Electrochemical Fluorination of Diols and Heterocyclic Compounds[1]

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Electrochemical fluorination of diols $(HO\text{-}CH_2\text{-}CH_2\text{-})_2X$ ($X=CH_2$, O, S, NH, NCH_3, NC_2H_5) afforded the corresponding perfluoro-heterocyclic compounds together with the cleaved products as a result of cyclization. Perfluoro-*p*-dioxane, a new compound having boiling point at 22.5—23.0 °C, was obtained from diethylene glycol. Electrochemical fluorination of heterocyclic compounds such as tetrahydropyran, *p*-dioxane, *p*-thioxane and morpholine was carried out and the results were compared with those obtained with diols.

Upon electrochemical fluorination, the formation of five- or six-membered perfluoro-heterocyclic compounds has been known to take place from the straight chain starting material containing a sufficient number of carbon atoms and hetero atom in proper position.[2-4]

We studied the electrochemical fluorination of such diols as 1,3-propanediol and 1,4-butanediol in order to obtain perfluoromalonic acid and perfluorosuccinic acid, respectively.[5,6] From 1,4-butanediol, perfluorotetrahydrofuran, formed as a result of cyclization, was obtained as the main product. It seems of interest to investigate the electrochemical fluorination of the compounds having two functional groups in order to obtain perfluoro-heterocyclic compounds.

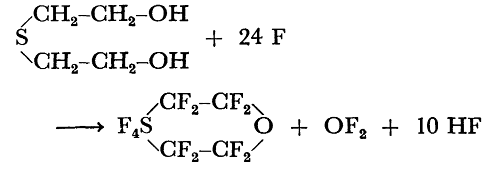
The aim of this work is to examine the ring formation upon electrochemical fluorination of the compounds of the type $(HO\text{-}CH_2\text{-}CH_2\text{-})_2X$ [$X=CH_2$(I), O(II), S(III), NH(IV), NCH_3(V), NC_2H_5(VI)], comparing the yields with those obtained from the fluorination of corresponding heterocyclic compounds and also to discuss the reaction mechanism. No detailed study has been reported on the fluorination of diols containing hetero atom, while the heterocyclic compounds dealt with in the present work were familiar starting material for the fluorination in electrochemical process.[4,7] As expected ring formed products, $\overline{CF_2CF_2CF_2CF_2CF_2O}$ (XI) was formed from I, $\overline{CF_2CF_2OCF_2CF_2O}$ (XII) from II, $\overline{CF_2CF_2OCF_2CF_2SF_4}$ (XIII) from III, $\overline{CF_2CF_2OCF_2CF_2NF}$ (XVI) from IV, $\overline{CF_2CF_2OCF_2CF_2N}CF_3$ (XV) from V and $\overline{CF_2CF_2OCF_2CF_2N}C_2F_5$ (XVI) from VI, respectively.

Experimental

Materials and Apparatus. All reagents except *p*-thioxane[8] were commercial products and used after purification when necessary. The purity of anhydrous hydrogen fluoride was higher than 99.5%.

All the features of the apparatus (capacity of the electrolytic cell, 1 l; electrodes, Ni plates; effective anodic surface area, 9.2 dm²) and the procedures were essentially the same as described previously.[5,9,10]

General Procedures. In order to compare the results with those obtained in each experiment, the conditions for fluorination were made to be the same; the electrolysis was carried out by batch (0.34 mol%), and cell temperatures and anodic current density were adjusted to 5—6 °C and 2.7 A/dm². The most important setting condition was the amount of electricity passed, *i.e.*, reaction time. Electrolysis was continued until the theoretical amount of electricity required to complete the reaction had passed. This was based on the amount of current assumed to be required to form fluorine which would react with the starting material. Taking an example in III (X=S), the following equation is available.



$$S(CH_2\text{-}CH_2\text{-}OH)_2 + 24\,F \longrightarrow F_4S\langle(CF_2\text{-}CF_2)_2\rangle O + OF_2 + 10\,HF$$

Thus 4.8 Faraday (128.7 A hr) is required to fluorinate 0.20 mol of the starting material. The value of yield (mol %) of six-membered perfluoro-cyclic ether should coincide with that of the current efficiency of the six-membered perfluoro-cyclic ether by the above equation.

