharin (**316**) as a CF_3S radical source enabled the photocatalytic trifluoromethylthiomethylation of alkenes **135** (Scheme 153).[171]

The reaction mechanism (Scheme 154) was confirmed by trapping the CF_3S radical (**317**) with 2-methyl-2-nitrosopropane used as a radical scavenger.

Scheme 151

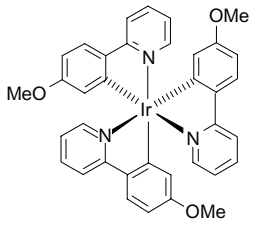


Scheme 152



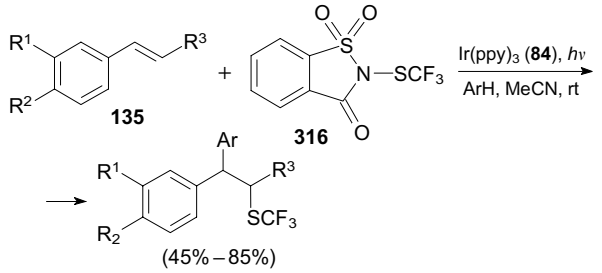
$R^1 = R^2 = R^3$ = H: Ar = Ph, 4-MeC_6H_4, 4-$Bu^tC_6H_4$, 4-$MeOC_6H_4$;
$R^1 = R^2$ = H, R^3 = Me: Ar = 4-$AcOC_6H_4$, 4-ClC_6H_4, *etc.*

314 =



[Ir(MeOppy)3]

Scheme 153

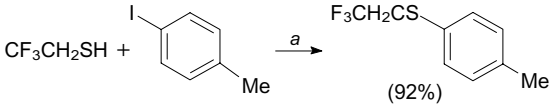


Ar = 2,4,6-$(MeO)_3C_6H_2$: $R^1 = R^3 = H$, R^2 = OMe, OAc, $NMeAc$, Ph, $N(Boc)_2$, NPhth; $R^1 = H$, R^2 = OMe, R^3 = Me, Ph; $R^1 = R^2$ = OMe, R^3 = Me; Ar = 3,4-$(MeO)_2C_6H_3$, 2,4-$(MeO)_2C_6H_3$, 3-Me, 4-$MeOC_6H_3$: $R^1 = H$, $R^2 = Bu^t$, *etc.*

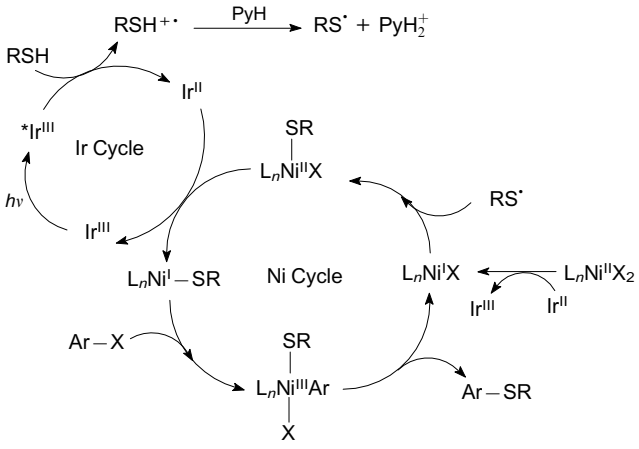
The practical method for the photocatalytic synthesis of trifluoromethylthio-substituted ketones **318** based on styrenes employs a combination of CF_3SO_2Na (**142**) and CS_2 as sources of the SCF_3 radical (**317**) (Scheme 155).[172]

Oderinde *et al.*[173] proposed a photocatalytic method for the introduction of the SCH_2CF_3 group into the aromatic ring in the presence of the $Ir[dF(CF_3)ppy]_2(dtb\text{-}bpy)PF_6$ (**73**) – $NiCl_2 \cdot glyme$ catalyst system (Scheme 156). The reaction mechanism presumably involves a double catalytic cycle with the participation of iridium (**73**) and nickel (**319**) catalysts.

