Electrochemical perfluoroalkoxylation of aromatic compounds

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New approaches to the electrochemical synthesis of aryl perfluoroalkyl ethers based on a) the electrooxidation of perfluorocarboxylic acid on a consumable PbO_2 anode and b) the simultaneous anodic oxidation of the "aromatic compound—alkaline perfluoroalkoholate" system on a platinum electrode were proposed.

Key words: perfluoroalkoxylation, electrochemical reaction.

The use of electrochemical methods for the synthesis of aryl perfluoroalkyl ethers is a poorly investigated area of chemistry. Thus, the preparation of perfluoroanisole *via* cross-coupling of the trifluoro- and pentafluorophenoxyl radicals formed during the electrooxidation of trifluoroacetic acid and pentafluorophenol on a Pt electrode has been described.[1] In nonfluorinated compounds, the use of anodic cross-coupling is limited to phenols that are difficult to oxidize because they contain several electron-withdrawing substituents, *e.g.*, picric acid. However, it is difficult to extend this method to unsubstituted or monosubstituted phenols because of their preference to undergo electrooxidation and to form polymeric products.

It is shown in this work that when an aromatic ring contains even such a strong electron-withdrawing substituent as a nitro group, *p*-nitrotrifluoroanisole is obtained in a yield of ~2.7%. The failure of the Kolbe cross-reaction of perfluorocarboxylic acids and phenols on a Pt anode seems to be due to the great difference in the adsorption and electrochemical behavior of these reagents.

The direct introduction of a fluoroalkoxy group to the aromatic ring through interaction between an aromatic substrate and fluoroalkoxyl radicals generated during the electrochemical process could be a more general method for the synthesis of aryl perfluoroalkyl ethers. A similar approach has been considered previously;[2] in the authors' opinion, the electrooxidation of trifluoroacetic acid on a glassy carbon anode in the presence of benzene and oxygen results in the formation of trifluoroanisole. We failed to reproduce this reaction and did not find even traces of trifluoromethoxybenzene.

In this work, two pathways for electrochemical synthesis of aryl perfluoroalkyl ethers were studied: a) the reaction of aromatic compounds with the fluoroalkoxyl radicals generated during anodic oxidation of perfluorocarboxylate anions followed by the reaction of the perfluoroalkyl radicals formed with oxygen from the material of the anode; b) anodic oxidation of the aromatic compound—alkaline perfluoroalcoholate system. Aryl fluoroalkyl ethers can be formed *via* three pathways: 1) two-electron oxidation of an aromatic compound followed by the addition of a nucleophile similarly to electrochemical acetoxylation,[3] 2) electrooxidation of perfluoroalcoholate to the fluoroalkoxyl radical and its further radical reaction with an aromatic compound; 3) simultaneous oxidation of the reagents through a mixed mechanism, when the overpotential values of electrooxidation of both the aromatic compound and the fluoroalcoholate are close to each other.

Results and Discussion

Electrolysis of trifluoroacetic acid on a PbO_2 anode in the presence of aromatic compounds

It has been shown[4] that the electrolysis of aqueous trifluoroacetic acid on a Pt anode results in the formation of bis-trifluoromethylperoxide and is accompanied by the degradation of the Pt electrode. This seems to occur[4] because the electrochemically generated trifluoromethyl radicals reduce the platinum oxides formed through oxidation of the platinum surface by the oxygen evolved. It has been proven[4] that $CF_3O^{\cdot}$ radicals are formed as a result of the reaction of $CF_3^{\cdot}$ radicals with PtO_x rather than through the reaction of electrochemically generated $CF_3^{\cdot}$ radicals with the oxygen evolved at the anode. Although this reaction allows for the $CF_3O^{\cdot}$ radical to be generated, it is impossible in fact to use this

Translated from *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 8, pp. 1505—1508, August, 1997.

1066-5285/97/4608-1441 $18.00

radical for electrosynthesis of the trifluoromethoxyl derivatives of aromatic compounds for two reasons: 1) platinum oxides are formed during the electrolysis of an aqueous solution of CF_3COOH only in the absence of organic compounds, since the latter are adsorbed and oxidized (*e.g.*, aromatic compounds in Refs. 5, 6), 2) when substances that are difficult to oxidize (*e.g.*, acetonitrile) are adsorbed, they inhibit the formation of an oxide layer.[7]

We suggested that a stronger oxidizing agent than PtO_x, *e.g.*, PbO_2, can be used as the anodic material in an attempt to generate the $CF_3O^{\cdot}$ radical during electrolysis of CF_3COOH in a nonaqueous solvent in the presence of aromatic compounds.