As a typical example, the procedures for the fluorination of pentamethylene-1,5-diol (I) will be described. Anhydrous hydrogen fluoride (about 1 l) was introduced into the cell. Prior to fluorination, electrolysis was carried out in order to remove a trace of impurity until the voltage rose to 6.5 V. The sample (20.8 g) of I was introduced into the cell, and electrolysis was carried out with an anodic current density of 2.7 A/dm², at a cell voltage of 4.8—6.1 V, and

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[1] This paper is designated Part 1 of a series "Studies on the Cyclization upon Electrochemical Fluorination."

[2] E. A. Kauck and J. H. Simons, U. S. 2644823 (1953); Saline Ludwigsshalle A. G., Ger. 1069639 (1959); Minnesota Mining and Manufacturing Co., Brit. 1007288 (1965); W. Blöchl, Fr. 1436269 (1966).

[3] J. A. Young, T. C. Simmons, and F. W. Hoffmann, *J. Amer. Chem. Soc.*, **78**, 5637 (1956); J. A. Young and R. D. Dresdner, *ibid.*, **80**, 1889 (1958).

[4] F. W. Hoffmann, T. C. Simmons, R. B. Beck, H. V. Holler, T. Katz, R. J. Koshar, E. R. Larsen, J. E. Mulvaney, F. E. Rogers, B. Singleton, and R. S. Sparks, *ibid.*, **79**, 3424 (1957).

[5] S. Nagase, T. Abe, and H. Baba, This Bulletin, **41**, 1921 (1968).

[6] Actually perfluorosuccinoyl fluoride was the product, and was easily led to perfluorosuccinic acid by subsequent hydrolysis.

[7] a) Minnesota Mining and Manufacturing Co., U. S. 2594272 (1952); b) Minnesota Mining and Manufacturing Co., U. S. 2500388 (1950); c) R. D. Dresdner and J. A. Young, *J. Amer. Chem. Soc.*, **81**, 574 (1959); d) T. C. Simmons, F. W. Hoffmann, R. B. Beck, H. V. Holler, T. Katz, R. J. Koshar, E. R. Larsen, J. E. Mulvaney, K. E. Paulson, F. E. Rogers, B. Singleton, and R. S. Sparks, *ibid.*, **79**, 3429 (1957): R. E. Banks and E. D. Burling, *J. Chem. Soc.*, **1965**, 6081.

[8] E. Fromm and B. Ungar, *Ber.*, **56**, 2288 (1923).

[9] T. Abe, S. Nagase, and K. Kodaira, This Bulletin, **43**, 957 (1970).

[10] T. Abe, S. Nagase, K. Kodaira, and H. Baba, *ibid.*, **43**, 1812 (1970).

a cell temperature of 5—6 °C. Electrolysis was conducted for 130.0 A hr (Theoretical; 128.7 A hr).

Gases evolving from the cell were passed through a reflux condenser kept at −25 °C, over NaF pellets and perflurocarboxylic acid fluoride absorber[11] (a couple of polyethylene bottles containing water), and then bubbled through an alkaline solution of sodium sulfite containing a small amount of potassium iodide in series of Ichinose gas washers in order to eliminate oxygen difluoride, and finally collected in traps immersed in liquid nitrogen. After electrolysis, the solution drained from the cell was checked, none of perfluorinated compounds being found.[12]

The reaction products (12.9 g) condensed in cold traps were subjected to low temperature distillation and separated into three fractions. Each fraction was subsequently analysed by glc (column; silica gel, Kel F # 3 30% on Chromosorb PAW, carrier; He). Compounds in Fractions 1, 2 and 3 were as follows. Fraction 1 (bp∼−77.9 °C, 0.8 g): CF_4,[13] C_2F_6, CHF_3, Fraction 2 (bp −77.8∼−56.5 °C, 1.5 g): C_3F_8, C_2HF_5, CF_3OCF_3, $CF_3OC_2F_5$, Fraction 3 (bp −56.4 °C∼r.t., 10.6 g): $\overline{CF_2CF_2CF_2CF_2CF_2O}$ (XI), $\overline{CF(CF_3)CF_2CF_2CF_2O}$, $\overline{CF_2CF_2CF_2CF_2O}$, C_3F_8, $CF_3OC_2F_5$, *n*-C_4F_{10}, *n*-C_5F_{12}. The first two compounds (XI, $\overline{CF(CF_3)CF_2CF_2CF_2O}$) were separated by repetitive glc and were analysed by IR, ^{19}F-NMR, Mass, and fluorine determination.

