Electrochemically induced nucleophilic substitution of perfluoroalkyl halides. An example of a dissociative electron-transfer-induced chemical reaction

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(w), 1363 (w), 1243 (s), 1076 (s), 996 (m) cm^{-1}; UV-vis (CH_2Cl_2) λ_{max} 422, 508, 577, 650 nm.

(*R*)-**3b**: yield 52%; high MS (FAB) *m/e* calcd for $^{12}C_{139}{}^{13}CH_{132}N_4O_{16}{}^{56}Fe$ 2181.902, found 2181.896 ($(M - Cl)^+$); IR (KBr) 2925 (s), 2854 (m), 1732 (w), 1650 (w), 1590 (m), 1458 (s), 1286 (w), 1252 (m), 1072 (s), 1003 (m) cm^{-1}; UV-vis (CH_2Cl_2) λ_{max} 421, 506, 580 nm.

Epoxidation of Styrene by Fe(Cl)[(*S*)-Binap(OMe)$_2$]$_4$TPP-eclipsed ((*S*)-1b) and Iodosobenzene. To a mixture of the catalyst (1 μmol), styrene (500 μmol), and *n*-tridecane (50 μmol) as a GLC internal standard in deaerated dry CH_2Cl_2 (1 mL) was added at once solid iodosobenzene (22 mg, 100 μmol), and the reaction mixture was stirred at a constant speed under an argon atmosphere. Aliquots (5 μL) were taken at appropriate intervals and quenched with a CH_2Cl_2 solution of PPh_3 (1.3 μmol). The formation of oxidized products was monitored by GLC, and their isolation was accomplished by silica-gel flash column chromatography, followed by identification by ^1H NMR spectroscopy. The optical yield (ee) was determined by the following method.

The trans β-proton of styrene oxide was analyzed by ^1H NMR spectroscopy in the presence of the chiral shift reagent tris[3-((heptafluoropropyl)hydroxymethylene)-(+)-camphorato]europium(III) (Eu(hfc)$_3$).[29] The proton showing the larger shift value was determined to be that of the *R* isomer.

Oxidation and analysis of the other olefins and oxidation by other catalysts were performed in the same manner with the exceptions noted in the text and Table II.

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Supplementary Material Available: A textual presentation of the experimental procedure for the preparation of compounds **5** and **6** and **8-17** (8 pages). Ordering information is given on any current masthead page.

(29) Fraser, P. R.; Petit, M. A.; Saunders, J. K. *J. Chem. Soc. D* **1971**, 1450.
(30) Tuschida, E.; Hasegawa, E.; Komatsu, T.; Nakata, T.; Nishide, H. *Chem. Lett.* **1990**, 389.
(31) Akimoto, H.; Yamada, S. *Tetrahedron* **1971**, *27*, 5999.
(32) Moneta, W.; Baret, P.; Pierre, J.-L. *Bull. Soc. Chim. Fr.* **1988**, 995.

Electrochemically Induced Nucleophilic Substitution of Perfluoroalkyl Halides. An Example of a Dissociative Electron-Transfer-Induced Chemical Reaction

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Abstract: Nucleophilic substitution of perfluoroalkyl halides can be induced electrochemically. The reaction mechanism is a slightly modified version of the classical $S_{RN}1$ mechanism in which the reaction is triggered by dissociative electron transfer, not involving the intermediacy of the anion radical of the substrate. Direct electrochemical induction is possible in principle with the iodides but not with the bromides because the reduction potentials of the substrate and of the perfluoroalkyl radical are too close in the latter case. This impossibility can be overcome by using as inductor an electrochemically generated outer-sphere electron donor. Thiolates react at the sulfur atom whereas phenoxide as well as imidazolate ions react at ring carbons rather than at the negatively charged heteroatom.

The work described in the following had two objectives. One was to contribute to the search of methods for introducing perfluoroalkyl groups into organic molecules. The second objective is of mechanistic nature. Electrochemically induced nucleophilic substitutions have been thoroughly investigated in the case of aromatic substrates.[1] This allowed the precise establishment of the reaction mechanisms of $S_{RN}1$[2a-c] aromatic nucleophilic substitution,[2d] of the nature of the competing side-reactions, and of the mechanics of the competition. In this case, the electron transfer that catalytically triggers the reaction is an outer-sphere process producing as the first intermediate the anion radical of the substrate. The aryl radical formed upon decomposition of this anion radical is the object of the nucleophilic attack but, at the same time, is a very good electron acceptor. Both facts—the intermediacy of the substrate anion radical and the high reducibility of the aryl radical—are the key ingredients that govern the outcome of the competition between substitution and hydrogenolysis of the substrate. As will be shown in the following discussion, in the present case, the electron transfer that triggers the reaction is dissociative, and therefore the feasibility of the substitution reaction directly depends upon the reducibility of the ensuing perfluoroalkyl free radical. In the case where the latter radical is not rapidly reduced by the electron donor used to trigger the reaction, other reactions, for example, H-atom abstraction from the solvent, may compete with the substitution process.

Introduction of fluoro substituents into organic molecules appears as an increasingly important goal in view of the applications of the resulting species as pharmaceutical and agrochemical agents or as precursors of tensioactive compounds. As regards more specifically the introduction of perfluoroalkyl groups, most of the reactions described so far seem to proceed via the prior formation

(1) (a) Pinson, J.; Savêant, J.-M. *J. Chem. Soc., Chem. Commun.* **1974**, 933. (b) For reviews, see ref 18c-e. (c) Savêant, J.-M. *Acc. Chem. Res.* **1980**, *13*, 323. (d) Savêant, J.-M. *Adv. Phys. Org. Chem.* **1990**, *26*, 1. (e) Pinson, J.; Savêant, J.-M. In *Festschrift in Honour of Manuel Baizer*; Little, R. D., Ed.; Marcel Dekker, New York, in press.
(2) (a) Kornblum, N.; Michel, R. E.; Kerber, R. C. *J. Am. Chem. Soc.* **1966**, *88*, 5662. (b) Russell, G. A.; Danen, W. C. *J. Am. Chem. Soc.* **1966**, *88*, 5663. (c) Kim, J. K.; Bunnett, J. F. *J. Am. Chem. Soc.* **1970**, *92*, 7463. (d) Bunnett, J. F. *Acc. Chem. Res.* **1978**, *11*, 413.

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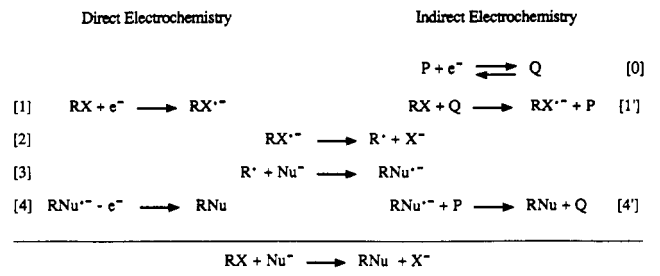
of perfluoroalkyl radicals. These $R_F^\bullet$ radicals may be produced from the parent perfluoroalkyl halides by photolysis[3a-i] or thermolysis.[3i-m] They have been allowed to react with unsaturated nitrogen,[3d,e] aromatic,[3i,m] and heterocyclic[3g,h,j-m] (imidazoles, pyrroles, thiophenes, furans) compounds. When investigated, the radical nature of these reactions has been assessed by use of radical traps. Perfluoroalkyl sulfonyl iodides[4a] decompose above −30 °C to give $R_F^\bullet$ radicals which can add to olefins; their bromide analogues[4b] seem to give ionic reactions in some cases but radical ones in other instances. Peroxides of general formula $C_nF_{2n+1}COOOCOC_nF_{2n+1}$[5] can be decomposed thermally to $R_F^\bullet$ radicals. The thermal decomposition of perfluoro carboxylic acids[6] in the presence of xenon difluoride[6a] or copper iodides[6b] also leads to $R_F^\bullet$ radicals which can react with aromatic and heteroaromatic compounds.

Electrochemistry has also been used as a means for generating $R_F^\bullet$ radicals. On the oxidative side, the Kolbe reaction applied to perfluoro carboxylic acids has been employed as a source of $R_F^\bullet$ radicals which have been reacted with olefins[7a-e] or with enols of β-diketones.[7f] On the reductive side, the indirect electrochemical reduction (using terephthalonitrile as a mediator) of CF_3Br in the presence of styrene leads to 1,1,1,6,6,6-hexafluoro-3,4-diphenylhexane, $CF_3CH_2CHC_6H_5CHC_6H_5CH_2CF_3$, the dimer of the radical adduct obtained by attack of $CF_3^\bullet$ on styrene.[8] In the presence of butyl vinyl ether, the mediator reacts with the adduct radical obtained upon attack of $CF_3^\bullet$ on the olefin.[8] Electrochemically generated $C_6F_{13}^\bullet$ radicals react with benzonitrile used as the solvent to give 4-perfluorohexylbenzonitrile.[9] Electrogenerated $SO_2^{\bullet-}$ reacts in a somewhat different fashion, abstracting a bromine atom from CF_3Br to give a $CF_3^\bullet$ radical which further reacts with $SO_2^{\bullet-}$ to give the trifluoromethyl sulfinate ion.[10] A related manner of preparing the latter compound was to use Zn as a reductant.[11] $R_F^\bullet$ radicals generated from the electrochemical reduction of perfluoroalkyl iodides react with acetylenic alcohols along a chain reaction leading to the addition of R_F and I to the triple bond.[12]

Scheme I



Metals or metal complexes[13] have been used to obtain substitution products from R_FX and aromatic of heteroaromatic compounds or addition products to olefins or carbonyl compounds. In the case of copper, perfluoroalkylcopper(I) complexes[13b-l] have been observed. In many cases the intermediacy of $R_F^\bullet$ radicals has been suggested and they were effectively trapped in some instances by diallyl ether or *tert*-butyl nitroxide.[13m,t]

Other substitution or addition reactions have been assumed to proceed via carbanionic or carbanionic-like intermediates: reactions of perfluoro organomagnesium[14] or organozinc[15] derivatives, addition of electrochemically generated R_F^- carbanions.[16] Perfluoroalkylphenyliodonium trifluoromethanesulfonates have been assumed to react with aromatics through carbocationic intermediates.[17]

The substitution of the halogen (chlorine, bromine, iodine) of perfluoroalkyl halides, R_FX, by nucleophiles is not an easy reaction.

