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Single electron-transfer processes in perfluoroalkyl halides reactions*

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Abstract

Reactions of nucleophiles, radical anions or metals with perfluoroalkyl bromides or iodides, which follow an electron-transfer (ET) mechanism, are reviewed. The nature of this step (classical, dissociative or associative ET) is not known with certainty. Proofs of the existence of an intermediate radical are based on inhibition and capture experiments. These reactions allow the preparation of fluorinated products, such as α-perfluoroalkyl ketones, perfluoroalkyl sulfides, perfluoroalkane sulfinates and perfluoroalkyl aromatic compounds

Introduction

Pioneer studies on the reactivity of perfluoroalkyl bromides and iodides have shown ready homolytic cleavage of the carbon–bromide (or iodide) bond and an X-philic attack on the voluminous halogen by hard nucleophilic reagents [1, 2]. However, since the mid-1970s, some reactions with soft nucleophilic reagents, metals and radical anions have been interpreted as single electron-transfer processes. The purpose of this short review is to discuss the proof supporting this mechanism and the remaining uncertainties about the nature of this process.

The electron-transfer (ET) process is possible when the halide is easily reducible and the reagent [D^- (charged nucleophile), $D^{\bullet -}$ (radical anion), D (neutral nucleophile) or M (metal)] is a good electron donor. Three kinds of ET can occur in the initial step of the reaction. A classical process can produce initially the corresponding perfluoroalkyl halide radical anion, which is transformed quickly to perfluoroalkyl radical and a halide anion. A dissociative process can lead directly to the same radical and the halide anion. An associative ET can give also this radical and a halogenated compound (Scheme 1).

Depending on the nature of the initial step, the ET may, or may not, involve the formation of the perfluoroalkyl halide radical anion as an intermediate, and of halogenated compound as a by-product. In all these cases, a perfluoroalkyl radical is a genuine intermediate of the ET process.

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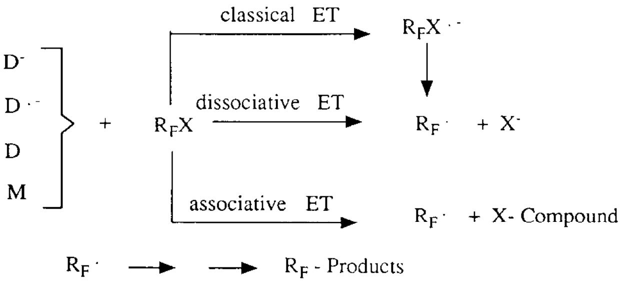
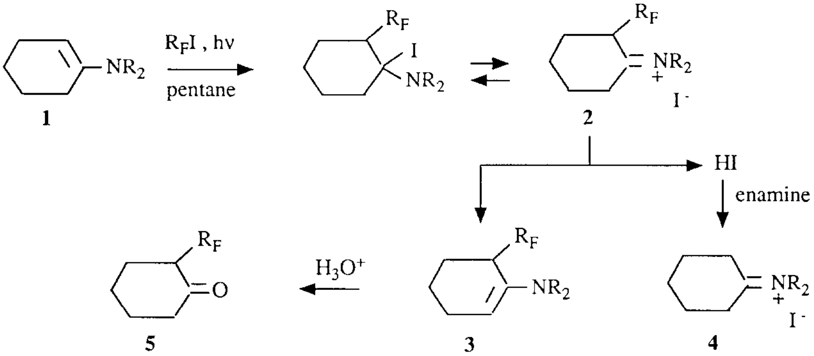
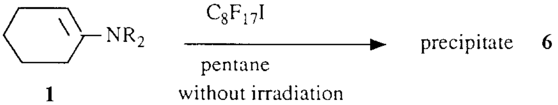


Scheme 1.



Scheme 2.



Scheme 3.

Initial observations

To the best of the author's knowledge, the first ET which was demonstrated in this area was the reaction of perfluoroalkyl iodides with enamines [3, 4]. In preparing this review, the author realizes that it has never been explained precisely how this mechanism came to be proposed. Consequently, he has chosen to begin with some words about the history of this study.