Results and Discussion

The reaction conditions for the fluorination of diols and heterocyclic compounds are given in Tables 1 and 2, respectively. The results obtained are summarized in Table 3.

We see that the formation of six-membered heterocyclic compounds were observed from corresponding diols, and their yields from diols and also from the fluorination products of heterocyclic compounds were significantly affected by the hetero atom.

Table 1. Conditions for the fluorination of diols
Anodic current density, 2.7 A/dm^2; cell temp., 5—6 °C; sample fed, 0.20 mol: general formula of the sample, $(HO\text{-}CH_2\text{-}CH_2\text{-})_2X$ (X represents a substituent).

Sample X	Cell voltage (V)	Electricity passed (A hr)	Products obtained (g)
CH_2 (I)	4.8—6.1	130.0	12.9
O (II)	4.8—5.1	102.2	4.3
S (III)	4.7—5.5	129.5	20.0
NH (IV)	4.9—5.3	117.6	8.6
NCH_3 (V)	4.9—5.3	137.5	12.7
NC_2H_5 (VI)	5.1—5.4	159.6	14.4

Table 2. Conditions for the fluorination of heterocyclic compounds
Anodic current density, 2.7 A/dm^2; cell temp., 5—6 °C; sample fed, 0.20 mol

Sample	Cell voltage (V)	Electricity passed (A. hr)	Products obtained (g)
tetrahydropyran (VII)	4.7—4.9	104.8	18.1
p-dioxane (VIII)	5.1—5.3	83.0	14.9
p-thioxane (IX)	5.6—6.6	107.5	27.1
morpholine (X)	4.9—5.1	93.8	17.0

Table 3. Results with the flourination of diols and heterocyclic compounds

Sample	Perfluoro-heterocyclic compound Yield (mol%)
I	XI (6.2),[a] $\overline{CF(CF_3)CF_2CF_2CF_2O}$ (4.3),[b] $\overline{CF_2CF_2CF_2CF_2O}$ (4.7)
II	XII (trace), $\overline{CF_2OCF_2CF_2O}$ (1.3)
III	XIII (1.3), $\overline{CF_2CF_2CF_2CF_2O}$ (0.8)
IV	XIV (0.1)
V	XV (2.7)
VI	XVI (7.1),[c] XV (1.1)
VII	XI (16.0), $\overline{CF(CF_3)CF_2CF_2CF_2O}$ (7.0), $\overline{CF_2CF_2CF_2CF_2O}$ (2.0)
VIII	XII (3.0), $\overline{CF_2OCF_2CF_2O}$ (1.0)
IX	XIII (9.7)
X	XIV (0.4)

a) Bp 32.0 °C (reported 32 °C).[7a] Found: F, 70.7%. Calcd: F, 71.3%.
b) Bp 26.5—27.0 °C. Found: F, 70.5%. Calcd: F, 71.3%.
c) Bp 67.6 °C. Found: F, 70.3%. Calcd: F, 70.8%.

Typical features of the fluorination products were observed in the fluorination of I and II. A considerable amount of the five-membered perfluoro-heterocyclic compounds ($\overline{CF(CF_3)CF_2CF_2CF_2O}$ and $\overline{CF_2CF_2CF_2CF_2O}$ from I, $\overline{CF_2OCF_2CF_2O}$ from II) was obtained as well as the expected six-membered compounds (XI from I and XII from II, respectively).