(3) (a) El Soueni, A.; Tedder, J. M.; Walton, J. C. *J. Fluorine Chem.* **1981**, *17*, 51. (b) El Soueni, A.; Tedder, J. M.; Walton, J. C. *J. Chem. Soc., Faraday Trans. 1* **1981**, *77*, 89. (c) Kato, M.; Yamabe, M. *J. Chem. Soc., Chem. Commun.* **1981**, 1173. (d) Tordeux, M.; Wakselman, C. *Tetrahedron* **1981**, *37*, 315. (e) Cantacuzène, D.; Wakselman, D.; Dorme, R. *J. Chem. Soc., Perkin Trans. 1* **1977**, 1365. (f) Girard, Y.; Atkinson, J. G.; Belanger, P. C.; Fuentes, J. J.; Rokach, J.; Rooney, C. S.; Remy, D. C.; Hunt, C. A. *J. Org. Chem.* **1983**, *48*, 3220. (g) Kimoto, H.; Shozo, F.; Cohen, L. A. *J. Org. Chem.* **1982**, *47*, 2867. (h) Kimoto, H.; Shozo, F.; Cohen, L. A. *J. Org. Chem.* **1984**, *49*, 1060. (i) Akiyama, T.; Kato, K.; Kajitani, M.; Sukugachi, Y.; Nakamura, J.; Hayashi, H.; Sugimari, A. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 3531. (j) Kobayashi, Y.; Yamamoto, K.; Kumadaki, I. *Tetrahedron Lett.* **1979**, *42*, 4071. (k) Birchall, J. M.; Irwin, G. P.; Boyson, R. A. *J. Chem. Soc., Perkin Trans. 2* **1975**, 435. (l) Kobayashi, Y.; Kumakadi, I.; Oshawa, A.; Murakami, S.; Nakano, T. *Chem. Pharm. Bull.* **1978**, *26*, 1247. (m) Cowell, A.; Tamborski, C. *J. Fluorine Chem.* **1981**, *17*, 345.

(4) (a) Huang, W. Y.; Hu, L. Q. *J. Fluorine Chem.* **1989**, *44*, 25. (b) Huang, W. Y.; Chen, J. L.; Qu, L. *Bull. Soc. Chim. Fr.* **1986**, 881.

(5) (a) Zhao, C.; El Tahiami, G. M.; Walling, C. *J. Org. Chem.* **1983**, *48*, 3908. (b) Yoshida, M.; Amemiya, H.; Kobayashi, M.; Sawada, M.; Hagii, M.; Aoshima, K. *J. Chem. Soc., Chem. Commun.* **1985**, 234. (c) Yoshida, M.; Moriya, K.; Sawada, H.; Kobayashi, M. *Chem. Lett.* **1985**, 755. (d) Sawada, H.; Yoshida, M.; Hagii, H.; Aoshima, K.; Kobayashi, M. *Bull. Chem. Soc. Jpn.* **1986**, *59*, 215. (e) Yoshida, M.; Yoshida, T.; Kamigata, N.; Kobayashi, M. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 3549. (f) Yoshida, M.; Yoshida, T.; Kobayashi, M.; Kamigata, N. *J. Chem. Soc., Perkin Trans. 1* **1989**, 909.

(6) (a) Tanake, Y.; Matsuo, N.; Ohno, N. *J. Org. Chem.* **1988**, *53*, 4582. (b) Carr, G. E.; Chambers, R. D.; Holmes, T. F.; Parker, D. G. *J. Chem. Soc., Perkin Trans. 1* **1988**, 921.

(7) (a) Brookes, C. J.; Coe, P. L.; Owen, D. M.; Pedler, A. E.; Tatlow, J. C. *J. Chem. Soc., Chem. Commun.* **1974**, 323. (b) Renaud, R. N.; Champagne, P. J. *Can. J. Chem.* **1975**, *53*, 529. (c) Brookes, C. J.; Coe, P. L.; Pedler, A. E.; Tatlow, J. C. *J. Chem. Soc., Perkin Trans. 1* **1978**, 202. (d) Renaud, R. N.; Champagne, P. J.; Savard, M. *Can. J. Chem.* **1979**, *57*, 2617. (e) Muller, N. *J. Org. Chem.* **1986**, *51*, 263. (f) Uneyama, K.; Ueda, K. *Chem. Lett.* **1988**, 853.

(8) Andrieux, C. P.; Gélis, L.; Savéant, J.-M. *Tetrahedron Lett.* **1989**, *30*, 4961.

(9) Andrieux, C. P.; Gélis, L.; Médebielle, M.; Pinson, J.; Savéant, J.-M. *J. Am. Chem. Soc.* **1990**, *112*, 3509.

(10) Andrieux, C. P.; Gélis, L.; Savéant, J.-M. *J. Am. Chem. Soc.* **1990**, *112*, 786.

(11) (a) Wakselman, C.; Tordeux, M. *J. Chem. Soc., Chem. Commun.* **1987**, 1701. (b) Tordeux, M.; Langlois, B.; Wakselman, C. *J. Chem. Soc., Perkin Trans. 1* **1990**, 2293.

(12) (a) Calas, P.; Commeyras, A. *J. Fluorine Chem.* **1980**, *16*, 553. (b) Calas, P.; Moreau, P.; Commeyras, A. *J. Chem. Soc., Chem. Commun.* **1982**, 433. (c) Commeyras, A.; Calas, P. Eur. Pat. Appl. EP 43, 758; *Chem. Abstr.* **1982**, *96*, 1321516x. (d) Amatore, C.; Gomez, L.; Calas, P.; Commeyras, A. *J. Fluorine Chem.* **1990**, *49*, 247.

(13) (a) Cu,[13b-j] Ni,[13m] Fe,[13n] Pd,[13o-s] Mg,[13t] Sn,[13u] Zn,[13v]. (b) Burdon, J.; Coe, P. L.; Marsh, C. R.; Tatlow, J. C. *Chem. Commun.* **1967**, 1259. (c) McLoughlin, V. C. R.; Thrower, J. *Tetrahedron* **1969**, *25*, 5921. (d) Burdon, J.; Coe, P. L.; Marsh, C. R.; Tatlow, J. C. *J. Chem. Soc., Perkin Trans. 1* **1972**, 639. (e) Coe, P. L.; Milner, N. E. *J. Organomet. Chem.* **1972**, *39*, 395. (f) Coe, P. L.; Milner, N. E. *J. Fluorine Chem.* **1972/73** *2*, 167. (g) Coe, P. L.; Milner, N. E. *J. Organomet. Chem.* **1974**, *70*, 147. (h) Leroy, J.; Rubinstein, M.; Wakselman, C. *J. Fluorine Chem.* **1985**, *27*, 291. (i) Chen, Q. Y.; Yang, Z. Y. *J. Fluorine Chem.* **1985**, *28*, 399. (j) Clark, J. H.; McClinton, M. A.; Blade, R. J. *J. Chem. Soc., Chem. Commun.* **1988**, 638. (k) Chen, G. J.; Tamborski, C. *J. Fluorine Chem.* **1989**, *43*, 207. (l) Chen, G. J.; Tamborski, C. *J. Fluorine Chem.* **1990**, *46*, 137. (m) Chen, Q. Y.; Yang, Z. Y. *J. Chem. Soc., Chem. Commun.* **1986**, 498. (n) Chen, Q. Y.; He, Y. B.; Yang, Z. Y. *J. Fluorine Chem.* **1986**, *34*, 255. (o) O'Reilly, N. J.; Maruta, M.; Ishikawa, N. *Chem. Lett.* **1984**, 517. (p) Huang, Y. Z.; Zhou, Q. *Tetrahedron Lett.* **1986**, *27*, 2397. (q) Fuchikami, T.; Shibata, Y.; Urata, H. *Chem. Lett.* **1987**, 521. (r) Matsubara, S.; Mitani, M.; Utimoto, K. *Tetrahedron Lett.* **1987**, *28*, 5857. (s) Chen, Q. Y.; Yang, Z. Y.; Zhao, C. X.; Qiu, Z. M. *J. Chem. Soc., Perkin Trans. 1* **1988**, 563. (t) Chen, Q. Y.; Qiu, Z. M. *J. Fluorine Chem.* **1988**, *39*, 289. (u) Kuroboshi, M.; Ishihara, T. *J. Fluorine Chem.* **1988**, *39*, 299. (v) Kitazume, T.; Ikeya, T. *J. Org. Chem.* **1988**, *53*, 2349.

(14) (a) Haszeldine, R. N. *J. Chem. Soc.* **1952**, 1423; **1953**, 148; **1954**, 1273. (b) Benson, D.; Smith, C. F.; Tamborski, C. *J. Fluorine. Chem.* **1973/1974**, *3*, 247. (c) Smith, C. F.; Soloski, E. J.; Tamborski, C. *J. Fluorine. Chem.* **1974**, *4*, 35. (d) Moreau, P.; Albadri, R.; Commeyras, A. *Nouv. J. Chim.* **1977**, *1*, 497. (e) Moreau, P.; Albadri, R.; Commeyras, A. *Nouv. J. Chim.* **1982**, *6*, 581. (f) Moreau, P.; Albadri, R.; Redwane, N.; Commeyras, A. *J. Fluorine. Chem.* **1980**, *6*, 581. (g) Moreau, P.; Redwane, N.; Commeyras, A. *Bull. Soc. Chim. Fr.* **1984**, 117. (h) Moreau, P.; Naji, N.; Commeyras, A. *J. Fluorine. Chem.* **1987**, *34*, 421.