Initially, this condensation was performed under UV irradiation. The adduct formed by a classical radical attack on a double bond was in fact the fluorinated immonium iodide **2**. Excess starting enamine transformed this salt into the perfluoroalkyl enamine **3**. Hydrolysis of the latter gave the corresponding ketone **5**. Thus, the secondary product was the simple non-fluorinated immonium iodide **4** (Scheme 2).

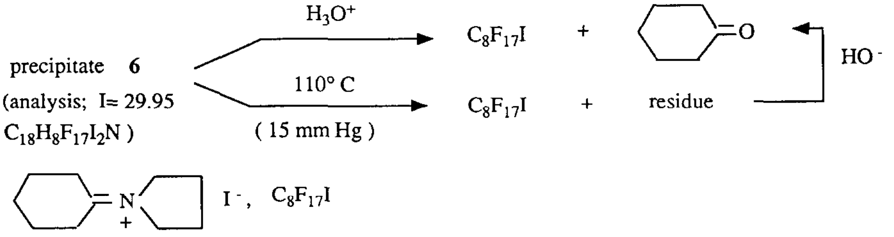
It should be remarked that a white powder **6** was formed simply by mixing the starting reactants before UV irradiation (Scheme 3).

The nature of precipitate **6** has been studied. Its acid hydrolysis gave the perfluoroalkyl iodide and the ketone which was used for the preparation of the enamine **1**. Its thermal decomposition under vacuum also produced the perfluoroalkyl iodide. Then, basic hydrolysis of the thermolysis residue furnished the same ketone. It appears that precipitate **6** was formed from the two starting reactants. What was impressive was the huge amount of iodine disclosed by the elemental microanalysis of compound **6** (Scheme 4).

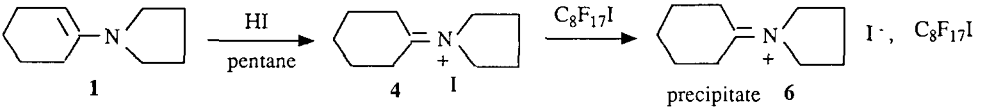
It seems that **6** contains two iodine atoms. On the basis of its analysis, this could correspond to a 1:1 combination between the perfluoroalkyl iodide and the simple immonium iodide **4**. An authentic sample of **4**, prepared from the starting enamine and hydroiodic acid, was mixed with the perfluoroalkyl iodide. The resulting solid product showed the same UV and NMR characteristics as precipitate **6** (Scheme 5).

The precise structure of the combination **6** was not known, but it was understood that the secondary product **4** could be readily formed simply by mixing the starting reactants, even before UV irradiation. Consequently, the supernatant layer of the reaction was hydrolyzed and the perfluoroalkyl ketone **5** was readily obtained. It appears that this condensation is the first spontaneous addition of a perfluoroalkyl halide to a double bond (Scheme 6).

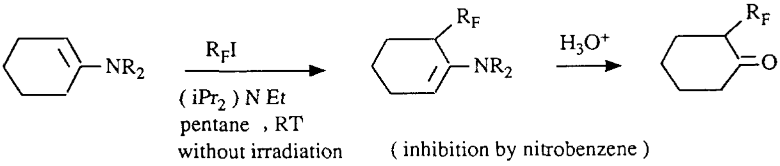
Moreover, it was observed that this condensation was inhibited by electron scavengers, such as nitrobenzene. Such inhibition shows the radical nature of the reaction.



Scheme 4.



Scheme 5.



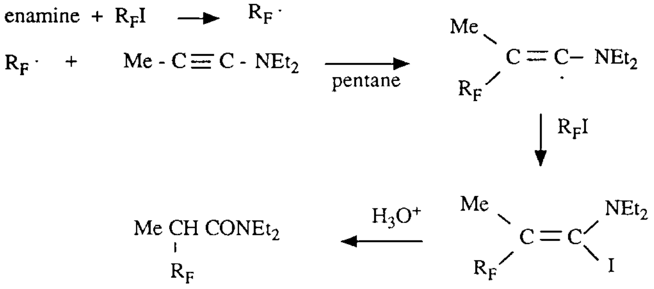
Scheme 6.

