Reactions of polyfluoroaromatic compounds with electrophilic agents. Part 20*. Nitrofluorination of pentafluorophenoxydifluoromethane and decafluorodiphenyl ether

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Abstract

When nitrofluorinated with HNO_3 in anhydrous HF, the pentafluorophenol ethers C_6F_5OR ($R = CHF_2$, C_6F_5) add the nitronium cation to the *para* and *ortho* positions with respect to the substituent or eventually to form the corresponding 3-nitrocyclohexa-1,4-dienes. The formation of the diene with a CFOR fragment, arising from nitronium cation addition to the *para* position, has been shown to be reversible in the case of $R = CHF_2$, unlike that from reaction at the *ortho* position which afforded the diene containing a $-CF_2-$ ring fragment.

Introduction

Pentafluoro- [2, 3] and tetrafluoro-benzene [4] derivatives with substituents such as hydrogen, chlorine, bromine and a methyl group, undergo nitrofluorination to form the 1,4-adducts with the location of the nitro group resulting from nitronium cation attack at positions *ortho* and *meta* to the non-fluorine substituent. Since in these cases, the substituent *para* to the position of primary attack is fluorine, capture of the fluoride anion by the intermediate nitrocyclohexadienyl cation during the second stage of the reaction leads to polyfluorinated cyclohexadienes with a very stable difluoromethylene group. The latter result affects decisively the properties and synthetic application of the primary product. Hence, it would to be of interest to ascertain the possibility of an attack *para* to the non-fluorine substituent, to form the cyclohexadiene adduct with the captured fluorine *ipso* to this substituent, and to reveal the modes of transformations of this adduct.

Since *meta* orientation in electrophilic attack with respect to the substituents mentioned above is apparently due to the predominance of the overall fluorine influence over the non-fluorine substituent effect, it seems reasonable to consider compounds of the type C_6F_5OR. In this case, one should expect the *para–ortho*-orientating effect of the OR substituent to

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*For Part 19, see ref. 1.

play the principal role, similar to the regioselectivity observed in the reactions of polyfluorinated hydroxyarenes with nitric acid [5–7]. By using substrates of this type with R other than hydrogen, one should expect a decreasing tendency towards bond cleavage in the intermediate arenium ions with the nitro group *ipso* to the fluorine, as compared to their analogues with R = H, and conversion of these intermediates to nitrocyclohexadienes rather than to nitrocyclohexadienones.

Attack of the nitronium cation on the position *para* to the OR group and *ipso* to a halogen, particularly fluorine, has been observed previously for reactions of phenol ethers with nitric acids in various media [8–10]. However, 2-nitro-4-halophenols were also formed in these reactions as by-products in amounts depending on the water content in the reaction medium. This dependence was attributed to competition between various routes of transformation of the intermediate σ-complex formed by *ipso* attack of the nitronium cation at the position *para* to the OR substituent [10].

On taking this into account, it was considered desirable in the present work to choose an OR group which diminishes the probability of phenol formation. In this connection, several transformation pathways for the σ-complex of type **1** (Scheme 1) into phenol would have *a priori* consideration, thus specifying and complementing the scheme [10] involving nucleophilic capture of the σ-complex **1** followed by conversion of the cyclohexadiene **2** formed into the cyclohexadienone **3**, a phenol precursor. It seems obvious that any transformation of the σ-complex **1**, except possibly intramolecular isomerization via 1,2-shift of the geminal substituent [11], occurs via the participation of a nucleophile. One should also bear in mind the possibility of σ-complex transformation into the cyclohexadienone **3** not only via formation of the cyclohexadiene **2** but also directly via nucleophilic attack of R at the α-carbon, since the resulting cyclohexadienone is an excellent leaving group (Scheme 1).