(15) (a) Kitazume, T.; Ishikawa, N. *J. Am. Chem. Soc.* **1985**, *107*, 5186. (b) Grondin, J. A.; Vottero, Ph. J. A.; Blancou, H.; Commeyras, A. *Actual. Chim.* **1987**, 57.

(16) (a) Sibille, S.; Mcharek, S.; Périchon, J. *Tetrahedron* **1989**, *45*, 1423. (b) Gélis, L. Thèse de Doctorat de l'Université de Paris VII, 1989.

(17) (a) Reactions of perfluoroalkyl phenyl iodoniums with carbanions,[17b,c] aromatic compounds,[17d,e] alkenes and alkadienes,[17f,g] thiols.[17h] (b) Umemoto, T.; Kuriu, Y. *Tetrahedron Lett.* **1981**, *22*, 5197. (c) Umemoto, T.; Gotoh, Y. *Bull. Chem. Soc. Jpn.* **1986**, *59*, 439. (d) Umemoto, T.; Kuriu, Y.; Shuyama, H. *Chem. Lett.* **1981**, 1663. (e) Umemoto, T.; Miyano, O. *Bull. Chem. Soc. Jpn.* **1984**, *57*, 3361. (f) Umemoto, T.; Furukawa, S.; Miyano, O.; Nakayama, S. I. *Nippon Kagaku Kaishi* **1985**, *11*, 2146. (g) Umemoto, T.; Kuriu, Y.; Nakayama, S. I. *Tetrahedron Lett.* **1982**, *23*, 1169. (h) Umemoto, T.; Kuriu, Y.; Nakayama, S. I.; Miyano, O. *Tetrahedron Lett.* **1982**, *23*, 1471. (i) Umemoto, T.; Kuriu, Y. *Chem. Lett.* **1982**, 65.

Because of the strongly electron-withdrawing properties of the perfluoroalkyl group,[18] S_N2 and S_N1 reactions are disfavored as compared with alkyl analogues. As regards nucleophilic substitution by the $S_{RN}1$ mechanism,[2] direct or indirect (by means of electrogenerated outer-sphere electron donors) electrochemistry has been shown to be an efficient means to trigger the reaction in the case of aromatic halides substrates and to allow rigorous demonstration of the nature of the mechanism and of the side reactions.[1] The principle of the reaction in the case of aromatic substrates is recalled in Scheme I.

The work reported in the following describes several examples of electrochemical induction of the nucleophilic substitution of perfluoroalkyl halides.[19]

Several substitution reactions involving perfluoroalkyl halides that are not triggered electrochemically have been previously described: photochemical perfluoroalkylation of aromatic thiols,[20a,b] sulfinic acids,[20c] selenols[20d] by CF_3I or $C_6F_{13}I$ in liquid ammonia; substitution of $C_6F_{13}I$ or $C_8F_{17}I$ (and the diiodo compounds $I(CF_2)_4I$) by the anion of 2-nitropropane leading to 2-perfluoroalkyl nitropropanes $R_FC(CH_3)_2NO_2$;[20e] and substitution by bisulfite,[20f] thiolates[20d,g-j] (which can be reacted not only with perfluoroalkyl iodides but also with the bromides[20h,i]), methylene bases of nitrogen heterocycles,[20j] diethyl malonate,[20k,l] ethyl acetoacetate,[20l] imidazole anions,[20m] and the anion of 5-nitrotetrahydro-1,3-oxazine.[20n] With malonates anions of the type $^-CH(COOR)_2$, the simple substitution product[20k] is not obtained. Owing to the acidic character of the proton in the α position of the terminal CF_2, a fluoride ion is eliminated to give $R_FCF{=}C(COOR)_2$ which can be attacked in its turn by the nucleophile to give $R_FCCH(COOR)_2{=}C(COOR)_2$. A similar reaction is observed in the case of acetyl acetate.[20l] When evidence for the $S_{RN}1$ character of the reaction was looked for, it was obtained from inhibition by nitrobenzene,[20h,i] *p*-dinitrobenzene,[20k-m] styrene, norbornene,[20o] or diallyl ether[20k-m] or by acceleration by light.[20k-m] Clearcut proofs were not always obtained by these procedures.

Since the work reported below consisted of attempts to trigger electrochemically the nucleophilic substitution of perfluoroalkyl halides, it is interesting to recall the main features of the direct and indirect electrochemistry of these compounds gathered in previous studies. On what seems to be the most inert electrode material available, namely, glassy carbon, the electrochemistry of several perfluoroalkyl halides (CF_3Br, CF_3I, $C_6F_{13}I$, $C_8F_{17}I$) has been investigated in some details[9] in aprotic solvents (acetonitrile, dimethylformamide (DMF) and dimethyl sulfoxide (DMSO)) containing tetraalkylammonium salts as supporting electrolyte[9] both in direct (at the electrode) and indirect (using anion radicals as mediators) fashion. The following conclusions emerged. With the iodides, the first cyclic voltammetric wave

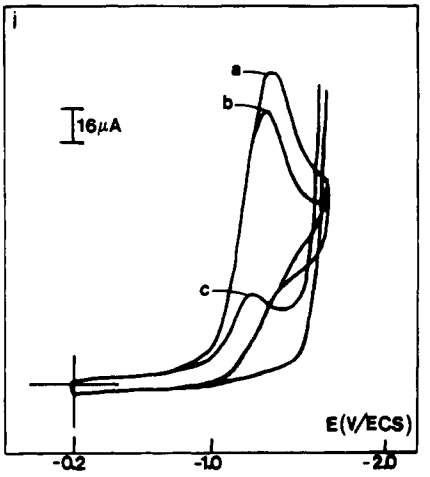
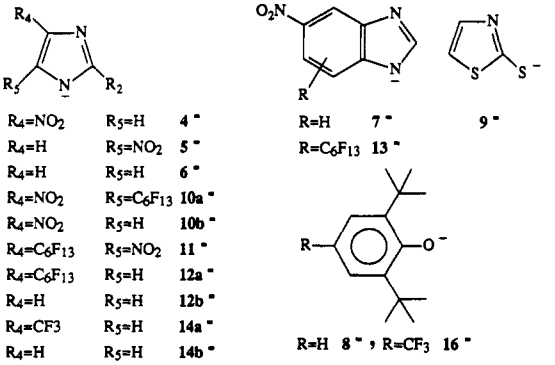


Figure 1. Cyclic voltammetry of $C_6F_{13}I$ (3) (4.52 mM) in CH_3CN + 0.1 M NBu_4BF_4 in the absence (a) and in the presence (b, c) of 4-nitroimidazole anion (4^-): (b) a + 4^- (21.6 mM); (c) a + (4^-) (47.9 mM); scan rate 0.2 V s^{-1}.

Chart I



(peak potentials: E_p = −1.52 V/SCE for CF_3I and E_p = −1.32 V/SCE for $C_6F_{13}I$ in DMF at 0.2 V s^{-1}) corresponds to the transfer of one electron. $R_F^\bullet$ radicals are then produced. Their reduction is observed at a more negative potential (E_p = −1.80 V/SCE for $CF_3^\bullet$ and $C_6F_{13}^\bullet$ in DMF at 0.2 V s^{-1}). In the case of CF_3Br, the reductions of the substrate and of the radical $CF_3^\bullet$ take place at nearly the same potential. (E_p = −2.10 V/SCE for CF_3Br in DMF at 0.2 V s^{-1}.) Both $CF_3^\bullet$ radicals and CF_3^- anions are thus produced at this potential. The formation of CF_3^- will be favored by direct reduction at potentials located behind the voltammetric peak, whereas the formation of $CF_3^\bullet$ is expected to be dominant at the foot of the wave or by indirect electrochemistry using mediators with standard potentials positive to the direct reduction of CF_3Br. Careful analysis of the electrochemical kinetics showed that in both cases the transfer of the first electron is concerted with the cleavage of the carbon–halogen bond. In other words, the direct and indirect electrochemical reductions do not go through the anion radical, the concerted pathway

$$R_FX + e^- \rightarrow R_F^\bullet + X^-$$

being energetically more advantageous. In organic solvents such as those mentioned above, the main fate of the perfluoroalkyl radicals thus generated is to abstract a hydrogen atom from the solvent. With $C_6F_{13}I$, but not with CF_3I and CF_3Br, a strong passivation of the electrode is observed upon reduction, which renders the triggering of any chemistry based on the production of the corresponding radicals quite difficult. This can, however, be achieved by use of redox catalysis. When $C_6F_{13}I$ is reduced at a mercury electrode, rather complex reactions are observed involving perfluoroalkyl mercury derivatives and ultimately leading to $C_6F_{13}H$.[21]

(18) (a) Sheppard, W. A.; Sharts, C. M. *Organic Fluorine Chemistry*; Benjamin: New York, 1969. (b) Chambers, R. D. *Fluorine in Organic Chemistry*; Wiley: New York, 1973. (c) Huheey, J. E. *J. Phys. Chem.* **1965**, *69*, 3284. (d) Pletnev, S. I.; Igumov, S. M.; Rozkhov, I. N.; Rempel, G. D.; Ponomarev, V. I.; Deev, L. E.; Shaidurov, V. S. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1989**, *9*, 2057. (e) Rempel, G. D.; Borisov, Yu. A.; Raevski, N. L.; Igumov, S. M.; Rozkhov, I. N. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1990**, *5*, 1059.

(19) (a) Preliminary results have been described in a brief communication.[19b] (b) Médebielle, M.; Pinson, J.; Savéant, J.-M. *Tetrahedron Lett.* **1990**, *31*, 1279.