An ynamine diluted in pentane did not react spontaneously with perfluoroalkyl iodides. However, this condensation was initiated by a decimolar quantity of an enamine (Scheme 7).

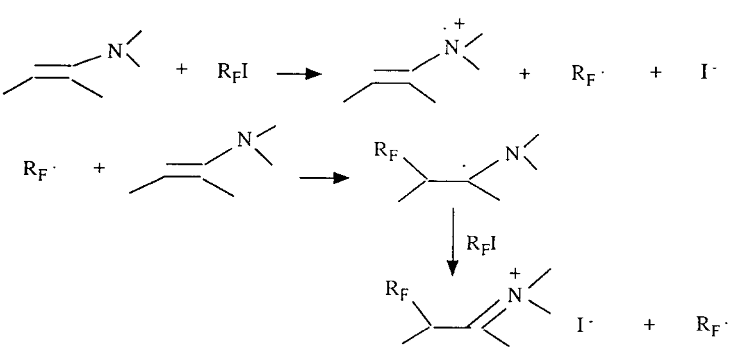
Capture of the perfluoroalkyl radical by the triple bond was in agreement with a chain mechanism. Consequently, the enamine reaction was interpreted as an SET process (Scheme 8).

At the same time, a radical-ion perfluoroalkylation of thiols was reported by the Yagupolskii group [5]. The reaction was performed under the conditions used by Bunnett for $S_{RN}1$ substitutions on aryl halides (UV irradiation in liquid ammonia). The formation of perfluoroalkyl sulfides was logically interpreted by an SET process (Scheme 9), but no additional proofs of this mechanism were given.

Comparison between Schemes 8 and 9 shows that both perfluoroalkylations are chain reactions initiated by electron transfer. In the thiol example propagation occurs by electron transfer, whereas in the enamine case this process involves iodine-atom transfer. However, the atom transfer could also be considered to follow an electron-transfer mechanism. A clearer example of a process in which a nucleophile (arylsulfinate ion) initiates by ET a radical chain process probably not involving ET was given later by Feiring [6].



Scheme 7.



Scheme 8.

$$RSH \xrightarrow[NH_3]{CF_3I\ ,\ h\nu} RSCF_3$$

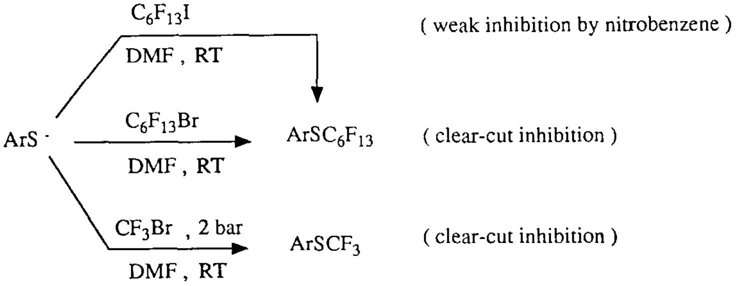
$$RS^- + CF_3I \longrightarrow RS\cdot + [\,CF_3I\,]^{\cdot -}$$

$$[\,CF_3I\,]^{\cdot -} \longrightarrow CF_3\cdot + I^-$$

$$RS^- + CF_3\cdot \longrightarrow [\,RS\cdot + CF_3^-\,] \longrightarrow [\,RSCF_3\,]^{\cdot -}$$

$$[\,RSCF_3\,]^{\cdot -} + CF_3I \longrightarrow RSCF_3 + [\,CF_3I\,]^{\cdot -}$$

Scheme 9.



Scheme 10.

Further examples

When thiolates are used instead of thiols, the reaction with perfluoroalkyl iodides does not need initiation by UV light. Several teams have shown that the mechanism involved is an SET process. In the condensation of perfluorohexyl iodide with sodium thiophenoxide [7], inhibition by nitrobenzene was not complete [8, 9]*. However, in the case of the less-reactive perfluoroalkyl bromides, a clear-cut inhibition was obtained [7] (Scheme 10).