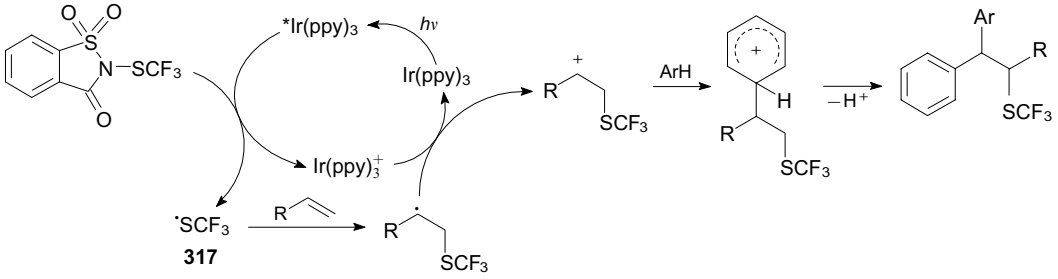
Scheme 156



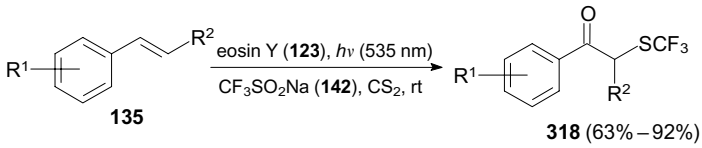
(*a*) Cat (**73**), $NiCl_2 \cdot glyme$ (**319**), *hv*, dtb-bpy, PyH, MeCN;



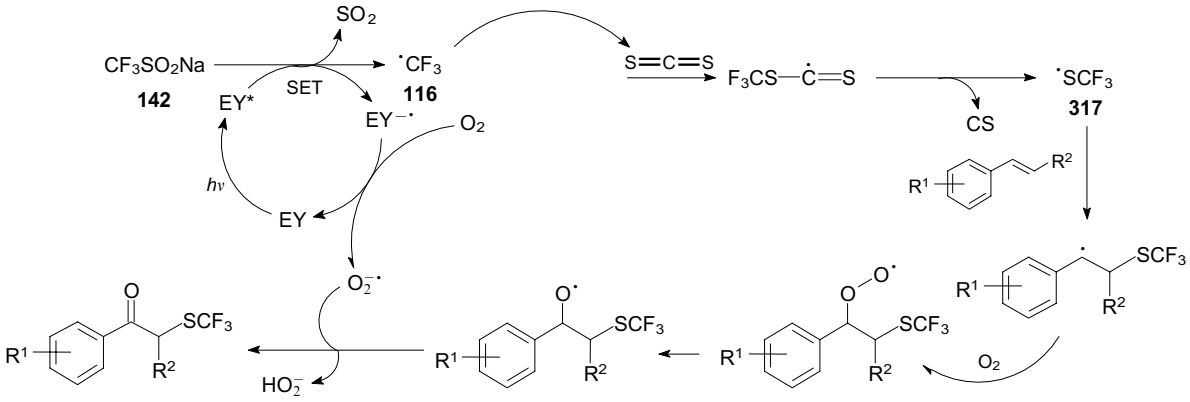
Scheme 154



Scheme 155



R^2 = H, R^1 = H, 4-Me, 4-EtO, 4-Bu^t, 3-Me, 4-Cl, 4-Br, 4-F, 3-Cl, 3-Br, 2-Cl, 4-NO_2, 4-$MeCO_2$; $R^1 = R^2$ = Ph, R^1 = 3-MeO, R^2 = CO_2H, *etc.*



9. Conclusion

This review shows that there is a great variety of methods for the synthesis of organofluorine compounds by photocatalysis. The design of new photocatalysts based on both organometallic and organic compounds, including those capable of being activated by visible light, has attracted extensive attention. The redox properties of photocatalysts and a wide range of substrates determined by experimental methods enabled chemists to develop rational methods for the synthesis of organofluorine compounds. Recent studies on photocatalytic fluorination demonstrated that these methods have a considerable potential in different fields of organic synthesis. Photocatalysis allows the defluorination of polyfluoroaromatic compounds without harmful metal-containing reagents, which have been employed earlier in such transformations. Photocatalysis proved to be efficient for generation of fluorinated alkyl radicals, enabling the synthesis of libraries of tri- and difluoromethylated arenes, hetarenes and other compounds, which can be used as biologically active compounds. Due to mild conditions, photocatalysis can be applied to introduce different fluorine-containing groups into organic molecules. It should be emphasized that these procedures require simple, safe and cheap fluorination reagents. The ease of light-induced functionalization of alkanes, alkenes, aromatic and natural compounds with fluorine-containing groups inspired chemists to develop new multistep processes, that include additional steps of cyclization, rearrangements, *etc*. These reactions provide synthetic routes to complex organic compounds inaccessible by other methods. Examples are the above-considered methods for the synthesis of fluorinated pyridines, indoles, acridines, phenanthridines, *etc*. The use of visible light as an initiator of organic reactions is attractive because it is not absorbed by organic compounds, thereby eliminating side reactions associated with typical photochemical processes initiated by ultraviolet light. In most cases, reactions are atom-economic. The use of visible light generally provides an environmentally friendly alternative to the classical synthetic methodology and, consequently, such procedures for fluorination of organic compounds follow green chemistry principles. Since photocatalytic processes involve radical steps, the enantioselectivity of reactions is sometimes difficult to control. The development of new chiral catalysts and catalytic systems makes it possible to perform enantioselective transformations in these cases also.