(20) (a) Boiko, V. N.; Schupak, G. M.; Yagupolsk'ii, L. M. *J. Org. Chem. USSR (Engl. Transl.)* **1977**, *13*, 972. (b) Boiko, V. I.; Kondratenko, N. V.; Sembur, V. P.; Yagupolsk'ii, L. M. *J. Org. Chem. USSR (Engl. Transl.)* **1977**, *13*, 1985. (c) Kondratenko, N. V.; Popov, V. I.; Boiko, V. N.; Yagupolsk'ii, L. M. *J. Org. Chem. USSR. (Engl. Transl.)* **1977**, *13*, 2086. (d) Voloschechuk, V. G.; Boiko, V. N.; Yagupolsk'ii, L. M. *J. Org. Chem. USSR (Engl. Transl.)* **1977**, *13*, 1866. (e) Feiring, A. E. *J. Org. Chem.* **1983**, *48*, 347. (f) Huang, W. Y.; Chen, J. L. *Acta Chim. Sinica* **1985**, 376. (g) Popov, V. I.; Boiko, V. N.; Yagupolsk'ii, L. M. *J. Fluorine Chem.* **1982**, *21*, 363. (h) Wakselman, C.; Tordeux, M. *J. Chem. Soc., Chem. Commun.* **1984**, 793. (i) Wakselman, C.; Tordeux, M. *J. Org. Chem.* **1985**, *50*, 4047. (j) Yagupolsk'ii, L. M.; Pazenok, S. V.; Kondratenko, N. V. *J. Org. Chem. USSR (Engl. Transl.)* **1984**, *33*, 1937. (k) Chen, Q. Y.; Qiu, Z. M. *J. Fluorine Chem.* **1986**, *31*, 301. (l) Cheng, Q. Y.; Qiu, Z. M. *J. Fluorine Chem.* **1987**, *35*, 343. (m) Chen, Q. Y.; Qiu, Z. M. *J. Chem. Soc., Chem. Commun.* **1987**, 1240. (n) Archibald, T. G.; Taran, C.; Baum, K. *J. Fluorine Chem.* **1989**, *43*, 243. (o) Feiring, A. E. *J. Fluorine Chem.* **1984**, *24*, 191.

(21) (a) Calas, P.; Moreau, P.; Commeyras, A. *J. Electroanal. Chem.* **1977**, *78*, 271. (b) Calas, P.; Commeyras, A. *J. Electroanal. Chem.* **1978**, *89*, 363. (c) Calas, P.; Commeyras, A. *J. Electroanal. Chem.* **1978**, *89*, 373.

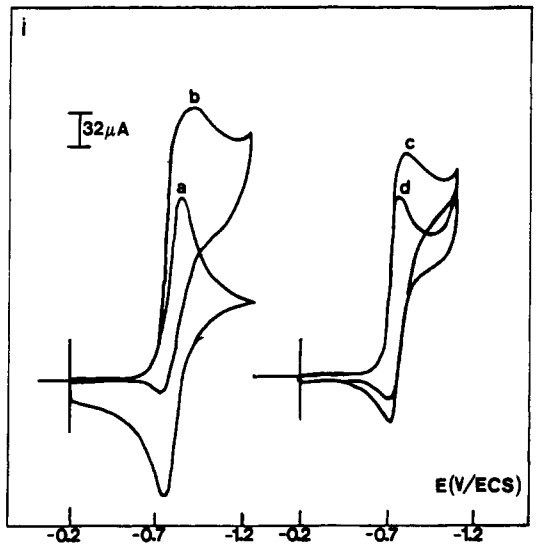


Figure 2. Redox catalysis of $C_6F_{13}I$ (**3**) by the anion radical of 4-nitropyridine *N*-oxide in CH_3CN + 0.1 M NBu_4BF_4 in the absence (a, b) and in the presence of 4-nitroimidazole anion (4^-) (c, d): (a) catalyst alone, C^0 = 3.0 mM; (b) a + $C_6F_{13}I$ (60 mM); (c) b + 4^- (80 mM); (d) b + 4^- (230 mM); scan rate 0.2 V s^{-1}.

Results

Substrates **1–3** [CF_3Br (**1**), C_4F_9I (**2**), $C_6F_{13}I$ (**3**)] and nucleophiles **4–9** were used. Compounds are shown in Chart I. The corresponding protonated species are numbered **4H**, **5H**, ...

In acetonitrile, on glassy carbon, perfluorohexyl iodide (**3**) shows a first one-electron cyclic voltammetric wave (E_p = −1.30 V/SCE at 0.2 V s^{-1}). In the presence of a 10-fold excess of the anion of 4-nitroimidazole (4^-),[22] this wave decreases to about 30% of its initial height (Figure 1). However, no wave could be observed which would correspond to the substituted product itself. On a second scan, a small wave appears at a potential positive to that of the substrate (E_p = −1.23 V/SCE at 0.2 V s^{-1}) which was assigned to the anion of the substituted product (10^-) on the basis of the following observations. If the substitution had taken place on the nitrogen, a reversible system would have been observed since N-alkylated nitroimidazoles show one-electron reversible systems at about −1.1 V/SCE.[23] **10H** (the protonated form of 10^-) exhibits an irreversible peak located at E_p = −0.80 V/SCE (at 0.2 V s^{-1}). This wave disappears in the presence of an excess of 4^- and a new irreversible peak appears at E_p = −1.23 V/SCE, while the wave of 4^- located at E_p = −2.00 V disappears, showing that the following reaction takes place:

$$\mathbf{10\text{-}H} + 4^- \rightleftarrows \mathbf{4\text{-}H} + 10^-$$

The reduction of **3** in the presence of 4^- was also examined by redox catalysis[1c,d,24] using 4-nitropyridine *N*-oxide as the mediator. This approach is made necessary at the preparative scale by the fact that the electrode is rapidly passivated upon direct electrolysis of $C_6F_{13}I$.[9] In the absence of **3**, the mediator shows a reversible one-electron wave with a standard potential E^0 = −0.79 V/SCE in CH_3CN. This wave increases upon addition of **3** and loses its reversibility (Figure 2). Upon addition of increasing amounts of the nucleophile, the wave decreases back and tends to recover its reversibility. We checked that the decrease of the wave is not due to a reaction between the catalyst (or its reduced form) and 4^-. As in direct electrochemistry, the peak of **10H** was not observed and the peak of 10^- could not be distinguished from the second peak of the catalyst. We carried out a preparative-scale electrolysis at the reduction potential of the catalyst in CH_3CN. Two cells were used: a two-compartment cell with a Nafion membrane as separator and a one-compartment cell with a soluble magnesium anode. Two isomers, 4-nitro-5-perfluorohexylimidazole (**10aH**) and 4-nitro-2-perfluorohexylimidazole (**10bH**),[25] were obtained with an overall yield of 94% (Table I) in both cases. It should be noted that the yield in $C_6F_{13}H$ was very low (<5%).

Similar voltammetric patterns were observed by direct electrochemistry of **2** and **3** in the presence of the anion of 2-methyl-5-nitroimidazole (5^-), also of **3** in the presence of the anion of 5-nitrobenzimidazole (7^-) as well as by redox catalyzed voltammetry of **3** in the presence of 5^-, 6^-, or 7^- and of **1** in the presence of 6^-. The results of the corresponding preparative-scale electrolyses are summarized in Table I. An attempt was made to use the anion of phenothiazine as the nucleophile. We observed that **3** and this anion react without electrochemical stimulation, leading to a 90% consumption of **3** to give $C_6F_{13}H$ and a small amount of perfluoroalkyl phenothiazine.

Table I. Preparative-Scale Electrolyses

substrate (mM)	nucleophile (mM)	catalyst (mM)	products % yields[a]	F/mol[b]
3 (25)[c,d]	4^- (190)	4-nitropyridine *N*-oxide (6.2)	**10aH** 94 (65)[e] **10bH** $C_6F_{13}H$ < (5)[f]	0.72
3 (25)[c,g]	4^- (190)	4-nitropyridine *N*-oxide (6.2)	**10aH** 70 (55)[h] **10bH**	1.10
3 (25)[c,d]	5^- (200)	4-nitropyridine *N*-oxide (6.2)	**11H** 63 (51) $C_6F_{13}H$ (25)	0.70
3 (25)[c,d]	6^- (140)	4-nitropyridine *N*-oxide (6.2)	**12aH** 70 (50)[i] **12bH**	0.2
1 (52.6)[k,d]	6^- (180)	terephthalonitrile (4.3)	**14aH**[l] **14bH**	
3 (25)[c,d]	7^-	4-nitropyridine *N*-oxide (6.2)	**13H** 54 (30)[j]	1.2
3 (32.4)[c,d]	8^- (110)	nitrobenzene (6.25)	**15H** 91 (57)	0.1
1 (46.5)[k,d]	8^- (73)	terephthalonitrile (6.25)	**16H**[m]	
3 (25)[c,d]	9^- (140)	*p*-nitrobenzonitrile (6.25)	**17H** 64 (48)	0.6

[a] Measured by ^{19}F NMR in the electrolyzed solution; in parentheses are isolated yields. [b] Per mole of substrate. [c] Electrolysis potential E = −0.90 V/SCE. [d] In a two-compartment cell. [e] Overall yield for the two isomers **10aH/10bH** = 0.65/0.35. [f] $C_6F_{13}H$ yield obtained by gas chromatography. [g] In a one-compartment cell with a soluble magnesium anode. [h] Overall yield for the two isomers **10aH/10bH** = 0.47/0.29; a third unidentified perfluoroalkylated product is observed by ^{19}F NMR (24% yield). [i] Overall yield for the two isomers **12aH/12bH** = 0.8/0.2. [j] Three isomers are obtained (see Experimental Section). [k] CF_3Br is continuously bubbled in the solution; electrolysis potential E = −1.60 V/SCE. [l] The overall production of the two isomers is 4.35 × 10^{-3} mol/h; **14aH/14bH** = 2/1. [m] The production of **16H** is 2.4 × 10^{-3} mol/h.