Similarly, ring contraction was observed in the fluorination of tetrahydropyran (VII) and *p*-dioxane (VIII). Thus ring expansion was expected to occur and an attempt was made to obtain XI by the fluorination of 2-methyltetrahydrofuran. When 2-methyltetrahydrofuran was subjected to electrochemical fluorination (reaction conditions: sample, 0.20 mol; anodic current density, 2.7 A/dm^2; electricity passed, 102.6 A hr; cell voltage, 4.8—5.1 V; cell temp., 5—6 °C), the product (29.4 g) mainly consisted of perfluoro-

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[11] The products in perfluorocarboxylic acid fluoride absorber were worked up in almost the same way as reported.[5] Perfluoroglutaric acid obtained was converted into silver salt prior to analysis because of its strong hygroscopic character. The perfluorocarboxylic acids obtained were as follows. Silver perfluoroglutarate (0.5 g); mono-basic acid sodium salt (4.6 g) [sodium trifluoroacetate (7 wt%), sodium perfluoropropionate (7), sodium perfluorobutyrate (19), sodium perfluorovalerate (67)].

[12] No perfluorinated products were found in the cell drainings throughout experiments.

[13] Arranged in the order of decrease in product composition (wt%).

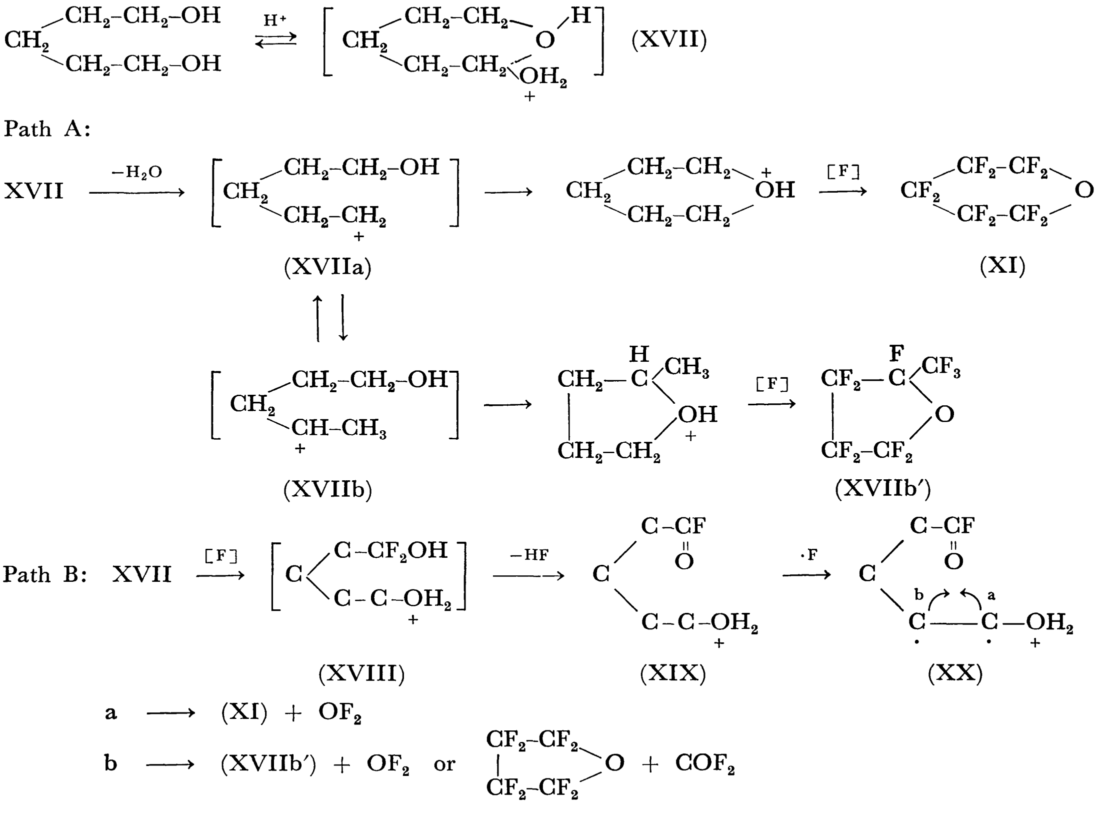
2-methyltetrahydrofuran, and XI produced as a result of the ring isomerization. The yields of the two compounds were 36.1% and 8.5%, respectively.