In this context, the above result may be attained by modifying the OR group in such a manner so as to decrease its basicity or inhibit nucleophilic attack of R at the α-carbon. Suitable modification appears to be fluorination at this carbon or substitution of R = Alk by R = Ar. In addition, the desired
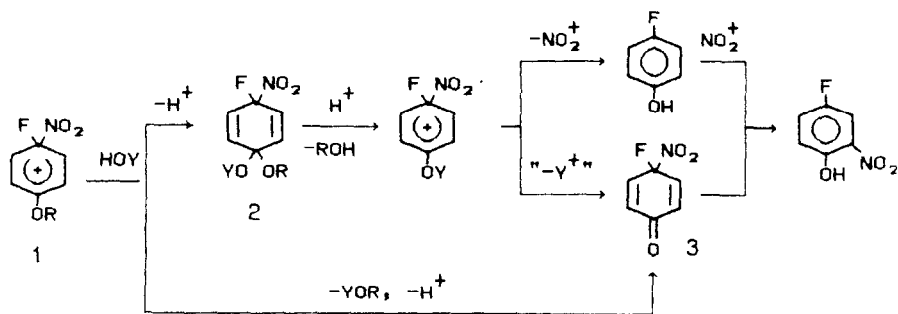
Scheme 1.

effect should also be achieved by diminishing the nucleophilicity of the medium. In this respect, suitable media seem to be those normally employed for the nitrofluorination of polyfluoroarenes.

The present work has been devoted to an investigation of the interaction of pentafluorophenoxydifluoromethane (**4**) and decafluorodiphenyl ether (**5**) with nitric acid ($d = 1.51$) in anhydrous hydrogen fluoride.

Experimental

NMR spectra were recorded on a Varian A56/60 instrument for CCl_4 solutions (15–25 wt.%) using C_6F_6 as the internal standard. IR spectra were recorded using a UR-20 spectrometer for CCl_4 solutions (5 wt.%). The molecular formula of diene **10** was obtained by high-resolution mass spectrometry on a Finnigan-MAT 8200 instrument. The spectral and elemental analysis data obtained are presented in Tables 1 and 2, respectively. The starting ethers were synthesized according to procedures described for compounds **4** [12] and **5** [13]. Hydrogen fluoride and nitric acid ($d = 1.51$) were of commercial origin and distilled before use.

Reaction of pentafluorophenoxydifluoromethane (4) with nitric acid in hydrogen fluoride

(a) The ether **4** (13.6 g) and a solution of HNO_3 (15 cm³) in HF (60 cm³) were shaken together for 22 h at 20 °C. The mixture was poured on to the mixture of methylene chloride (20 cm³) and crushed ice. The organic layer was separated, washed with water and dried with magnesium sulphate. The solvent was evaporated using a column to afford the residual oil (13.8 g) which was shown by NMR spectroscopy to consist of the starting material (13%) and the isomers **6** and **7**. The mixture of nitrodienes **6** and **7** (1:6 ratio, 4.2 g, 24%) was obtained for elemental analysis by distillation under reduced pressure (25 mm Hg) as a fraction boiling at 45–51 °C.

(b) The ether **4** (10.0 g) and a solution of HNO_3 (11 cm³) in HF (25 cm³) were shaken together for 5 h at 20 °C. The mixture was worked up as described above. The resulting methylene chloride solution was shown by NMR spectroscopy to contain the starting material (30%) and isomers **6** and **7** in a 1:9 ratio.

(c) Similarly, after shaking up ether **4** (12.0 g) with HNO_3 (14 cm³) and HF (80 cm³), a mixture of **4, 6, 7** and **10** was obtained in a ~3:4:2:1 ratio.

Reaction of nitrodienes 6 and 7 with hydrogen fluoride

A mixture of isomers **6** and **7** (1:5 ratio, 1.9 g) and HF (16 cm³) were shaken together for 24 h at 20 °C. After standard work up (*vide supra*), the residual methylene chloride solution contained **10** and **4** in a 15:85 ratio.