Table II. Decrease of the Catalytic Peak Obtained with 4-Nitropyridine *N*-oxide as the catalyst and **3** as the Substrate upon Addition of Increasing Amounts of Nucleophiles[a]

nucleophile		4^-		5^-		7^-		9^-	
[Nu^-] (M)	0	0.04	0.08	0.16	0.04	0.08	0.23	0.04	0.08	0.04	0.08
i_p/i_p^0	1.77	1.74	1.45	1.21	1.70	1.53	1.19	1.71	1.26	1.43	1.13

[a] Temp, 20 °C; scan rate, 0.2 V/s.

(22) (a) That imidazoles could act as nucleophiles in $S_{RN}1$ reactions was first shown by Bowman et al.[22b-e] using *p*-nitrobenzyl chloride as a substrate. (b) Adebayo, A. T. O. M.; Bowman, W. R.; Salt, W. G. *Tetrahedron Lett.* **1986**, *27*, 1943. (c) Adebayo, A. T. O. M.; Bowman, W. R.; Salt, W. G. *J. Chem. Soc., Perkin Trans. 1* **1987**, 2819. (d) Adebayo, A. T. O. M.; Bowman, W. R.; Salt, W. G. *J. Chem. Soc., Perkin Trans. 1* **1989**, 1415. (e) Bowman, W. R.; Symons, M. C. R. *J. Chem. Soc., Perkin Trans. 2* **1988**, 1077.

(23) Roffia, S.; Gottardi, C.; Vianello, E. *J. Electroanal. Chem.* **1982**, *142*, 263.

(24) (a) Andrieux, C. P.; Savéant, J.-M. Electrochemical Reactions. In *Investigations of Rates and Mechanisms of Reactions (Techniques of Chemistry)*; Bernasconi, C. F., Ed.; Wiley: New York, 1986; Vol. VI/4E, Part 2, pp 305–390. (b) Andrieux, C. P.; Dumas-Bouchiat, J.-M.; Savéant, J.-M. *J. Electroanal. Chem.* **1980**, *113*, 19. (c) Swartz, J. E.; Stenzel, T. T. *J. Am. Chem. Soc.* **1984**, *106*, 2520. (d) Amatore, C.; Oturan, M. A.; Pinson, J.; Savéant, J.-M.; Thiébault, A. *J. Am. Chem. Soc.* **1984**, *106*, 6318.

(25) Kimoto, H.; Fujii, S.; Muramatsu, Y.; Maki, Y.; Hirata, N.; Kamoshita, K.; Hamada, T.; Yoshida, A. Jap. Patent 61 286 370; *Chem. Abstr.* **1987**, *106*, 156476c.

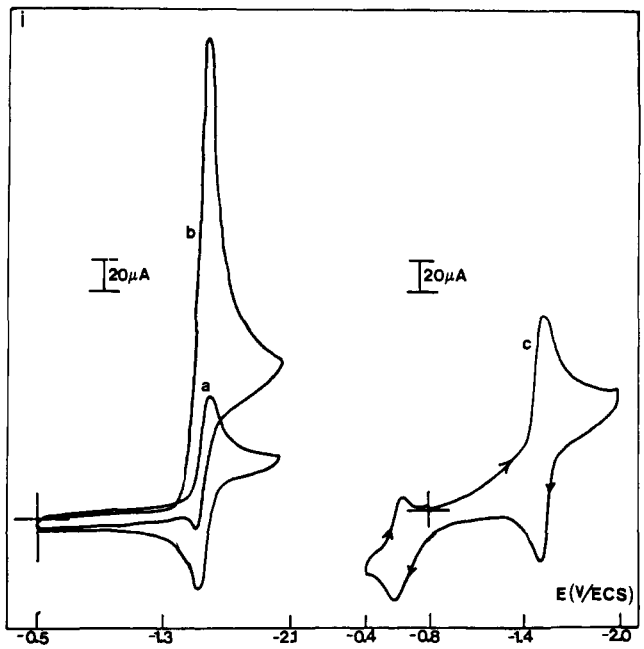
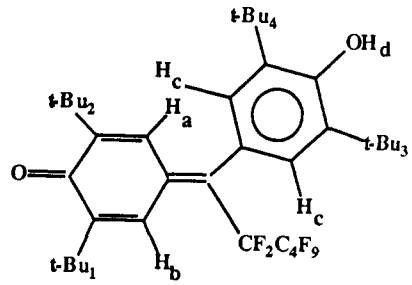


Figure 3. Redox catalysis of CF_3Br (**1**) by the anion radical of terephthalonitrile in DMF + 0.1 M NBu_4BF_4 in the absence (a, b) and in the presence (c) of (8^-): (a) catalyst alone, C^0 = 3.0 mM; (b) a + **1** (60 mM); (c) b + 8^- (40.0 mM), scan rate 0.2 V s^{-1}.

The decrease of the catalytic peak obtained with 4-nitropyridine *N*-oxide as the catalyst and **3** as the substrate upon addition of increasing amounts of nucleophiles was measured under the same experimental conditions in the aim of investigating the kinetics of the substitution reaction. The results are summarized in Table II.

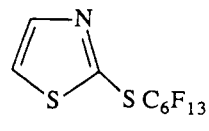
The 2,6-di-*tert*-butylphenoxide ions (8^-) was chosen as an example of an oxygen nucleophile. In the presence of CF_3Br (**1**), terephthalonitrile (E^0 = −1.57 V/SCE) shows a large catalytic wave which decreases upon adding 8^- (Figure 3). On the reverse scan, a reversible oxidation peak is observed (E^0 = −0.59 V/SCE). **16H**, the substitution product at the carbon in para of the phenolic group, is obtained by preparative-scale electrolysis (Table I). The cyclic voltammetry of this compound shows the same reversible oxidation wave as that observed in the redox catalysis cyclic voltammetric experiment.

With the same nucleophile, a similar behavior is observed with **3** as the substrate and with nitrobenzene as the catalyst. However, unlike the preceding case, the simple substitution product is not obtained upon preparative-scale electrolysis. **15H**, a dimeric product in which two fluorine atoms have been lost, is obtained instead with an excellent yield (Table I).



15H

The anion of 2-mercaptothiazoline (9^-) was chosen as an example of a sulfur nucleophile. With **3** as the substrate and *p*-nitrobenzonitrile (E^0 = −0.85 V/SCE) as the catalyst, addition of the nucleophile makes the catalytic wave decrease and a new cathodic wave appear at E_p = −1.40 V/SCE which can be assigned to the substitution product. Electrolysis at −1.00 V/SCE yields the substitution product **17**. It exhibits the same wave at E_p = −1.40 V/SCE as observed in the redox catalysis experiment. It should be noted that this wave is irreversible, indicating that the anion radical of **17** is not very stable similarly to what has been previously observed in the case of PhSPh.[27]



17

Attempts to trigger the substitution reaction by direct electrochemical reduction in the case of CF_3Br (**1**) were unsuccessful as revealed by the lack of variation of the cyclic voltammetric wave upon addition of nucleophiles (in some cases a small decrease of the peak is observed with concentrations of nucleophiles above 1 M).

Scheme II

$$P + e^- \rightleftharpoons Q \qquad [0]$$

$$R_FX + Q \xrightarrow{k_E} R_F^{\bullet} + X^- + P \qquad [1'+2]$$

$$R_F^{\bullet} + Nu^- \xrightarrow{k_{Nu}} R_FNu^{\bullet -} \qquad [3]$$

$$[4'] \quad R_FNu^{\bullet -} + P \longrightarrow R_FNu + Q \quad \text{or} \quad R_FNu^{\bullet -} + R_FX \longrightarrow R_FNu + R_F^{\bullet} + X^- \quad [4'']$$

$$R_FX + Nu^- \longrightarrow R_FNu + X^-$$

Discussion

The cyclic voltammetric redox catalysis experiments described above clearly show that the substitutions demonstrated by the preparative-scale electrolyses are electron-transfer-induced reactions. Since the direct or mediated electrochemical reduction of perfluoroalkyl halides involves a concerted electron-transfer–bond-breaking process, the classical $S_{RN}1$ mechanism[1] recalled in Scheme I is not exactly followed in the sense that the reaction does go through the intermediacy of the anion radical of the substrate. The reaction is triggered by a dissociative electron transfer that directly produces the perfluoroalkyl radical that reacts with the nucleophile leading to the anion radical of the substituted product (Scheme II). The latter species transfers its unpaired electron to the best electron acceptor present in the reaction medium. This may be the oxidized form of the mediator in the case of redox-mediated electrochemical induction as investigated here or the substrate itself in which case a chain process is set up. In redox catalysis, the mediator couple is selected so as to be rapid in terms of electron-transfer kinetics and to have a standard potential positive to the reduction potential of the substrate. It has thus a better opportunity to accept the unpaired electron of the anion radical of the substituted product than has the starting halide.

This change in the mechanism as compared to that of aryl halides[1] and the difference in the electron-accepting properties of perfluoroalkyl and aryl radicals have important consequences in terms of the feasibility of the reaction and of the nature of the competing side reactions. Aryl radicals are very easy to reduce, much more than the parent aryl halides. The feasibility of direct electrochemical induction of the substitution reaction is then a consequence of the fact that electron transfer to the aryl halide substrate is not concerted with the breaking of the carbon–halogen bond.[1c] The aryl radical is thus formed away from the electrode surface, the farther the slower the decomposition of the aryl halide anion radical. Had it been formed at the electrode surface, it would have been immediately reduced, leaving no opportunity to the nucleophilic attack to take place. It remains that the electron-transfer reduction of the aryl radical at the electrode is a powerful competing pathway, the more so the more rapidly decomposed the $ArX^{\bullet -}$ radical and thus the shorter the distance the aryl radical has to travel to reach back the electrode surface. For slower decomposing $ArX^{\bullet -}$ radicals, another electron-transfer reaction competes with the nucleophilic attack, namely, electron transfer from the anion radical of the substituted product. This is, however, reached at maximum the diffusion limit and can thus be overrun by strong nucleophiles introduced in sufficient excess. The usefulness of the redox catalytic approach in the case of fast cleaving $ArX^{\bullet -}$ radical derives from the same reason since the aryl

(26) (a) This behavior is the same as that observed previously with 2,4,6-tri-*tert*-butylphenol[26b] (E^0 = −0.30 V/SCE) with, as expected from the electron-withdrawing effect of the C_6F_{13} group a more negative standard potential. (b) Evans, D. H. *Acc. Chem. Res.* **1977**, *10*, 313.