Perfluoro-*p*-dioxane[14] (XII) was produced as the ring formed product from II, and also the fluorination product of VIII, though the electrochemical fluorination of VIII yielded only perfluoro-1,2-dimethoxyethane as a cleaved product.[7b]

Fluorination of IV afforded a trace of perfluoromorpholine (XIV), which was obtained also in poor yield from morpholine (X). However, when *N*-alkyldiethanolamines (V and VI) were subjected to electrochemical fluorination, the production of an increased amount of the ring formed products (perfluoro-*N*-alkylmorpholines, XV and XVI) was observed as compared with that from IV.[15]

Mechanism. For the formation of perfluoroheterocyclic compounds from diols, there seems to be two conceivable mechanisms operating simultaneously during the course of electrochemical fluorination. One involves cyclization *via* oxonium compound followed by dehydration (Path A), and the other involves cyclization by radicals formed on the carbon chain of the same molecule (Path B). It is well-known that oxonium compounds are formed when alcohols and ethers are dissolved in anhydrous hydrogen fluoride.[16] In the case of pentamethylene-1,5-diol (I), oxonium compound (XVII) is formed when I is dissolved in anhydrous hydrogen fluoride, XVIIa and XVIIb being then formed by dehydration followed by isomerization. Formation of tetrahydropyran including a trace of methyltetrahydrofuran from I in hydrogen fluoride was ascertained in the following experiment, and it is strongly suggested that this type of cyclization (Path A) could occur: 5 g of I was added to 50 ml anhydrous hydrogen fluoride in a 300 ml flask made of poly(chlorotrifluoroethylene), fitted with a reflux condenser (−25 °C). After being left standing 2 hr at room temperature, the solution was diluted with water (200 ml) extracted with ether, the ethereal solution (about 300 ml) being then neutralized by alkaline solution. After removing ether by distillation, the distillation residue (0.5 g) was analysed by glc (column; Carbowax 4000 20% on Celite 545, carrier; He). glc analysis showed the presence of tetrahydropyran (major) and trace of 2-methyltetrahydrofuran.

On the other hand, fluoro-alcohol (XVIII) carrying fluorine atom in α position, which is considered to be formed during the course of electrochemical fluorination of primary alcohol, eliminates hydrogen fluoride and changes into acid fluoride (XIX). The acid fluoride thus obtained may proceed to perfluorocarboxylic acid fluorides[11] (perfluoroglutaryl fluoride, perfluorovaleryl fluoride and other degradaded perfluoroacid fluorides), but part of it (XIX) may be subjected to radical attack by the carbon radical of



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[14] Bp 22.5—23.0 °C. ^{19}F-NMR (chemical shift from external CF_3COOH); 10.7 ppm (singlet, CF_2). On the other hand, perfluoro-1,2-dimethoxyethane had a bp of 9.0—10.0 °C (reported 13 °C). ^{19}F-NMR; −20.5 ppm (triplet, CF_3), 14.2 ppm (quartet, CF_2).

[15] Alkylamines give the corresponding perfluoroalkylamines in the best yield in the case of tertiary amines. *Cf. e. g.*, E. A. Kauck and J. H. Simmons, U. S. 2616927 (1952); Brit. 666733 (1952).

[16] See for example, "The Chemistry of Non-Aqueous Solvents," Vol. II, ed. by J. J. Lagowski, Academic Press Inc., New York (1967), p. 81; "Protonated Heteroaliphatic Compounds," by G. A. Olah and A. M. White, *Chem. Rev.*, **70**, 561 (1970).

the same molecule resulting from the hydrogen abstraction by fluorine radical creating the bond in either way, B-a or -b.

Accordingly, Path A may be the first step in the reaction, while Path B may occur during the course of electrochemical fluorination. The usual poor yield of the ring formed products from diols which contain a hetero atom may be explained to be due to an undesirable influence of the protonated hetero atom on the stability of the carbonium ion formed (XVIIIa, XVIIb) and also an easier fission of the bond of the carbon-hetero atom.

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