TABLE 1

NMR and IR data for polyfluorinated cyclohexadienes and cyclohexadienones

Structure type and number	x	y	z	Fluorine chemical shifts[a] (δ_F, ppm) δ_1	δ_2	δ_3	δ_4	δ_5	δ_6	Spin coupling constant (J, Hz)[b]	IR data (ν, cm^{-1})
6 (n.c.)	OCHF$_2$	F	NO$_2$	80.3	23.8	50.8–52.2	12.7	11.5	29.6	22.5 (5, 6); ~21 (2, 3; 3, 4); 9.5 (3, 5); ~6 (2, 6; 4, 6); 15.5; (F¹, 2); 74 (H, F in CHF$_2$)	1045–1110 (CF$_2$); 1340, 1615 (NO$_2$); 1730 (C=C)
7[c,d]	F	OCHF$_2$	NO$_2$	6.8	14.5	38.4 40.5 77.0 (CHF$_2$)	14.5	6.8	25.9 26.5	22 (2, 3; 3, 4; 5, 6); ~9 (2, 6; 4, 6); ~6 (1, 3; 3, 5); 72 (H, F in CHF$_2$)	1340, 1615 (NO$_2$); 1730, 1745 (C=C)
8	OC$_6$F$_5$	F	NO$_2$		14.5	53.4	14.0	12.1	32.2	e	1000–1050 (CF$_2$); 1340, 1615 (NO$_2$)
9[c,d]	F	OC$_6$F$_5$	NO$_2$	10.5	18.3	42.6 44.7	18.3	10.5	29.1 30.9	21–22 (1, 6; 2, 3; 3, 4); ~9 (1, 3; 3, 5); 6 (2, 6; 4, 6)	1530 (C$_6$F$_5$); 1730, 1740 (C=C)
10	OCHF$_2$	F	F	81.5	18.2	51.3	5.7	8.4	54.0	~20 (2, 3; 3, 4; 5, 6); ~10 (2, 6; 3, 5; 4, 6); 75 (H, F in CHF$_2$)	1070, 1090, 1110 (CF$_2$); 1730 (C=C)
13 (n.c.)	OCHF$_2$	F	–	78.8	29.9	46.7	16.7	11.8		21.5; (2, 3); 21 (3, 4); 10 (3, 5); 6 (2, 4); 4 (2, 4; 4, 5); 3 (2, 5); 76 (H, F in CHF$_2$)	1690, 1715 (C=O), (C=C)
14	F	OCHF$_2$	–	6.9	18.3 77.5 (CHF$_2$)	35.7 (CHF$_2$)	18.3	6.9		23.5 (2, 3; 3, 4); 8 (1, 3; 3, 5); 3 (1, 2; 1, 4; 2, 5); 71 (H, F in CHF$_2$)	1725 (C=O, C=C)

[a]From C$_6$F$_5$ as internal reference.   [b]Coupling atoms are shown in parentheses.   [c]A mixture of geometrical isomers.   [d]The most probable assignment is presented.   [e]Signal resolution unsatisfactory.
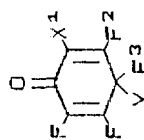
TABLE 2

Elemental analyses of polyfluorinated cyclohexadienes and cyclohexadienones

Compound No.	Found (%)				Formula	Required (%)			
	C	H	F	N		C	H	F	N
6 (n.c.)	28.3	0.55	50.3	4.74	$C_7HF_8NO_3$	28.1	0.34	50.8	4.68
	28.4	0.50	50.0	4.52					
7[a]	28.4	0.60	50.2	4.74	$C_7HF_8NO_3$	28.1	0.34	50.8	4.68
	28.4	0.55	49.9	4.52					
8, 9	35.4		50.8	3.42	$C_{12}F_{11}NO_3$	34.7		50.4	3.38
(mixture)	35.2		50.9	3.57					
13 (n.c.)	33.2	0.41	52.8		$C_7HF_7O_2$	33.6	0.40	53.2	
	33.0	0.35	52.9						
14[b]	33.1	0.35	52.9		$C_7HF_7O_2$	33.6	0.40	53.2	
	32.8	0.44	52.7						

[a]Contained a 10% admixture of isomer **6**.
[b]Contained a 10% admixture of isomer **13**.

1-Difluoromethoxy-6-nitro-2,3,3,4,5,6-hexafluorocyclohexa-1,4-diene (6) (n.c.)

A mixture (9.0 g) of **4, 6, 7** and **10** (3:4:2:1) and HF (40 cm³) were shaken together for 2.5 h at 20 °C. After standard work up, the residue (7.0 g) consisted of **4, 6** and **10** in a 5:4:1 ratio. The individual compound **6** (1.2 g) was isolated by distillation under reduced pressure as a fraction boiling at 43–46 °C (5 Torr).

1-Difluoromethoxy-2,3,3,4,5,6,6-heptafluorocyclohexa-1,4-diene (10) (n.c.)