Our experiments showed that the electrooxidation of the CF_3COOK—CF_3COOH system on the PbO_2 anode in the range of potentials corresponding to the occurrence of the Kolbe reaction (anodic current density 200 mA cm^{-2}) in anhydrous acetonitrile in the presence of benzonitrile seems to result in the formation of trifluoromethoxy derivatives of benzonitrile. The ^{19}F NMR spectrum has three groups of signals: a group of signals (less than 3%, possibly isomers) of very weak intensity at $\delta \approx -20$ ppm, singlets (three isomers, 16%) in the region characteristic of trifluoromethyl benzonitrile derivatives at $\delta = -14$—-16 ppm, and a group of signals (81%) at $\delta \approx -2.0$ ppm that can be assigned to the trifluoroacetoxy benzonitrile derivatives.

The results obtained showed only that it is feasible to use an oxygen-enriched electrode to generate the $CF_3O^{\cdot}$ radical, because the main electrochemical process occurring at the PbO_2 anode was oxidation of the aromatic compound. The absence of electron-withdrawing groups in the molecule of the aromatic compound leads to decrease in its oxidation potential. This makes it difficult to attain the potentials at which oxidation of the carboxylate and the generation of $CF_3O^{\cdot}$ radicals are possible.

The electrooxidation of the CF_3COOK—CF_3COOH system at the PbO_2 anode in anhydrous acetonitrile in the presence of benzene resulted mainly in the formation of phenol and polymeric products.

Anodic oxidation of the "aromatic compound—alkaline perfluoroalcoholate" system

In order to elucidate the sequence of the electrochemical and chemical stages of anodic oxidation of the ArH—$R_fO^-M^+$ system, we studied the electrochemical behavior of benzotrifluoride on a Pt electrode in MeCN with 0.1 *M* Bu_4NBF_4 or 0.6 *M* $(CF_3)_2CFOCs$.

Figure 1 shows the voltammogram* of a Pt microelectrode in acetonitrile with 0.1 *M* Bu_4NBF_4 and in the presence of an aromatic compound (curves *1* and *2*, respectively). This figure presents also the voltammograms

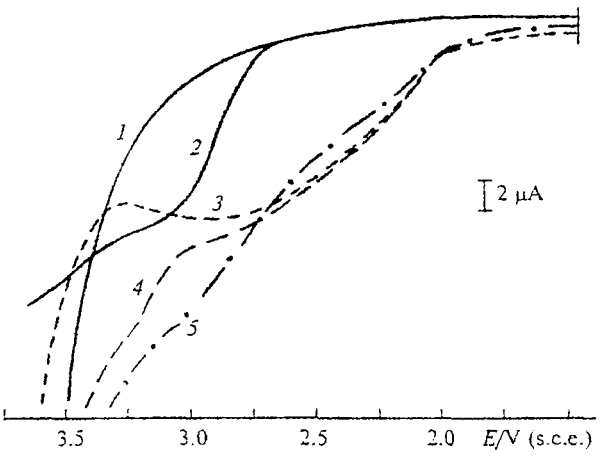

Fig. 1. Voltammograms (Pt electrode, $S = 2 \cdot 10^{-3}$ cm^2) in MeCN with 0.1 *M* Bu_4NBF_4 (*1*); in the presence of $2 \cdot 10^{-3}$ *M* $PhCF_3$ (*2*); with 0.6 *M* $(CF_3)_2CFOCs$ (*3*); with 0.6 *M* $(CF_3)_2CFOCs$ in the presence of $2 \cdot 10^{-3}$ *M* $PhCF_3$ (*4*); with 0.6 *M* $(CF_3)_2CFOCs$ in the presence of 0.1 *M* H_2O (*5*). Scan rate is 200 mV s^{-1}, $E_{init} = 1.5$ V.