(27) Amatore, C.; Combellas, C.; Pinson, J.; Oturan, M. A.; Robveille, S.; Savéant, J.-M.; Thiébault, A. *J. Am. Chem. Soc.* **1985**, *107*, 4846.

radical is then formed far from the electrode surface and is only subject to electron-transfer reduction by $ArNu^{\bullet-}$ radicals and/or by the reduced form of the mediator. Besides the electron-transfer deactivations of the aryl radical, H-atom transfer may also play an important role as a competing side reaction in organic solvents.[1c]

With perfluoroalkyl derivatives, the direct electrochemical induction of the substitution reaction produces the perfluoroalkyl radical at the electrode surface. The feasibility of the substitution thus hinges upon the rate of reduction of the perfluoroalkyl radical at the electrode surface compared with that of the nucleophilic attack at the potential where the induction is attempted, i.e., at the reduction potential of the perfluoroalkyl halide. This falls in line with the observation that the direct electrochemical induction is possible with the iodides and almost unsuccessful with the bromides, since the reduction potential of the perfluoroalkyl radicals is close to that of the bromides and much more negative than that of the iodides. Redox catalysis of the electrochemical reduction makes the induction possible in the case of the bromides because the perfluoroalkyl radicals are then formed far from the electrode surface. In addition, since the standard potential of the mediator couple is positive to the reduction potential of the substrate, the reduction of the perfluoroalkyl radical by the reduced form of the mediator is not a fast reaction and thus ceases to be an important competing pathway. Under these conditions the main competing side reaction, leading to the hydrogenolysis product, R_FH, is H-atom abstraction from the solvent. Although possible in principle, the direct electrochemical induction is not of much practical value in the case of $C_6F_{13}I$ because of electrode passivation. This difficulty is successfully circumvented by the use of redox catalysis. In these conditions, the electron-transfer reduction of the perfluoroalkyl radical by the reduced form of the mediator is even much slower than in the case of bromides since mediator couples having a much more positive standard potential are used because the reduction potentials of the iodides are much positive than those of the bromides. Thus, the only competing reaction is H-atom abstraction from the solvent.

In this connection, the kinetic data displayed in Table II can be used to estimate the rate constants of the reaction of the $C_6F_{13}^{\bullet}$ radical with the listed nucleophiles, or at least their ratio with the rate constant of H-atom abstraction from acetonitrile. As shown elsewhere,[28] the following procedure can be used on the basis of the mechanism shown in Scheme II (in which reaction 4′ is assumed to overrun reaction 4″) and of the competing reaction:

$$R_F^{\bullet} + CH_3CN \xrightarrow{k_H} R_FH + \text{products}$$

In the absence of nucleophile, the catalytic increase of the mediator cyclic voltammetric wave, i_p/i_p^0 (i_p^0 = height of the mediator cathodic peak in the absence of substrate, i_p = height of the catalytic peak), is a function of two parameters: a rate parameter $\lambda_E = (RT/F)(k_E[\text{mediator}]/v)$ and an excess parameter $\gamma = [R_FX]/[\text{mediator}]$. Upon addition of the nucleophile, i_p/i_p^0 decreases and is equal to the value it would have in the absence of the nucleophile for a value of the excess factor $\gamma' = \gamma k_H/(k_H + k_{Nu}[Nu^-])$.[28] λ_E is thus determined first from the catalytic experiments in the absence of nucleophile already using computed working curves[24b] (in the present case, $\lambda_E = 0.45$, $k_E = 10^3$ M^{-1} s^{-1}). The same set of working curves is then used for constructing the theoretical variation of i_p/i_p^0 with the excess factor, and this curve is used for obtaining the value of γ/γ' for each nucleophile and each value of its concentration. The experimental variations of γ/γ', which is predicted to be equal to $1/\{1 + k_{Nu}[Nu^-]/k_H\}$, are shown in Figure 4. The following values of k_{Nu}/k_H (in M^{-1}) were derived from the slopes of the straight lines thus obtained.

Nu^-	4^-	5^-	7^-	9^-
k_{Nu}/k_H	18	14	22	70

The imidazolates have thus similar reactivities toward the perfluorohexyl radical while the thiolate seems a little more reactive.

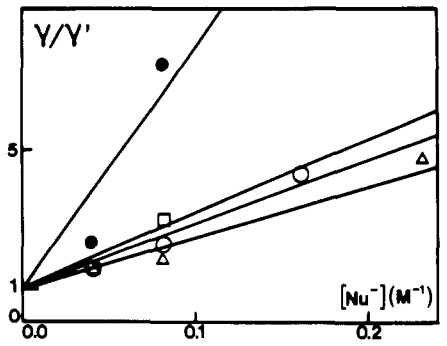


Figure 4. Analysis of the cyclic voltammetric kinetics of the redox catalysis electrochemical induction of the substitution of $C_6F_{13}I$ (6 mM) by 4^- (○), 5^- (△), 7^- (□), 9^- (●): mediator, 5-nitropyridine *N*-oxide (3 mM); scan rate, 0.2 V s^{-1}; solvent, acetonitrile; temp 22 °C.

The value of k_H in acetonitrile is not known but should not be too different from that estimated for DMF (4×10^5 s^{-1}).[9] The rate constants of the nucleophilic attack thus fall in the 10^7–10^8 M^{-1} s^{-1} range.

The triggering of the reaction by mediator redox couples, as described above, allows a better understanding of the inhibition effects previously observed in nucleophilic substitutions of perfluoroalkyl halides triggered by other means. Inhibitors of $S_{RN}1$ reactions are generally of two types, namely, electron traps and radical traps.[1c] It has been observed that nitrobenzene inhibits the substitution of $C_6F_{13}Br$ by thiophenate ions but not that of $C_6F_{13}I$.[20h] This can be explained as follows. As seen above, the nitrobenzene anion radical works as an electron-transfer inductor for the reactions of $C_6F_{13}I$ while this would not be possible from bromides in view of the large difference between the standard potential of $PhNO_2/PhNO_2^{\bullet-}$ coupld ($E^0 = -1.10$ V/SCE) and the reduction potential of perfluoroalkyl bromides (around −2 V/SCE instead of −1.30 V/SCE for the iodides). Perfluoroalkylphenyl sulfides have a quite negative reduction potential (around −1.9 V/SCE). The electron trapping reaction:

$$C_6F_{13}SPh^{\bullet-} + PhNO_2 \rightleftarrows C_6F_{13}SPh + PhNO_2^{\bullet-}$$

thus possesses a considerable driving force toward the right-hand side whatever the starting halide. It would thus seem that this should inhibit the reaction by interupting the chain propagation:

$$C_6F_{13}SPh^{\bullet-} + C_6F_{13}X \rightarrow C_6F_{13}SPh + C_6F_{13}^{\bullet} + X^-$$

in all cases. However, in the case of the iodides, the $PhNO_2^{\bullet-}$ anion radicals thus generated are able to immediately restart the propagation by electron transfer to the substrate, whereas this is not possible with the bromides. In the case of $C_6F_{13}I$, the reaction is inhibited by styrene, but this plays the role of a radical trap rather than that of an electron trap.

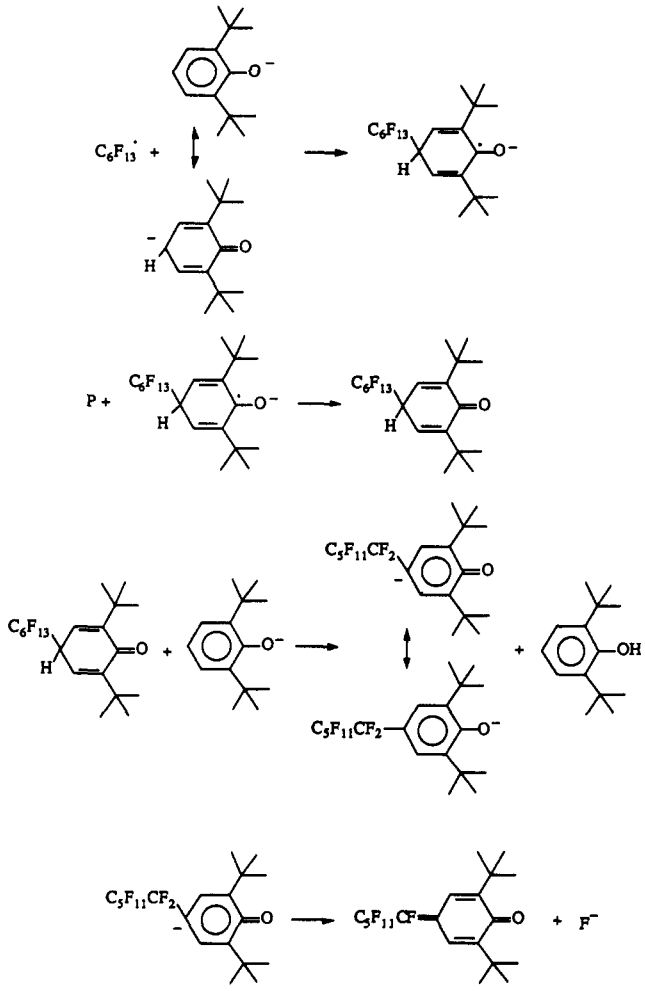
With the sulfur nucleophile 9^-, the reaction takes place at the negatively charged heteroatom as with other thiolates.[20] This is not the case either with the phenoxide or the imidazolates ions. In the former case, we observe the same kind of reaction as previously observed with aromatic substrates.[29] With CF_3Br and 8^-, a simple perfluoroalkylation of the carbon in the para position of the phenoxy groups occurs. This is also the primary reaction with $C_6F_{13}I$, although the resulting compound is further converted into **15H**. This transformation can be rationalized as depicted in Scheme III. The deprotonated adduct is not stable, unlike the case of CF_3 substitution. It loses a fluoride ion,[30] thus giving rise to a quinone methide compound. This is then attacked by the starting phenoxide ion, thus yielding **15H** with the loss of a second fluoride ion.