At the same time, Feiring showed that the intermediate perfluoroalkyl radical could be captured by norbornene [10]. Moreover, he reported inhibition of the thiolate condensation by styrene. In that case, the benzylic radical formed was relatively stable and poorly reactive; its reaction with the perfluoroalkyl iodide was rather slow, and consequently the chain reaction was broken (Scheme 11).

Numerous groups have examined the reaction of perfluoroalkyl halides with metals. Some of them have interpreted the initial step as an SET process [11–13]. Recently, we have shown that the perfluoroalkyl radical formed in the reaction of trifluoromethyl bromide with zinc can be captured by an

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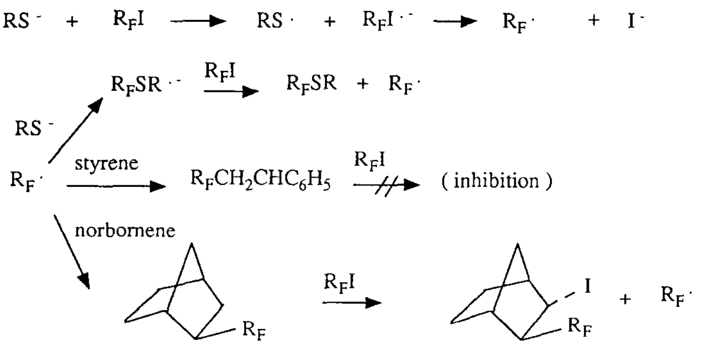
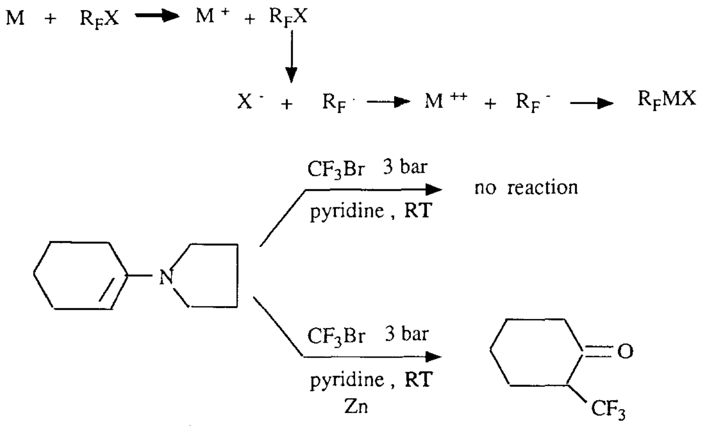
*In a recent publication [8], Savéant *et al.* have interpreted our study [7] as an absence of inhibition. In fact, we have stated that the inhibition by nitrobenzene of the benzene thiolate condensation with perfluorohexyl iodide is less efficient than that of the corresponding bromide. In the experimental part of another of our publications [9],it has been demonstrated that the perfluorohexyl iodide conversion dropped from 85% to 30% in the presence of nitrobenzene. A clear-cut inhibition was observed with perfluorohexyl bromide.



Scheme 11.



Scheme 12.

enamine [13] (Scheme 12). The observation of enamine reactivity under Barbier conditions could be the result of a chain process initiated at the zinc surface.

Reaction of the same halide with zinc and sulfur dioxide under slight pressure led to the formation of a triflinate salt [11, 14]. We have interpreted the main pathway of this reaction by the initial reduction of SO_2 to its corresponding radical anion (which is known to be in equilibrium with a dithionite salt), followed by an SET process between this radical anion and the perfluoroalkyl bromide [11, 13] (Scheme 13). Obviously, this condensation requires a stoichiometric amount of reductant. The mechanism was written as a non-chain process.