This review is an attempt to summarize the state-of-the-art in photocatalysis applied to the synthesis of organofluorine compounds, which is a rapidly growing field of research. An investigation of the mechanism of photocatalytic transformations will give deeper understanding of relevant theoretical concepts and provide the basis for the development of selective fluorination reactions. The issue of selectivity of photocatalysis is closely related to the study of properties of reactive intermediates, such as radicals, carbocations and radical ions, involved in the reactions. The use of quantum chemical methods will give better insight into the properties of these species and provide the basis for understanding the detailed mechanism of these reactions. Further investigations in the field of organic photocatalysis should be focused on the development of practical selective fluorination methods using readily available and cheap starting reagents and photocatalysts. Photofluorination reactions should be predictable, which requires a deep knowledge of their mechanism. The unique way of photocatalytic activation of organic compounds combined with the employment of fluorinated building blocks or fluorinating reagents creates the basis for the development of new methodologies in organofluorine chemistry.

References

1. J.Miró, C.del Pozo. *Chem. Rev.*, **116**, 11924 (2016)
2. M.G.Campbell, T.Ritter. *Chem. Rev.*, **115**, 612 (2015)
3. T.Liang, C.N.Neumann, T.Ritter. *Angew. Chem., Int. Ed.*, **52**, 8214 (2013)
4. P.A.Champagne, J.Desroches, J.-D.Hamel, M.Vandamme, J.-F.Paquin. *Chem. Rev.*, **115**, 9073 (2015)
5. Y.Zeng, C.Ni, J.Hu. *Chem. – Eur. J.*, **22**, 3210 (2016)
6. J.R.Wolstenhulme, V.Gouverneur. *Acc. Chem. Res.*, **47**, 3560 (2014)
7. S.V.Kohlhepp, T.Gulder. *Chem. Soc. Rev.*, **45**, 6270 (2016)
8. M.Fagnoni, D.Dondi, D.Ravelli, A.Albini. *Chem. Rev.*, **107**, 2725 (2007)
9. D.Ravelli, D.Dondi, M.Fagnoni, A.Albini. *Chem. Soc. Rev.*, **38**, 1999 (2009)
10. S.Protti, M.Fagnoni, D.Ravelli. *ChemCatChem*, **7**, 1516 (2015)
11. M.-Y.Cao, X.Ren, Z.Lu. *Tetrahedron Lett.*, **56**, 3732 (2015)
12. J.D.Weaver. *Synlett*, **25**, 1946 (2014)
13. J.D.Nguyen, E.M.D'Amato, J.M.R.Narayanam, C.R.J.Stephenson. *Nat. Chem.*, **4**, 854 (2012)
14. A.McNally, C.K.Prier, D.W.C.MacMillan. *Science*, **334**, 1114 (2011)
15. J.M.R.Narayanam, C.R.J.Stephenson. *Chem. Soc. Rev.*, **40**, 102 (2011)
16. S.Fukuzumi, K.Ohkubo. *Org. Biomol. Chem.*, **12**, 6059 (2014)
17. C.K.Prier, D.A.Rankic, D.W.C.MacMillan. *Chem. Rev.*, **113**, 5322 (2013)
18. T.Besset, T.Poisson, X.Pannecoucke. *Chem. – Eur. J.*, **20**, 16830 (2014)
19. S.D.Halperin, H.Fan, S.Chang, R.E.Martin, R.Britton. *Angew. Chem., Int. Ed.*, **53**, 4690 (2014)
20. D.Staveness, I.Bosque, C.R.J.Stephenson. *Acc. Chem. Res.*, **49**, 2295 (2016)
21. T.Chatterjee, N.Iqbal, Y.You, E.J.Cho. *Acc. Chem. Res.*, **49**, 2284 (2016)
22. M.A.Ischay, T.P.Yoon. *Eur. J. Org. Chem.*, 3359 (2012)
23. D.Ravelli, M.Fagnoni, A.Albini. *Chem. Soc. Rev.*, **42**, 97 (2013)
24. A.V.Vorontsov, A.V.Arsentyev. *Curr. Org. Chem.*, **17**, 2459 (2013)
25. M.Reckenthäler, A.G.Griesbeck. *Adv. Synth. Catal.*, **355**, 2727 (2013)
26. J.Xu, X.Liu, Y.Fu. *Tetrahedron Lett.*, **55**, 585 (2014)
27. W.Zhu, J.Wang, S.Wang, Z.Gu, J.L.Aceña, K.Izawa, H.Liu, V.A.Soloshonok. *J. Fluorine Chem.*, **167**, 37 (2014)
28. T.Koike, M.Akita. *J. Fluorine Chem.*, **167**, 30 (2014)
29. M.-C.Belhomme, T.Besset, T.Poisson, X.Pannecoucke. *Chem. – Eur. J.*, **21**, 12836 (2015)
30. S.-M.Wang, J.-B.Han, C.-P.Zhang, H.-L.Qin, J.-C.Xiao. *Tetrahedron*, **71**, 7949 (2015)
31. S.Barata-Vallejo, S.M.Bonesi, A.Postigo. *Org. Biomol. Chem.*, **13**, 11153 (2015)
32. M.Akita, T.Koike. *C.R. Chim.*, **18**, 742 (2015)
33. I.Ghosh, L.Marzo, A.Das, R.Shaikh, B.König. *Acc. Chem. Res.*, **49**, 1566 (2016)
34. C.R.Jamison, L.E.Overman. *Acc. Chem. Res.*, **49**, 1578 (2016)
35. J.Chen, J.Cen, X.Xu, X.Li. *Catal. Sci. Technol.*, **6**, 349 (2016)
36. A.C.Hernandez-Perez, S.K.Collins. *Acc. Chem. Res.*, **49**, 1557 (2016)