(28) Médebielle, M.; Pinson, J.; Savéant, J.-M. *J. Electroanal. Chem.*, in press.

(29) Alam, N.; Amatore, C.; Combellas, C.; Pinson, J.; Savéant, J.-M.; Thiébault, A.; Verpeaux, J. N. *J. Org. Chem.* **1988**, *53*, 1496.

(30) (a) The loss of a fluoride ion from carbanions containing perfluoroalkyl groups is precedented.[20k,l,30b,c] (b) Bunnett, J. F.; Galli, C. *J. Chem. Soc., Perkin Trans 1* **1985**, 2515. (c) Bunnett, J. F.; Mitchel, E.; Galli, C. *Tetrahedron* **1985**, *41*, 4119.

Scheme III



The fact that imidazolate ions react at the ring carbons rather than at the negatively charged nitrogen is in sharp contrast with what has been observed previously with a variety of nitroalkyl halides (*p*-nitrobenzyl chloride, 2-bromo- or 2-chloronitropropane) where the N-alkylated products were obtained in all cases.[22c,d]

Experimental Section

For cyclic voltammetry we used a home-built potentiostat[31] equipped with a positive feedback ohmic drop compensation and a Tacussel GSTP4 signal generator. The working electrode was a glassy-carbon (Tokai Corp.) disk (3-mm diameter) and the reference electrode a saturated calomel electrode (SCE).

Electrolyses and coulometric measurements were carried out in a 125-mL glassy-carbon (Carbone-Lorraine V25) crucible, used as the electrode, equipped with a glass cover with ground joints for the electrodes, nitrogen, and CF_3Br inlets. The system is made gas-tight by means of O-rings. As anode we used in most cases a platinum wire separated by a no. 4 glass frit or by a Nafion 125 (Dupont) membrane from the cathodic compartment. In one case the anode was a magnesium wire with no separation from the cathodic compartment. The acetonitrile used as solvent was a reagent grade product. Tetrabutylammonium tetrafluoroborate in 0.1 M concentration was used as supporting electrolyte except in the preparative-scale electrolyses where either NBu_4ClO_4 (for the ^{19}F NMR examination of the solutions) or NEt_4BF_4 (soluble in water for extraction of the products) were used. Perfluoroalkyl iodides (Aldrich) were used as received. CF_3Br, $C_6F_{13}H$, and $C_{12}F_{26}$ were kindly given by the Atochem Co. The nucleophiles were prepared as tetramethylammonium salts; the corresponding acids (all of commercial origin, Aldrich) were mixed with stoichiometric amounts of $NMe_4OH\cdot 5H_2O$ (Aldrich) in methanol. The solution was dried over $MgSO_4$, filtered, evaporated to give an oil which was dried under vacuum, and recrystallized in CH_3CN/ether mixtures. The resulting hygroscopic solids were kept under vacuum over P_2O_5.

(31) Garreau, D.; Savéant, J.-M. *J. Electroanal. Chem.* **1972**, *35*, 309.

The solutions were analyzed by gas chromatography on a Girdel 30 apparatus using a 4-m column filled with 30% SE30 on Chromosorb W100/120. The temperature was programmed at 5 °C/min from 60 to 130 °C and maintained at this value. The FT NMR spectra were recorded on a 235-MHz Bruker spectrometer. The chemical shifts are given in ppm by reference to CCl_3F (^{19}F NMR) and TMS (^1H NMR and ^{13}C NMR). The relative amounts of the products at the end of electrolyses were determined by reference to an internal standard ($C_6H_5CF_3$) of known concentration.

Electrolysis of $C_6F_{13}I$ with 4-Nitroimidazolate Anion (4^-). In a two-compartment cell 4-nitropyridine *N*-oxide (0.087 g, 0.62 mmol) was dissolved in 100 mL of CH_3CN containing 0.1 M NBu_4BF_4; $C_6F_{13}I$ was added (1.11 g, 2.5 mmol) and then the nucleophile (3.54 g, 19 mmol). The potential was set at −0.90 V/SCE and the electrolysis was stopped when all $C_6F_{13}I$ has been consumed as checked by gas chromatography. An aliquot of the solution was examined by ^{19}F NMR to determine the yields of perfluoroalkylated products. The solution was neutralized with 1 N HCl. Upon cooling in the refrigerator 4-nitroimidazole precipitated. The aqueous solution was extracted with ether. The ether extracts were dried and evaporated to give 1.54 g of an orange oil which crystallizes upon cooling. The solid was purified by chromatography (SiO_2; CH_2Cl_2/MeOH 9:1) to give 720 mg (65%) of a mixture of two isomers which can be separated by chromatography (SiO_2). These two isomers were identified by comparison (NMR, TLC) with authentic samples offered by Dr. H. Kimoto.[25] 4-Nitro-2-perfluorohexylimidazole (**10Hb**): ^{19}F NMR (DMSO-d_6/$CFCl_3$) δ −80.0 (CF_3, 3 F) −110.3 (α-CF_2, 2 F), −120.9 (β-CF_2, 2 F), −121.4 (γ-CF_2, 2 F), −122.0 (δ-CF_2, 2 F), −125.3 (ϵ-CF_2, 2 F); ^1H NMR (DMSO-d_6/TMS) δ 6.0 (−NH), 8.3 (H_5). 4-Nitro-5-perfluorohexylimidazole (**10Hb**): ^{19}F NMR (DMSO-d_6/$CFCl_3$) δ −80.0 (CF_3, 3 F), −105.8 (α-CF_2, 2 F), −119.9 (β-CF_2, 2 F), −120.9 (γ-CF_2, 2 F), −121.8 (δ-CF_2, 2 F), −125.2 (ϵ-CF_2, 2 F); ^1H NMR (DMSO-d_6/TMS) δ 6.0 (NH), 8.0 (H_2). If the electrolysis was carried out in a one-compartment cell with a soluble magnesium anode, the ^{19}F NMR ($CDCl_3$/$CFCl_3$) spectrum of the solution showed the presence of **10Ha** and **10Hb** and of a third compound characterized by a signal at −114.8 ppm.

Electrolysis of $C_6F_{13}I$ (3) with the Anion of 2-Methyl-5-nitroimidazole (5^-). The electrolysis was performed in CH_3CN as in the preceding experiment (concentration of nucleophile 0.20 M). The ethereal extracts were dried and evaporated to give 1.5 g of a yellow solid which was purified by chromatography (SiO_2; EtOAc/MeOH 95:5) and then recrystallized (ethyl acetate/pentane) to give 570 mg (51%) of a yellow solid, 2-methyl-5-nitro-4-perfluorohexylimidazole (**11H**): mp 156 °C; ^{19}F NMR (DMSO-d_6/$CFCl_3$) δ −79.4 (CF_3, 3 F), −105.7 (α-CF_2, 2 F), −119.6 (β-CF_2, 2 F), −120.7 (γ-CF_2, 2 F), −121.6 (δ-CF_2, 2 F), −124.9 (ϵ-CF_2, 2 F); ^1H NMR (DMSO-d_6/TMS) δ 2.31 (s, 3 H). Mass (CI, NH_3) *m/e* 446 ($M + H^+$), 463 ($M + NH_4^+$). Anal. Calcd for $C_{10}H_4F_{13}N_3O_2$: C, 26.96; H, 0.90; N, 9.43. Found: C, 27.20; H, 1.12; N, 6.94.

Electrolysis of $C_6F_{13}I$ (3) with the Anion of Imidazole (6^-). An intense blue color was observed upon mixing perfluorohexyl iodide and the anion of imidazole (**6**); this color is likely due to the formation of a charge-transfer complex.[20m] The electrolysis was performed in CH_3CN as in the first experiment in a two-compartment cell. After analysis of the products on the raw electrolysis solution by ^{19}F NMR and ether extraction, 1.6 g of an oil was obtained which was purified by chromatography (SiO_2, CH_2Cl_2) to give 550 mg of a white solid (50% yield) identified by comparison with the spectroscopic data of Cohen and Kimoto[38] as a mixture of 2-perfluorohexylimidazole (**12bH**) and 4-perfluorohexylimidazole (**12aH**): ^{19}F NMR ($CDCl_3$ + DMSO-d_6/$CFCl_3$) δ −77.5 ($2CF_3$, 6 F), −105.4 (α-CF_2, 2 F) for the 4-isomer; −107.0 (α-CF_2, 2 F) for the 2-isomer; −118.5 ($2CF_2$, 4 F), −119.3 ($2CF_2$, 4 F), −119.6 ($2CF_2$, 4 F), −122.8 ($2CF_2$, 4 F) (**12aH**/**12bH**) = 0.8/0.2. ^1H NMR ($CDCl_3$ + DMSO-d_6/TMS) δ 7.0 (4-H of the 2-perfluorohexylimidazole (**12bH**)), 7.1 (5-H of **12aH**), 7.35 (5-H of 4-perfluorohexylimidazole (**12aH**)), 7.65 (2-H of **12bH**).

Electrolysis of $C_6F_{13}I$ (3) in the Presence of the Anion of 5-Nitrobenzimidazole (7^-). By operating as in the first experiment, 922 mg of a yellow oil was obtained which was purified by chromatography (SiO_2; CH_3COOEt/CH_3OH: 91/2) to give 325 mg (50% yield) of yellow crystals which was a mixture of three isomers (**13H**). ^{19}F NMR ($CDCl_3$/$CFCl_3$): isomer A δ −79.3 (CF_3, 3 F), −110.7 (CF_2, 2 F), −120.2 (CF_2, 2 F), −120.4 (CF_2, 2 F), −121.3 (CF_2, 2 F), −124.7 (CF_2, 2 F); isomer B δ −79.3 (CF_3, 3 F), −103.2 (CF_2, 2 F), −115.5 (CF_2, 2 F), −116.6 (CF_2, 2 F), −120.2 (CF_2, 2 F), −122.8 (CF_2, 2 F). The ratio of the three isomers is A = 0.55; B = 0.33; C = 0.12. Mass (CI, NH_3) *m/e* 482 ($M + H^+$), 500 ($M + NH_4^+$). Anal. Calcd for $C_{13}H_4F_{13}N_3O_2$: C, 32.43; H, 0.83; N, 8.73. Found: C, 32.88; H, 1.13; N, 9.03.