The sulfinato dehalogenation of liquid perhalogenoalkyl halides by sodium dithionite has been reported by the Huang group [15, 16]. Similarly, we have been able to transform the gaseous and poorly reactive trifluoromethyl bromide into sodium trifluoromethane sulfinate, but under modified reaction conditions [17] (Scheme 14). The SET process involved is analogous to that of the zinc–sulfur dioxide reaction.

$$Zn + SO_2 \xrightarrow[DMF]{CF_3Br \quad 3\ bar} CF_3SO_2ZnBr$$

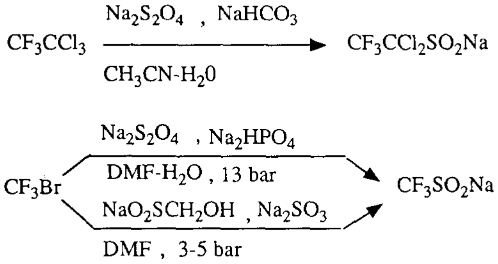
$$Zn + SO_2 \longrightarrow Zn^{+} \; SO_2^{\cdot -} \qquad (SO_2^{\cdot -} \rightleftarrows S_2O_4^{2-})$$

$$SO_2^{\cdot -} + CF_3Br \longrightarrow SO_2 + CF_3Br^{\cdot -}$$

$$CF_3Br^{\cdot -} \longrightarrow Br^{-} + CF_3^{\cdot}$$

$$CF_3^{\cdot} + SO_2^{\cdot -} \longrightarrow CF_3SO_2^{-}$$

Scheme 13.



$$CF_3CCl_3 \xrightarrow[CH_3CN\text{-}H_2O]{Na_2S_2O_4\ ,\ NaHCO_3} CF_3CCl_2SO_2Na$$

$$CF_3Br \xrightarrow[DMF\text{-}H_2O\ ,\ 13\ bar]{Na_2S_2O_4\ ,\ Na_2HPO_4} CF_3SO_2Na$$

$$CF_3Br \xrightarrow[DMF\ ,\ 3\text{-}5\ bar]{NaO_2SCH_2OH\ ,\ Na_2SO_3} CF_3SO_2Na$$

Scheme 14.

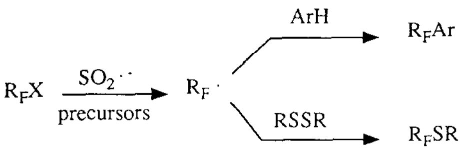
$$SO_2 \xrightarrow[DMF]{e^-} SO_2^{\cdot -} \xrightarrow{CF_3Br} CF_3SO_2^{-}$$

Scheme 15.

This triflinate salt has also been obtained electrochemically [18, 19] (Scheme 15). Two different non-chain processes requiring a stoichiometric source of electrons have been proposed. The first one [18] was a classical ET, similar to Scheme 13. The second one [19] was an associative ET (see Scheme 19).

Later, we reported that the intermediate perfluoroalkyl radical formed in the reaction of perfluoroalkyl halides with various sulfoxylate radical-anion precursors could react with electron-rich aromatic compounds [20] and disulfides [21] to give perfluoroalkyl aromatics and perfluoroalkyl sulfides, respectively (Scheme 16). In the latter case, a stoichiometric amount of reductant was required. Consequently, a non-chain process was considered. In the first case, a decimolar equivalent of the reductant was sufficient to promote the reaction. We proposed that SO_2 which is formed can be reduced back to its radical anion by an intermediate cyclohexadienyl radical. This step could induce chain formation of the perfluoroalkyl radical [20].

Since the earlier studies, all the proofs given in favour of SET processes in perfluoroalkyl halides reactions have been based on trapping the intermediate perfluoroalkyl radicals and on inhibition experiments.



Scheme 16.

$$SO_2^{\cdot -} + CF_3Br \longrightarrow {}^{\cdot}SO_2CF_3 + Br^-$$

$${}^{\cdot}SO_2CF_3 \longrightarrow CF_3^{\cdot} + SO_2$$

$$CF_3^{\cdot} + SO_2^{\cdot -} \longrightarrow CF_3SO_2^-$$

Scheme 17.

$$SO_2^{\cdot -} \xrightarrow{RX} RSO_2^- \xrightarrow{RX} RSO_2R$$

	$k\ s^{-1}\ M^{-1}$
CH_3Br	10^{-1}
$(CH_3)_2CHI$	10^{1}
$C_6H_5CH_2Br$	10^{2}
CF_3Br	10^{3}

$$(CF_3SO_2^- \xrightarrow{CF_3Br} \!\!\!\!/\!\!/\;\; CF_3SO_2CF_3)$$

Scheme 18.