37. R.Ciriminna, R.Delisi, Y.-J.Xu, M.Pagliaro. *Org. Process Res. Dev.*, **20**, 403 (2016)
38. T.Gensch, M.N.Hopkinson, F.Glorius, J.Wencel-Delord. *Chem. Soc. Rev.*, **45**, 2900 (2016)
39. E.J.Cho. *Chem. Rec.*, **16**, 47 (2016)
40. G.Wei, C.Basheer, C.-H.Tan, Z.Jiang. *Tetrahedron Lett.*, **57**, 3801 (2016)
41. X.Pan, H.Xia, J.Wu. *Org. Chem. Front.*, **3**, 1163 (2016)
42. S.Roslin, L.R.Odell. *Eur. J. Org. Chem.*, 1993 (2017)
43. C.Zhang. *Adv. Synth. Catal.*, **359**, 372 (2017)
44. S.Senaweera, J.D.Weaver. *Aldrichim. Acta*, **49**, 45 (2016)
45. P.Kirsch. *Modern Fluoroorganic Chemistry. Synthesis, Reactivity, Applications*. (Weinheim: Wiley-VCH, 2004)
46. R.P.Singh, J.M.Shreeve. *Acc. Chem. Res.*, **37**, 31 (2004)
47. K.Uneyama. *Organofluorine Chemistry*. (Oxford: Blackwell, 2006)
48. J.Baudoux, D.Cahard, in *Organic Reactions*. Vol. 69. (Ed. L.E.Overman). (Hoboken: Wiley, 2007). P. 347
49. G.I.Borodkin, V.G.Shubin. *Russ. Chem. Rev.*, **79**, 259 (2010)
50. L.Manral. *Synlett*, 807 (2006)
51. S.Bloom, J.L.Knippel, T.Lectka. *Chem. Sci.*, **5**, 1175 (2014)
52. S.Bloom, M.McCann, T.Lectka. *Org. Lett.*, **16**, 6338 (2014)
53. C.R.Pitts, M.S.Bloom, D.D.Bume, Q.A.Zhang, T.Lectka. *Chem. Sci.*, **6**, 5225 (2015)
54. J.-B.Xia, C.Zhu, C.Chen. *J. Am. Chem. Soc.*, **135**, 17494 (2013)
55. D.Cantillo, O.de Frutos, J.A.Rincón, C.Mateos, C.O.Kappe. *J. Org. Chem.*, **79**, 8486 (2014)
56. J.-B.Xia, C.Zhu, C.Chen. *Chem. Commun.*, **50**, 11701 (2014)
57. D.D.Bume, C.R.Pitts, R.T.Jokhai, T.Lectka. *Tetrahedron*, **72**, 6031 (2016)
58. C.W.Kee, K.F.Chin, M.W.Wong, C.-H.Tan. *Chem. Commun.*, **50**, 8211 (2014)
59. D.D.Bume, C.R.Pitts, F.Ghorbani, S.A.Harry, J.N.Capilato, M.A.Siegler, T.Lectka. *Chem. Sci.*, **8**, 6918 (2017)
60. Patent WO 2015000076A1 (2015)
61. M.B.Nodwell, A.Bagai, S.D.Halperin, R.E.Martin, H.Knustc, R.Britton. *Chem. Commun.*, **51**, 11783 (2015)
62. M.Xiang, Z.-K.Xin, B.Chen, C.-H.Tung, L.-Z.Wu. *Org. Lett.*, **19**, 3009 (2017)
63. J.G.West, T.A.Bedell, E.J.Sorensen. *Angew. Chem., Int. Ed.*, **55**, 8923 (2016)