of a Pt electrode in acetonitrile with 0.6 *M* $(CF_3)_2CFOCs$ and in the presence of benzotrifluoride (curves *3* and *4*, respectively). It can be seen that in MeCN with either 0.1 *M* Bu_4NBF_4 (potentials $E = 2.6$—3.0 V) or 0.6 *M* $(CF_3)_2CFOCs$, one can observe a wave of the electrooxidation of an aromatic compound that is somewhat shifted to more anodic potentials ($E = 3.0$—3.5 V). The curves measured in the presence of 0.6 *M* $(CF_3)_2CFOCs$ differ from those obtained with 0.1 *M* Bu_4NBF_4 only by the presence of the wave in the 2.1—3.0 V region. As our experiments showed, this wave is of diffusion nature and is due to the presence of traces of water, which can favor the formation of hexafluoroacetone hydrate. Actually, the addition of a small amount of water to the electrolyte results in the appearance on the wave of its oxidation at the same potential. At a high water concentration this process is not limited by diffusion in the region of potentials studied (see Fig. 1, curve *5*).

Thus, one can assume that the electrooxidation of aromatic compounds in the presence of $(CF_3)_2CFOCs$ results in the formation of perfluoroalkoxy derivatives through a mechanism similar to that of acetoxylation, since the overpotential of the electrooxidation of the heptafluoroisopropoxy anion is significantly higher than that of an aromatic compound.

In fact, the anodic oxidation of benzotrifluoride under the conditions of preparative electrolysis in the presence of $(CF_3)_2CFOCs$ yields a mixture of three isomers of heptafluoroisopropoxybenzotrifluoride and two isomers of bis(heptafluoroisopropoxy)benzotrifluoride. The process is likely to occur according to the ECE mechanism:

* The authors wish to acknowledge S. M. Peregudova for measurement of voltammograms.

$$ArH + R_fO^- - 2e \rightarrow ArOR_f + H^+,$$

$$ArOR_f + R_fO^- - 2e \rightarrow Ar(OR_f)_2 + H^+.$$

As can be seen from the presented equations, this process is accompanied by the formation of protons.

The overpotential of proton reduction is high at a Hg cathode, and acidification of the medium occurs, since the reduction of Cs^+ ions is the main cathodic process (in order to bind the protons, electrolysis was carried out in the presence of excess CsF).

It is noteworthy that in the case under consideration, unlike in the anodic trifluoromethylation of aromatic compounds,[8] simultaneous introduction of two R_fO groups to the aromatic ring takes place. This result seems to indicate that the electrooxidation of the perfluoroalkoxy derivatives obtained at the first stage proceeds more easily than electrooxidation of the trifluoromethyl derivatives.

Similarly, we were able to perform the trifluoromethoxylation of $PhCF_3$ by electrolysis in a solution of CF_3OCs in anhydrous MeCN. However, the yield of trifluoromethoxybenzotrifluoride is extremely low, and in spite of the feasibility of anodic trifluoromethoxylation of arenes, this reaction could scarcely be considered to be a preparative method.

The analogs of this reaction are not available in the literature, and the reaction found by us seems to be the first example of the electrochemical perfluoroalkoxylation of aromatic compounds.

Thus, this work showed the practicability of the trifluoromethoxylation of benzonitrile through the anodic oxidation of the CF_3COOK—CF_3COOH system on a PbO_2 anode in the region of potentials corresponding to the occurrence of the Kolbe reaction. The novel electrochemical perfluoroalkoxylation of some aromatic compounds *via* cooxidation of an alkaline perfluoroalcoholate and an aromatic compound on a Pt electrode in anhydrous acetonitrile was found.

Experimental

A 25 mL glass three-electrode cell with a bubbler for purging an inert gas, a water jacket for thermostatting, and separated anodic and cathodic compartments was used to measure the voltammograms. Before measurements platinum electrodes were treated in a hot mixture of concentrated H_2SO_4 and H_2O_2, then thoroughly washed with bidistilled water and dried in a vacuum dessicator. Before recording voltammograms, all solutions were thoroughly purged with purified argon to remove oxygen. Potentials were measured and are presented *vs.* an aqueous saturated calomel electrode (s.c.e.).

Pt gauze electrodes preliminarily treated in the flame of a gas burner to remove impurities were used for preparative electrosynthesis as well as 30—100 mL glass electrochemical cells equipped with a water jacket and a reflux condenser. The electrolyte was magnetically stirred.