Nature of the electron transfer

The mechanism of the reaction between trifluoromethyl bromide and sulfoxylate radical anion has been questioned by the Savéant group [19]. The rate of this reaction was found to be four orders of magnitude higher than that of an aromatic radical anion having the same standard potential (extrapolated value). By assuming that this latter reaction was a genuine dissociative ET, it was initially concluded that the $SO_2^{\cdot -}$ reaction was a S_N2 process; its rate was calculated [22] from the mechanism written as Scheme 17.

The authors [19, 22] remarked that the rate was higher than that of the very reactive benzyl bromide [23] (Scheme 18; this table gives a summary of the rate values calculated from electrochemical data by Wille *et al.* for simple alkyl halides [23], and by Savéant *et al.* for CF_3Br [19, 22]).

However, we have recently performed qualitative competitive experiments between these two halides, using a formic acid/sodium hydrogen sulfite mixture as the sulfoxylate radical anion precursor in DMF. On following the reaction by NMR spectroscopy, we observed that trifluoromethyl bromide was less reactive than benzyl bromide under these conditions. Its reactivity was comparable to that of isopropyl iodide [23] (Scheme 18) in similar competitive experiments [24]. Nevertheless, this value is still in a higher range than that of the aromatic radical anion of the same standard potential.

We have suggested that the mechanism written in Scheme 17 seems unlikely. In the reaction of $SO_2^{\cdot -}$ with usual alkyl halides, sulfinate salts were not isolated because they reacted further with the starting halide by a second S_N2 process to readily give dialkyl sulfonates [23]. The absence of the corresponding fluorinated sulfone (Scheme 18) in the reaction of trifluoromethyl bromide was in agreement with the known resistance of perfluoroalkyl halides to S_N2 processes.

An alternative associative mechanism was then suggested by the Savéant team [19, 22] (Scheme 19).

This associative ET does not involve the trifluoromethyl bromide radical anion as an intermediate. The existence of this latter was considered to be unlikely in a polar solvent such as DMF [25], because of weakening of the charge-polarizable dipole interaction between the trifluoromethyl radical and the bromide anion.

However, the existence of trifluoromethyl halide radical anions has been demonstrated by different methods: these species have been detected by ESR spectroscopy in weakly polar solid matrixes at 77 K upon γ-irradiation [26, 27] and by mass spectrometry in the gas phase upon collision with alkali-metal atoms [28, 29].

It is possible that a halogen-exchange reaction observed recently in our laboratory could be indicative of the presence of the trifluoromethyl iodide radical anion, even in a polar solvent [30] (Scheme 20).

The trifluoromethyl radical, formed by reaction of trifluoromethyl bromide with a sulfoxylate radical anion precursor, leads to trifluoromethyl iodide in the presence of sodium iodide in DMF at room temperature. A triple collision between $CF_3^{\cdot}$, I^- and CF_3Br appears unlikely. Although other mechanisms

$$CF_3Br + SO_2^{\cdot -} \longrightarrow CF_3^{\cdot} + BrSO_2^-$$

$$CF_3^{\cdot} + SO_2^{\cdot -} \longrightarrow CF_3SO_2^-$$

Scheme 19.

$$NaI \xrightarrow[\text{HCOOH, NaHSO}_3\text{; DMF, RT, 3h}]{CF_3Br\text{, 4 bar}} CF_3I$$

$$\begin{tikzcd}
CF_3^{\cdot} + I^- \arrow[r, shift left] & CF_3I^{\cdot -} \arrow[l, shift left] \arrow[d, "CF_3Br"] \\
 & CF_3I + CF_3Br^{\cdot -}
\end{tikzcd}$$

Scheme 20.

can be written, the simpler one seems the reaction of the radical with the iodide anion (Scheme 20). However, this observation cannot be considered as proof of radical-anion formation in the initial step of the SET process.

On the other hand, the associative mechanism (Scheme 19) involves the formation of the bromosulfinate anion $BrSO_2^-$. This species is known to be relatively stable at room temperature and to be detectable in polar solvents [31, 32]. However, such a halogenated compound was not observed in the reaction of CF_3Br with $SO_2^{\bullet-}$ [19, 22].