64. S.D.Halperin, D.Kwon, M.Holmes, E.L.Regalado, L.-C.Campeau, D.A.DiRocco, R.Britton. *Org. Lett.*, **17**, 5200 (2015)
65. S.Bloom, D.D.Bume, C.R.Pitts, T.Lectka. *Chem. – Eur. J.*, **21**, 8060 (2015)
66. M.Rueda-Becerril, O.Mahé, M.Drouin, M.B.Majewski, J.G.West, M.O.Wolf, G.M.Sammis, J.-F.Paquin. *J. Am. Chem. Soc.*, **136**, 2637 (2014)
67. S.Ventre, F.R.Petronijevic, D.W.C.MacMillan. *J. Am. Chem. Soc.*, **137**, 5654 (2015)
68. X.Wu, C.Meng, X.Yuan, X.Jia, X.Qian, J.Ye. *Chem. Commun.*, **51**, 11864 (2015)
69. S.Kohtani, T.Kurokawa, E.Yoshioka, H.Miyabe. *Appl. Catal., A: General*, **521**, 68 (2016)
70. K.Ohkubo, A.Fujimoto, S.Fukuzumi. *J. Phys. Chem. A*, **117**, 10719 (2013)
71. S.I.Scherbinina, O.V.Fedorov, V.V.Levin, V.A.Kokorekin, M.I.Struchkova, A.D.Dilman. *J. Org. Chem.*, **82**, 12967 (2017)
72. L.I.Panferova, V.O.Smirnov, V.V.Levin, V.A.Kokorekin, M.I.Struchkova, A.D.Dilman. *J. Org. Chem.*, **82**, 745 (2017)
73. S.M.Senaweera, A.Singh, J.D.Weaver. *J. Am. Chem. Soc.*, **136**, 3002 (2014)
74. L.Flamigni, A.Barbieri, C.Sabatini, B.Ventura, F.Barigelletti. *Top. Curr. Chem.*, **281**, 143 (2007)
75. S.M.Senaweera, J.D.Weaver. *J. Org. Chem.*, **79**, 10466 (2014)
76. X.Liu, Z.Wang, X.Zhao, X.Fu. *Inorg. Chem. Front.*, **3**, 861 (2016)
77. P.Dai, J.Ma, W.Huang, W.Chen, N.Wu, S.Wu, Y.Li, X.Cheng, R.Tan. *ACS Catal.*, **8**, 802 (2018)
78. R.Naumann, F.Lehmann, M.Goez. *Angew. Chem., Int. Ed.*, **57**, 1078 (2018)
79. H.Yin, Y.Wada, T.Kitamura, S.Yanagida. *Environ. Sci. Technol.*, **35**, 227 (2001)
80. S.Kohtani, Y.Ohama, Y.Ohno, I.Tsuji, A.Kudo, R.Nakagaki. *Chem. Lett.*, **34**, 1056 (2005)
81. J.Lu, N.S.Khetrapal, J.A.Johnson, X.C.Zeng, J.Zhang. *J. Am. Chem. Soc.*, **138**, 15805 (2016)
82. P.L.Watson, T.H.Tulip, I.Williams. *Organometallics*, **9**, 1999 (1990)
83. A.U.Meyer, T.Slanina, C.-J.Yao, B.König. *ACS Catal.*, **6**, 369 (2016)
84. S.Senaweera, J.D.Weaver. *J. Am. Chem. Soc.*, **138**, 2520 (2016)
85. A.Singh, J.J.Kubik, J.D.Weaver. *Chem. Sci.*, **6**, 7206 (2015)
86. A.Singh, C.J.Fennell, J.D.Weaver. *Chem. Sci.*, **7**, 6796 (2016)
87. M.B.Khaled, R.K.El Mokadem, J.D.Weaver III. *J. Am. Chem. Soc.*, **139**, 13092 (2017)