An amalgamated Cu electrode was used as the counter-electrode in preparative electrosyntheses involving the perfluoroisopropoxyl anion.

Voltammograms were recorded with a Pi-50.1 potentiostat on a two-coordinate N-308 recorder. The same potentiostat was used for electrosynthesis under galvanostatic conditions.

Acetonitrile for electrochemical measurements and preparative electrolysis was purified by treatment with $KMnO_4$ followed by double distillation over P_2O_5. Trifluoroacetic acid and water were twice distilled. All aromatic compounds were purified according to known procedures. Bu_4NBF_4 was obtained from Bu_4NBr and $NaBF_4$ and dried and reprecipitated from EtOH by diethyl ether. Bu_4NBF_4 was dried *in vacuo* over P_2O_5 and stored in a dry box in an argon atmosphere over P_2O_5. For the kinetic measurements and the electrolysis, the compounds $(CF_3)_2CFOCs$ and CF_3OCs were synthesized directly in the electrochemical cell through the introduction of hexafluoroacetone or difluorophosgene to an acetonitrile solution with excess cesium fluoride. This procedure for obtaining $(CF_3)_2CFOCs$ and CF_3OCs ruled out hydrolysis by air moisture.

The gaseous and liquid reaction products were analyzed by GLC (Poropak Q, 30 °C and 10% FS-1265 on Chromosorb or Krytox, respectiveiy) at the corresponding temperatures. When the concentration of the products formed during electrolysis was low, chromatomass spectrometry (GC/MS) was used for their identification. The chromatomass spectra were recorded on a VG-7070 instrument (ionization energy 70 eV, phase OV-101, 30—35 °C min^{-1}). ^{19}F NMR spectra were recorded on a Bruker WP-200 SY spectrometer (188 MHz) (CF_3COOH as the external standard).

PbO_2 was obtained by anodic deposition at 18—20 °C and pH 1—2 onto Ni gauze or a Pt microelectrode from an electrolyte of the following composition: 1 *M* $Pb(NO_3)_2$ + 0.4 *M* $Cu(NO_3)_2$ + 0.2 *M* $Al(NO_3)_3$. The current density was 0.25—6.0 A dm^{-2}. The thickness of the PbO_2 deposite was 1—2 mm; the current yield of PbO_2 was 90—100%.

Examples of electrosynthesis. 1. The cell was charged with CF_3Ph (2.6 g, 17 mmol), $(CF_3)_2CFOCs$ (18 mmol) (obtained from $(CF_3)_2CO$ (3 g, 18 mmol) and CsF (5 g, 33 mmol)), and 60 mL of acetonitrile. The electrolysis was carried out on a Pt anode (a 22 cm^2 gauze) and a cathode of amalgamated copper (a rod 8 mm in diameter, length 20 mm) in a galvanostatic regime at 30 mA current. After passing 0.005 F of electricity, the electrolysis was stopped and the reation mixture was extracted with pentane (3×30 mL), and the extract was evaporated *in vacuo*. The residue (2 g) was analyzed by GLC, ^{19}F NMR, and GC/MS.

The ^{19}F NMR spectrum, δ: 1.3 (d, 6 F, CF—O—); 58 (hept, 1 F, $(CF_3)_2C$); −14.2 (m, 3 F, CF_3Ph, J_{CF_3-CF} = 3 Hz).

GLC data (FS-1265, 3 m, 134 °C) showed the presence of a new peak that corresponded to a 10% current yield of aryl perfluoroalkyl ethers.

Mass-spectrometry indicated the presence of compounds corresponding to the empirical formula $i\text{-}C_3F_7OC_6H_4CF_3$ (three isomers): m/z (I_{rel} (%)): 330 $[M]^+$ (40), 311 $[M-F]^+$ (15), 145 $[C_7H_4F_3]^+$ (100), 133 $[C_6H_4F_3]^+$ (18), 69 $[CF_3]^+$ (10). The mass-spectrum of one isomer is presented, the other two possess similar fragmentation with somewhat different intensities of the peaks of some ions.