Reaction of $C_6F_{13}I$ (3) with the Anion of Phenothiazine. **3**, 1.11 g ($2.5\cdot10^{-3}$ mol) was dissolved in DMSO (100 mL), and 8.41 g (20×10^{-3}

mol) of phenothiazine anion was added under nitrogen (the orange solution became dark green upon addition of the nucleophile). After 15 min the solution was analyzed by gas chromatography showing that 90% of $C_6F_{13}I$ had reacted to give a 71% yield of $C_6F_{13}H$. The ^{19}F NMR spectrum of the electrolysis solution showed the formation of a small amount of perfluorophenothiazine: ($CDCl_3/CFCl_3$) δ −79.1 (CF_3, 3 F), −108.6 (α-CF_2, 2 F), −119.8 (CF_2, 2 F), −120.2 (CF_2, 2 F), −121.1 (CF_2, 2 F), −124.5 (CF_2, 2 F). ^1H NMR ($CDCl_3$/TMS) δ 6.93 (m), 6.25 (m). The position of α-CF_2 shows that the perfluoroalkyl group is bonded to a carbon and not to a nitrogen. Mass (CI, NH_3) *m/e* 518 ($M + H^+$) (1), corresponding to a perfluorophenothiazine besides peaks corresponding to the dimer and the trimer of phenothiazine.

Electrolysis of $C_6F_{13}I$ (3) in the Presence of 2,6-Di-*tert*-butylphenoxide (8^-). Upon mixing **3** (3.24×10^{-2} M) with the nucleophile (0.11 M) in CH_3CN, a blue color was observed but there was no consumption of **3** even after 24 h. The electrolysis in CH_3CN was carried out until all $C_6F_{13}I$ had been consumed as checked by gas chromatography. After acidification and extraction by ether of the electrolyzed solution, 3.5 g of an orange oil was obtained. This oil was purified by chromatography (SiO_2; CH_2Cl_2/heptane 80/20) to give orange crystals which were recrystallized in CH_3OH/H_2O (1.27 g, 57% yield). A second preparative thin-layer chromatography was necessary (SiO_2; pentane/CH_2Cl_2 80/20) to obtain analytically pure samples of **15H**: mp 112 °C: ^{19}F NMR ($CDCl_3/CFCl_3$) δ −79.1 (CF_3, 3 F), −97.9 (α-CF_2, 2 F), −117.6 (CF_2, 2 F), −120.7 (CF_2, 2 F), −124.4 (CF_2, 2 F); ^1H NMR ($CDCl_3$/TMS) δ 1.10 (t-Bu_2, H); 1.30 (t-Bu_1, 9 H), 1.50 (t-Bu_3 and t-Bu_4, 18 H), 5.40 (OH_d, 1 H), 6.70 (H_a, 1 H), 7.0 (H_c, 2 H), 7.5 (H_b, 1 H); ^{13}C NMR ($CDCl_3$/TMS) δ 186.4 (C=O), 154.7 (C–OH), 129.8–135.6 (α-CF_2 to δ-CF_2), 119.5 (CF_3), 30.3 (t-Bu_3 and t-Bu_4), 29.5 (t-Bu_1), 29.3 (t-Bu_2). IR (KBr pellet) 1629 cm^{-1} (s, C=O), 1645 (w, C=C), 3642 (OH, s). Mass (CI, NH_3) *m/e* 691 ($M + H^+$), 710 ($M + NH_4^+$). Anal. Calcd for $C_{34}H_{41}F_{11}O_2$: C, 59.13; H, 5.94; F, 30.28. Found: C, 58.80; H, 6.25; F, 29.90.

Electrolysis of $C_6F_{13}I$ (3) with the Anion of 2-Mercaptothiazoline (9^-). The electrolysis was carried out in CH_3CN (100 mL); it was stopped when $C_6F_{13}I$ had been consumed as observed by gas chromatography. The solution was neutralized with HCl (1 N, 250 mL) and extracted with ether (4 × 100 mL); the combined organic layer was washed with a solution of $NaHCO_3$ (2 × 50 mL) and NaCl (2 × 50 mL). After drying the organic solutions were evaporated to give a brown solid which was purified by chromatography (SiO_2; ether) to give 524.4 mg (48%) of an orange oil, 2-perfluorohexylthiothiazoline (**17H**): ^{19}F NMR ($CDCl_3$/$CFCl_3$) δ −80.2 (CF_3, 3 F), −82.9 (α-CF_2, 2 F), −117.9 (CF_2, 2 F), −120.1 (CF_2, 2 F), −121.2 (CF_2, 2 F), −124.6 (CF_2, 2 F); ^1H NMR ($CDCl_3$/TMS) δ 3.8 (m).

Electrolysis of CF_3Br (1) with the Anion of Imidazole (6^-). The concentration of CF_3Br in DMF was determined as follows. CF_3Br is soluble at 4% by weight at atmospheric pressure. From this saturation concentration known concentrations of CF_3Br could be obtained by diluting CF_3Br with N_2 with the help of an Alphagaz mass flow regulator. If the pressure at the outlet of the flowmeter is the standard pressure (p) and the flows f are related by $p(CF_3Br) + p(N_2) = 1$ atom and $f(CF_3Br)/f(N_2) = p(CF_3Br)/p(N_2)$, thus $p(CF_3Br) = f(CF_3Br)/[f(CF_3Br) + f(N_2)]$. To obtain a concentration of 5.26×10^{-2} M in DMF the flow of nitrogen was set at 45 cm^3/min and the flow of CF_3Br at 11 cm^3/min. After saturation of 100 mL of DMF with the CF_3Br/N_2 mixture, terephthalonitrile (0.055 g, 0.43 mmol) and tetramethylammonium imidazolate (**6**) (2.5 g, 0.18 M) were added. The potential was set at −1.60 V/SCE and the electrolysis was stopped arbitrarily after 21.3 C. The solution was neutralized with 15 mL of HCl (1 N) and poured into 200 mL of water and 200 mL of ether. The aqueous layer was separated and extracted with 50 mL of ether. The combined organic layers were washed with water, dried, and evaporated to give 545.2 mg of a yellow solid which was purified by chromatography (SiO_2; CH_2Cl_2) to give 345.2 mg of a white solid which was a mixture of the isomers of trifluoromethylimidazole, as determinated by comparison with literature[3g,h] spectroscopic data. ^{19}F NMR ($CDCl_3$ + DMSO-d_6/$CFCl_3$) δ −61.0 (CF_3, 4-trifluoromethylimidazole (**14bH**)), −62.0 (CF_3, 2-trifluoromethylimidazole (**14aH**)). The ratio of isomers was (**14aH**/**14bH**) = 0.67/0.33. ^1H NMR ($CDCl_3$ + DMSO-d_6/TMS) δ 7.13 (4-H or 5-H of 2-trifluoromethylimidazole (**14aH**); 7.2 (4-H or 5-H of 4-trifluoromethylimidazole (**14bH**), 7.70 (2-H (**14bH**)).

Electrolysis of CF_3Br with 2,6-Di-*tert*-butylphenoxide (8^-). In this case the electrolysis was stopped after consumption of 90 C. After workup as in experiment 7, an oil (856 mg) was obtained which was purified by chromatography (SiO_2, CH_2Cl_2) to give (332 mg) of 2,6-di-*tert*-butyl-4-trifluoromethylphenol,[32] mp 82–84 °C (lit.[32] 78–80 °C): ^{19}F NMR ($CDCl_3/CFCl_3$) δ −59.2 (CF_3, 3 F); ^1H NMR ($CDCl_3$/$CFCl_3$) δ −1.40 (s, 9 H, t-Bu), 5.25 (s, OH), 7.6 (s, 2 H).

Conclusion

The main conclusions that emerge from the preceding results are as follows. Nucleophilic substitution of perfluoroalkyl halides can be induced electrochemically. The reaction mechanism is a slightly modified version of the classical $S_{RN}1$ mechanism in which the reaction is triggered by dissociative electron transfer, thus not involving the intermediacy of the anion radical of the substrate. Indirect electrochemistry using an electrogenerated outer-sphere electron donor as mediator is to be preferred to direct electrochemical induction both with CF_3Br and $C_6F_{13}I$ for, however, different reasons. In the first case, the reduction potential of the substrate, at which the perfluoroalkyl radical is produced, is slightly negative to the reduction potential of the radical. Since the radical is produced at the electrode surface, it is immediately reduced by rapid electron transfer from the electrode which prevents its reaction with the nucleophile. Indirect electrochemical induction is then made possible by the fact that the mediator couple is positive to the reduction potential of CF_3Br and also to that of $CF_3^\bullet$. With $C_6F_{13}I$, direct electrochemical induction is possible in principle since the induction potential is largely positive to the reduction potential of the C_6F_{13} radical. It is, however, of little practical value because of rapid passivation of the electrode. The mediated induction avoids this drawback. Under these conditions, the main reaction competing with the substitution process is H-atom transfer from the solvent leading to hydrogenolysis. Thiolates react at the sulfur atom whereas phenoxide as well as imidazolate ions react at ring carbons rather than at the negatively charged heteroatom. While in the first case the reaction is clearly of the $S_{RN}1$ type, it may rather be regarded as a homolytic aromatic substitution in the second.

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(32) Stahly, J. P.; Bell, D. R. *J. Org. Chem.* **1989**, *54*, 2873.