88. K.Müller, C.Faeh, F.Diederich. *Science*, **317**, 1881 (2007)
89. S.Purser, P.R.Moore, S.Swallow, V.Gouverneur. *Chem. Soc. Rev.*, **37**, 320 (2008)
90. W.K.Hagmann. *J. Med. Chem.*, **51**, 4359 (2008)
91. D.A.Nicewicz, D.W.C.MacMillan. *Science*, **322**, 77 (2008)
92. D.A.Nagib, M.E.Scott, D.W.C.MacMillan. *J. Am. Chem. Soc.*, **131**, 10875 (2009)
93. V.Pham, D.A.Nagib, D.W.C.MacMillan. *Angew. Chem., Int. Ed.*, **50**, 6119 (2011)
94. D.Cantillo, O.de Frutos, J.A.Rincón, C.Mateos, C.O.Kappe. *Org. Lett.*, **16**, 896 (2014)
95. N.Iqbal, S.Choi, E.Ko, E.J.Cho. *Tetrahedron Lett.*, **53**, 2005 (2012)
96. Y.Su, K.P.L.Kuijpers, N.König, M.Shang, V.Hessel, T.Noël. *Chem. – Eur. J.*, **22**, 12295 (2016)
97. D.A.Nagib, D.W.C.MacMillan. *Nature (London)*, **480**, 224 (2011)
98. H.Jiang, C.Huang, J.Guo, C.Zeng, Y.Zhang, S.Yu. *Chem. – Eur. J.*, **18**, 15158 (2012)
99. Y.Yasu, T.Koike, M.Akita. *Angew. Chem., Int. Ed.*, **51**, 9567 (2012)
100. R.Tomita, Y.Yasu, T.Koike, M.Akita. *Beilstein J. Org. Chem.*, **10**, 1099 (2014)
101. Y.R.Malpani, B.K.Biswas, H.S.Han, Y.-S.Jung, S.B.Han. *Org. Lett.*, **20**, 1693 (2018)
102. S.Jana, A.Verma, R.Kadu, S.Kumar. *Chem. Sci.*, **8**, 6633 (2017)
103. X.Sun, S.Yu. *Chem. Commun.*, **52**, 10898 (2016)
104. B.Sahoo, J.-L.Li, F.Glorius. *Angew. Chem., Int. Ed.*, **54**, 11577 (2015)
105. S.B.Woo, D.Y.Kim. *J. Fluorine Chem.*, **178**, 214 (2015)
106. A.Carboni, G.Dagousset, E.Magnier, G.Masson. *Synthesis*, **47**, 2439 (2015)
107. H.S.Han, E.H.Oh, Y.-S.Jung, S.B.Han. *Org. Lett.*, **20**, 1698 (2018)
108. G.-L.Gao, C.Yang, W.Xia. *Chem. Commun.*, **53**, 1041 (2017)
109. L.Li, Q.-Y.Chen, Y.Guo. *J. Fluorine Chem.*, **167**, 79 (2014)
110. Y.-C.Yuan, H.-L.Liu, X.-B.Hu, Y.Wei, M.Shi. *Chem. – Eur. J.*, **22**, 13059 (2016)
111. L.Zhu, L.-S.Wang, B.Li, B.Fu, C.-P.Zhang, W.Li. *Chem. Commun.*, **52**, 6371 (2016)
112. N.Iqbal, S.Choi, E.Kim, E.J.Cho. *J. Org. Chem.*, **77**, 11383 (2012)
113. B.Li, D.Fan, C.Yang, W.Xia. *Org. Biomol. Chem.*, **14**, 5293 (2016)
114. X.Liu, Z.Wu, Z.Zhang, P.Liu, P.Sun. *Org. Biomol. Chem.*, **16**, 414 (2018)