Another question arises from the comparison of the behaviour of various radical anions having approximately the same standard potential. No detectable reaction of the superoxide radical anion $O_2^{\bullet-}$ with trifluoromethyl bromide has been observed [19, 22], showing that this possible transformation is very much slower than that of $SO_2^{\bullet-}$ [33][*]. Two cases can be considered. In the first hypothesis, the $O_2^{\bullet-}$ reaction rate can be equivalent to that of an aromatic radical anion having the same standard potential. This latter reaction has been interpreted as a dissociative ET [19, 22]. By analogy, the superoxide anion reaction could follow a dissociative process. In this case, the behaviour of $SO_2^{\bullet-}$ would be rather peculiar. In the second hypothesis, the rate of reaction of $O_2^{\bullet-}$ could be lower than that of the aromatic radical anion. In that case, should it be an associative ET process? If so, this would mean that the rates of very different radical anions having about the same standard potential, and reacting by the same ET process, do not lie on the same curve[†].

The nature of an electron transfer might vary depending on whether the donor is an odd or even electron species. Intuitively, it seems that an associative process is less likely for a species such as $PhSCF_3^{\bullet-}$ than for PhS^-, if for no other reason than a steric effect[‡]. Moreover, the associative ET should give $PhS(X)CF_3^-$. Its structure could correspond more to a transition state than to a real intermediate. A similar question can be asked about the perfluoroalkylation of other nucleophiles, such as the 2-nitropropyl anion [36]. A dissociative or a classical ET appears more likely for these steps.

The peculiar associative ET proposed for the sulfoxylate anion-radical reaction [19, 22] could be due to the absence of a steric effect in that case. However, the same argument should be valid for the superoxide anion-radical reaction (*vide supra*). The different behaviour of these two reagents could

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[*] Very recently, the reaction of a more reactive perfluoroalkyl iodide with the superoxide anion radical has been described [33].

[†] Dr. B. Smart has remarked that the various aromatic radical anions have similar basicities. It seems logical that the relation between the rates of their reactions with trifluoromethyl bromide and their respective standard potentials should follow a straight line [19, 22]. Based on the Edwards equation [34, 35],the nucleophilic strengths of donors depend not only on their polarizabilities but also on their basicities. Compared to carbon nucleophiles, sulfur and oxygen donors have very different basicities. Consequently, sulfur radical anions could constitute a second family, and oxygen radical anions a third one; their reactivities could be represented on curves different from that of the aromatic radical anions.

[††] The author thanks the referee for this interesting remark.

be due to the formation of a more stable product in the first case [37]. But, as already pointed out, the bromosulfinate anion, $BrSO_2^-$, was not detected.

Conclusions

The existence of intermediate radicals has been clearly demonstrated in various reactions of perfluoroalkyl halides with soft nucleophiles, radical anions and reductive metals in agreement with a single electron-transfer mechanism.

However, the nature of this process is not known with certainty. Is it a classical, a dissociative or an associative electron transfer? Recently, Savéant has laid emphasis on the differences between these processes. Arguments in favour or against the involvement of the perfluoroalkyl halide radical anion or that of the halogenated secondary product, formed in an associative process, can be given. Whatever the genuine answer, these SET reactions can be used as new methods for the introduction of perfluoroalkyl groups into organic molecules (Scheme 1).

Acknowledgments

The author thanks his coworkers whose names appear in the references, and particularly Dr Marc Tordeux for his recent contributions. He is also grateful to Dr Bruce Smart for having attracted his attention to the importance of the nucleophilic strengths which can be analyzed by the Edwards equation.