A compound corresponding to the empirical formula $(i\text{-}C_3F_7O)_2C_6H_3CF_3$ (two isomers) is also identified in the products: m/z (I_{rel} (%)): 514 $[M]^+$ (72), 495 $[M-F]^+$ (42), 348 $[M-C_3F_6O]^+$ (90), 329 $[M-C_3F_7O]^+$ (100), 179 $[M-C_6F_{13}O]^+$ (65), 163 $[M-C_6F_{13}O_2]^+$ (100), 151 $[M-C_7F_{13}O_2]^+$ (48), 132 $[M-C_7F_{14}O_2]^+$ (25), 101 $[M-C_8F_{15}O_2]^+$ (18), 69 $[CF_3]^+$ (10). The second isomer differs by the presence of the fragment 345 $[M-C_3F_7]^+$ (100) and by a highly intense peak corresponding to the fragment 69 $[CF_3]^+$ (100).

Thus, a mixture of three isomers of heptafluoroisopropoxybenzotrifluoride and two isomers of bis(heptafluoroisopropoxy)benzotrifluoride is formed in the reaction.

2. Electrolysis was carried out under conditions similar to those described above, but a solution of cesium trifluoromethoxylate in acetonitrile was used as the background electrolyte.

The mass-spectra showed the presence of compounds of the empirical formula $CF_3OC_6H_4CF_3$. *m/z* (I_{rel} (%)): 230 $[M]^+$ (100), 211 $[M-F]^+$ (20), 180 $[M-CF_2]^+$ (5), 161 $[M-CF_3]^+$ (9), 145 $[M-OCF_3]^+$ (25), 133 $[C_6H_4F_3]^+$ (30), 114 $[C_6H_4F_2]^+$ (20), 69 $[CF_3]^+$ (72).

No products containing two CF_3O groups in the molecule of the aromatic compound were observed. However, this result seems to be due to the extremely low concentration of $CF_3OC_6H_4CF_3$ formed.

3. The cell was charged with CF_3COOH (7.5 g, 65 mmol), $O_2NC_6H_4ONa$ (1.04 g, 6.5 mmol), and 27 mL of a MeOH—sulfolane mixture (8 : 1). The electrolysis was carried out on a Pt anode (20 cm^2 gauze) and a Ni cathode (2 cm^2 wire) in a galvanostatic regime at 2 A current. After passing 0.024 F of electricity, the electrolysis was stopped and the reaction mixture was poured into cool water and extracted with diethyl ether (3×30 mL). The extract was evaporated *in vacuo*. The residue (1.0 g) was analyzed by ^{19}F NMR and GC/MS.

The ^{19}F NMR spectrum (δ: −19.5 (s, CF_3—O), as well as a group of signals at −2.0—0) corresponds to CF_3COOH and its derivatives, *e.g.*, $CF_3COOC_6H_4NO_2$. According to NMR, up to 10% of the isolated mixture is the target product, nitro-α,α,α-trifluoroanisole. The current yield was 2.7%, the substance yield was 7.4%.

Using GC/MS, we found CF_3COOMe (*m/z* (I_{rel} (%)): 128 $[M-H]^+$ (1), 69 $[CF_3]^+$ (62), 59 $[COOCH_3]^+$ (80), 15 $[CH_3]^+$ (100)) and CF_3COOH (*m/z* (I_{rel} (%)): 114 $[M]^+$ (1), 69 $[CF_3]^+$ (72), 45 $[COOH]^+$ (100)). (Totally up to 90%.)

Mass-spectrometry showed the presence of compounds corresponding to the empirical formula $O_2NC_6H_4OCF_3$ (*m/z* (I_{rel} (%)): 207 $[M]^+$ (90), 191 $[M-O]^+$ (5), 177 $[M-NO]^+$ (30), 161 $[M-NO_2]^+$ (20), 122 $[M-CF_3O]^+$ (15), 95 $[C_6H_4F]^+$ (100), 69 $[CF_3]^+$ (42), 30 $[NO]^+$ (15), up to 10%), as well as traces of compounds of the empirical formula $O_2NC_6H_3(OCF_3)CF_3$ (*m/z* (I_{rel} (%)): 275 $[M]^+$ (70), 256 $[M-F]^+$ (20), 229 $[M-NO_2]^+$ (8), 190 $[M-CF_3O]^+$ (10), 163 $[M-COF_2-NO_2]^+$ (100), 129 $[M-F_4-NO_2]^+$ (20), 69 $[CF_3]^+$ (75)).

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Received November 12, 1996;
in revised form December 11, 1996