115. L.M.Kreis, S.Krautwald, N.Pfeiffer, R.E.Martin, E.M.Carreira. *Org. Lett.*, **15**, 1634 (2013)
116. X.Yu, S.M.Cohen. *J. Am. Chem. Soc.*, **138**, 12320 (2016)
117. X.-L.Yu, J.-R.Chen, D.-Z.Chen, W.-J.Xiao. *Chem. Commun.*, **52**, 8275 (2016)
118. Z.Gonda, F.Béke, O.Tischler, M.Petró, Z.Novák, B.L.Tóth. *Eur. J. Org. Chem.*, 2112 (2017)
119. Q.Lefebvre, N.Hoffmann, M.Rueping. *Chem. Commun.*, **52**, 2493 (2016)
120. J.W.Lee, D.N.Spiegowski, M.-Y.Ngai. *Chem. Sci.*, **8**, 6066 (2017)
121. F.Narjes, R.F.Koehler, U.Koch, B.Gerlach, S.Colarusso, C.Steinkühler, M.Brunetti, S.Altamura, R.De Francesco, V.G.Matassa. *Bioorg. Med. Chem. Lett.*, **12**, 701 (2002)
122. Y.Xu, L.Qian, A.V.Pontsler, T.M.McIntyre, G.D.Prestwich. *Tetrahedron*, **60**, 43 (2004)
123. M.A.Chowdhury, K.R.A.Abdellatif, Y.Dong, D.Das, M.R.Suresh, E.E.Knaus. *J. Med. Chem.*, **52**, 1525 (2009)
124. Q.-Y.Lin, Y.Ran, X.-H.Xu, F.-L.Qing. *Org. Lett.*, **18**, 2419 (2016)
125. Q.-Y.Lin, X.-H.Xu, K.Zhang, F.-L.Qing. *Angew. Chem., Int. Ed.*, **55**, 1479 (2016)
126. N.Noto, T.Koike, M.Akita. *Chem. Sci.*, **8**, 6375 (2017)
127. C.-Y.He, J.Kong, Xue.Li, Xiao.Li, Q.Yao, F.-M.Yuan. *J. Org. Chem.*, **82**, 910 (2017)
128. G.Yin, M.Zhu, W.Fu. *J. Fluorine Chem.*, **199**, 14 (2017)
129. J.Liu, W.Ding, Q.-Q.Zhou, D.Liu, L.-Q.Lu, W.-J.Xiao. *Org. Lett.*, **20**, 461 (2018)
130. L.I.Panferova, A.V.Tsymbal, V.V.Levin, M.I.Struchkova, A.D.Dilman. *Org. Lett.*, **18**, 996 (2016)
131. L.I.Panferova, M.I.Struchkova, A.D.Dilman. *Synthesis*, **49**, 4124 (2017)
132. Y.-b.Wu, G.-P.Lu, B.-j.Zhou, M.-j.Bu, L.Wan, C.Cai. *Chem. Commun.*, **52**, 5965 (2016)
133. G.N.Chernov, V.V.Levin, V.A.Kokorekin, M.I.Struchkova, A.D.Dilman. *Adv. Synth. Catal.*, **359**, 3063 (2017)
134. X.-J.Wei, W.Boon, V.Hessel, T.Noël. *ACS Catal.*, **7**, 7136 (2017)
135. Y.Arai, R.Tomita, G.Ando, T.Koike, M.Akita. *Chem. – Eur. J.*, **22**, 1262 (2016)
136. W.Sha, W.Zhang, S.Ni, H.Mei, J.Han, Y.Pan. *J. Org. Chem.*, **82**, 9824 (2017)
137. Z.-B.Yin, J.-H.Ye,W.-J.Zhou, Y.-H.Zhang, L.Ding, Y.-Y.Gui, S.-S.Yan, J.Li, D.-G.Yu. *Org. Lett.*, **20**, 190 (2018)
138. V.I.Supranovich, V.V.Levin, M.I.Struchkova, A.A.Korlyukov, A.D.Dilman. *Org. Lett.*, **19**, 3215 (2017)
139. Y.Choi, C.Yu, J.S.Kim, E.J.Cho. *Org. Lett.*, **18**, 3246 (2016)
140. S.S.Ashirbaev, V.V.Levin, M.I.Struchkova, A.D.Dilman. *J. Fluorine Chem.*, **191**, 143 (2016)
141. Y.-M.Su, Y.Hou, F.Yin, Y.-M.Xu, Y.Li, X.Zheng, X.-S.Wang. *Org. Lett.*, **16**, 2958 (2014)
142. M.Daniel, G.Dagousset, P.Diter, P.-A.Klein, B.Tuccio, A.-M.Goncalves, G.Masson, E.Magnier. *Angew. Chem., Int. Ed.*, **56**, 3997 (2017)
143. C.W.Suh, D.Y.Kim. *Tetrahedron Lett.*, **56**, 5661 (2015)