References

1 C. Wakselman and C. Kaziz, *J. Fluorine Chem.*, *33* (1986) 347.
2 C. Wakselman and A. Lantz, in R. E. Banks, B. E. Smart and J. C. Tatlow (eds.), *Organofluorine Chemistry: Principles and Commercial Applications*, Plenum, New York, in preparation.
3 D. Cantacuzène and C. Wakselman, *Fr. Pat. 2 354 310* (1975). [*Chem. Abs.*, *89* (1978) 146 428e].
4 D. Cantacuzène, C. Wakselman and R. Dorme, *J. Chem. Soc., Perkin Trans. 1*, (1977) 1365.
5 V. N. Boiko, G. M. Schchupak and L. M. Yagupolskii, *Zh. Org. Khim.*, (1977) 1057.
6 A. E. Feiring, *J. Org. Chem.*, *50* (1985) 3629.
7 C. Wakselman and M. Tordeux, *J. Chem. Soc., Chem. Commun.*, (1984) 793.
8 M. Medebielle, J. Pinson and J. M. Savéant, *J. Am. Chem. Soc.*, *113* (1991) 6872.
9 C. Wakselman and M. Tordeux, *J. Org. Chem.*, *50* (1985) 4047.
10 A. E. Feiring, *J. Fluorine Chem.*, *24* (1984) 191.
11 C. Wakselman and M. Tordeux, *Bull. Soc. Chim. Fr.*, (1986) 868.
12 D. J. Burton and Z. Y. Yang, *Tetrahedron*, *48* (1992) 189 and references therein.
13 M. Tordeux, C. Francèse and C. Wakselman, *J. Chem. Soc., Perkin Trans. 1*, (1990) 1951.
14 C. Wakselman and M. Tordeux, *Fr. Pat. 2 564 829* (1984) [*Chem. Abs.*, *105* (1986) 171 845v].
15 W. Y. Huang, B. N. Huang and J. L. Chen, *Acta Chim. Sinica*, *42* (1984) 1114 [*Chem. Abs.*, *102* (1985) 78 313g].

16 W. Y. Huang, *J. Fluorine Chem.*, *32* (1986) 179.
17 M. Tordeux, B. Langlois and C. Wakselman, *J. Org. Chem.*, *54* (1989) 2452.
18 J. C. Folest, J. Y. Nedelec and J. Perichon, *Synth. Commun.*, *18* (1988) 1491.
19 C. P. Andrieux, L. Gélis and J. M. Savéant, *J. Am. Chem. Soc.*, *112* (1990) 786.
20 M. Tordeux, B. Langlois and C. Wakselman, *J. Chem. Soc., Perkin Trans. 1*, (1990) 2293.
21 C. Wakselman, M. Tordeux, J. L. Clavel and B. Langlois, *J. Chem. Soc., Chem. Commun.*, (1991) 993.
22 L. Gélis, *Thesis*, Paris VII University, 1988.
23 H. J. Wille, B. Kastening and D. Knittel, *J. Electroanal. Chem.*, *214* (1986) 221.
24 M. Tordeux and C. Wakselman, unpublished results.
25 C. P. Andrieux, L. Gélis, M. Medebielle, J. Pinson and J. M. Savéant, *J. Am. Chem. Soc.*, *112* (1990) 3509.
26 A. Hasgawa and F. Williams, *Chem. Phys. Lett.*, *46* (1977) 66.
27 A. Hasgawa, M. Shiotani and F. Williams, *Faraday Discuss. Chem. Soc.*, *63* (1977) 157.
28 R. N. Compton, P. W. Reinhardt and C. D. Cooper, *J. Chem. Phys.*, *68* (1978) 4360.
29 A. Kühn and E. Illenberger, *J. Phys. Chem.*, *93* (1989) 7060.
30 M. Tordeux and C. Wakselman, unpublished results.
31 A. Salama, S. B. Salama, M. Sobeir and S. Wasif, *J. Chem. Soc. A*, (1971) 1112.
32 E. Milanova and P. L. Benoit, *Can. J. Chem.*, *55* (1977) 2807.
33 C. Dapremont-Avignon, P. Calas, A. Commeyras and C. Amatore, *J. Fluorine Chem.*, *51* (1991) 357.
34 J. O. Edwards, *J. Am. Chem. Soc.*, *76* (1954) 1540.
35 J. O. Edwards, *J. Am. Chem. Soc.*, *78* (1956) 1819.
36 A. E. Feiring, *J. Org. Chem.*, *48* (1983) 347.
37 J. M. Savéant, personal communication.