144. N.Zhou, P.Xu, W.Li, Y.Cheng, C.Zhu. *Acta Chim. Sinica*, **75**, 60 (2017)
145. S.B.Nagode, A.K.Chaturvedi, N.Rastogi. *Asian J. Org. Chem.*, **6**, 453 (2017)
146. Y.Xiang, Y.Li, Y.Kuang. J Wu. *Chem. – Eur. J.*, **23**, 1032 (2017)
147. J.Rong, L.Deng, P.Tan, C.Ni, Y.Gu, J.Hu. *Angew. Chem., Int. Ed.*, **55**, 2743 (2016)
148. L.-C.Yu, J.-W.Gu, S.Zhang, X.Zhang. *J. Org. Chem.*, **82**, 3943 (2017)
149. J.Jung, E.Kim, Y.You, E.J.Cho. *Adv. Synth. Catal.*, **356**, 2741 (2014)
150. F.Ding, Y.Jiang, K.Lin, L.Shi. *Org. Biomol. Chem.*, **16**, 1812 (2018)
151. H.Xiang, Q.-L.Zhao, P.-J.Xia, J.-A.Xiao, Z.-P.Ye, X.Xie, H.Sheng, X.-Q.Chen, H.Yang. *Org. Lett.*, **20**, 1363 (2018)
152. J.J.Douglas, H.Albright, M.J.Sevrin, K.P.Cole, C.R.J.Stephenson. *Angew. Chem., Int. Ed.*, **54**, 14898 (2015)
153. L.Wang, X.-J.Wei, W.-L.Lei, H.Chen, L.-Z.Wu, Q.Liu. *Chem. Commun.*, **50**, 15916 (2014)
154. W.Huang, J.Chen, D.Hong, W.Chen, X.Cheng, Y.Tian, G.Li. *J. Org. Chem.*, **83**, 578 (2018)
155. K.Chen, N.Berg, R.Gschwind, B.König. *J. Am. Chem. Soc.*, **139**, 18444 (2017)
156. W.-Q.Hu, X.-H.Xu, F.-L.Qing. *J. Fluorine Chem.*, **208**, 73 (2018)
157. Y.Duan, W.Li, P.Xu, M.Zhang, Y.Cheng, C.Zhu. *Org. Chem. Front.*, **3**, 1443 (2016)
158. J.-X.Li, L.Li, M.-D.Zhou, H.Wang. *Org. Chem. Front.*, **5**, 1003 (2018)
159. C.-Y.He, J.-W.Gu, X.Zhang. *Tetrahedron Lett.*, **58**, 3939 (2017)
160. S.Barata-Vallejo, D.E.Yerien, A.Postigo. *Eur. J. Org. Chem.*, 7869 (2015)
161. D.E.Yerien, R.Conde, S.Barata-Vallejo, B.Camps, B.Lantaño, A.Postigo. *RSC Adv.*, **7**, 266 (2017)
162. T.Yajima, M.Ikegami. *Eur. J. Org. Chem.*, 2126 (2017)
163. X.Geng, F.Lin, X.Wang, N.Jiao. *J. Photochem. Photobiol., A: Chem.*, **355**, 194 (2018)
164. X.Geng, F.Lin, X.Wang, N.Jiao. *Org. Lett.*, **19**, 4738 (2017)
165. M.R.Torviso, D.Mansilla, S.Garcia, B.Lantaño, S.Barata-Vallejo, A.Postigo. *J. Fluorine Chem.*, **197**, 42 (2017)
166. X.Sun, W.Wang, Y.Li, J.Ma, S.Yu. *Org. Lett.*, **18**, 4638 (2016)
167. S.Tang, L.Yuan, Z.-Z.Li, Z.-Y.Peng,Y.-L.Deng, L.-N.Wang, G.-X.Huang, R.-L.Sheng. *Tetrahedron Lett.*, **58**, 2127 (2017)
168. V.I.Supranovich, V.V.Levin, M.I. Struchkova, A.D.Dilman. *Org. Lett.*, **20**, 840 (2018)
169. S.Mukherjee, B.Maji, A.Tlahuext-Aca, F.Glorius. *J. Am. Chem. Soc.*, **138**, 16200 (2016)
170. Y.Li, T.Koike, M.Akita. *Asian J. Org. Chem.*, **6**, 445 (2017)
171. G.Dagousset, C.Simon, E.Anselmi, B.Tuccio, T.Billard, E.Magnier. *Chem. – Eur. J.*, **23**, 4282 (2017)
172. A.K.Yadav, K.N.Singh. *Chem. Commun.*, **54**, 1976 (2018)
173. M.S.Oderinde, M.Frenette, D.W.Robbins, B.Aquila, J.W.Johannes. *J. Am. Chem. Soc.*, **138**, 1760 (2016)