The diene **6** (0.5 g) and HF (5 cm) were shaken together for 15 h at 50 °C. After standard work up, the diene **10** (0.25 g, 55%) was isolated by distillation as a fraction boiling at 100–105 °C under atmospheric pressure. Found: M, 271.9879. C_7HF_9O requires: 271.9883.

2-Difluoromethoxy-3,4,4,5,6-pentafluorocyclohexa-2,5-diene-1-one (13) (n.c.)

The nitroether **6** (0.4 g) was heated for 4 h at 130 °C. Vacuum distillation (10 Torr, bath temperature 60–65 °C) of the residue gave, after standard work-up, dienone **13** (0.25 g, 75%).

Thermolysis of nitrodienes 6 and 7

A mixture of **6** and **7** (1:9, 1.63 g) was heated for 3 h at 160 °C. After standard work up, the residue was distilled at atmospheric pressure to give a mixture of dienones **13** and **14** (1:9 ratio) as a fraction boiling at 150–151 °C.

Reaction of decafluorodiphenyl ether (5) with nitric acid in hydrogen fluoride

The ether **5** (7.9 g) and a solution of HNO_3 (5 cm^3) in HF (15 cm^3) were shaken together for 7 h at 20 °C. The mixture was worked up as described above. After evaporation of methylene chloride (7.0 g, 75%), the residual oil was shown by NMR spectroscopy to consist of the nitroethers **8** and **9** (1:3 ratio).

Results and discussion

We have found that reaction of ethers **4** at 20 °C or **5** at 60 °C with HNO_3 in HF give mixtures of 2- and 6-difluoromethoxy- or 2- and 6-pentafluorophenoxy-3-nitrohexafluorocyclohexa-1,4-dienes [(**6, 7**) for R = CHF_2, (**8, 9**) for R = C_6F_5], respectively (Scheme 2.)

All product structures were assigned on the basis of ^{19}F NMR and IR spectral data (Table 1) which, in our opinion, do not require detailed analysis as compared to the data obtained earlier for related compounds [1–4, 12]. It should only pointed be out that, as judged from the ^{19}F NMR spectra, the nitroethers **7** and **9** were mixtures of geometrical isomers in a ratio of ~1:1 in both cases.

The ratio of isomeric nitrodienes **8** and **9** derived from nitrofluorination of ether **5** was 1:3. The composition of the mixture of nitrodienes **6** and **7** is significantly dependent on the reaction time and the ratio of components in the nitrating system HNO_3–HF: the greater the reaction time and the smaller the percentage of HNO_3, the greater the content of **6** in the final mixture at the expense of isomer **7**. This variation of isomer product ratio apparently arises from the reversible formation of nitrodiene **7** from ether **4**, as indicated by the fact that treatment of the mixture of isomers **6** and **7** with HF at 20 °C for 12 h resulted in complete transformation of **7** into **4**. In contrast, ether **6** did not revert to **4**, but 1-di-fluoromethoxy-2,3,3,4,5,6,6-heptafluorocyclohexa-1,4-diene (**10**) was formed by slow displacement of the nitro group in **6** by fluorine (cf. refs. 2–4). This result has enabled us to isolate the individual isomer **6**. Interaction of the mixture of **6** and **7** with HF at elevated temperature (50 °C) gave ether **4** and diene **10**.

Conversion of nitrodiene **7** into ether **4** apparently involves the acid-catalyzed elimination of a fluoride anion during the first step leading to the

4,5   6,8   7,9

4,6,7 R = CHF_2; 5,8,9 R = C_6F_5
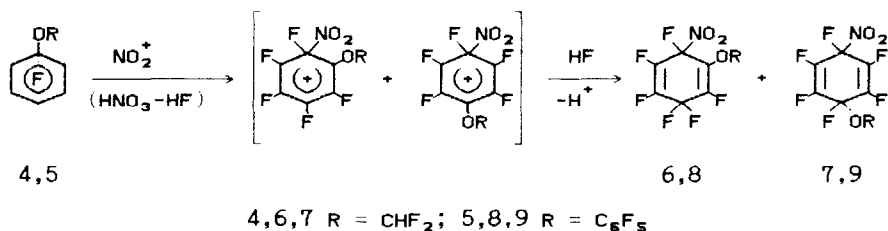
Scheme 2.

benzenium ion **11**. The latter is stabilized by the *para*-alkoxy group and loses the nitronium cation to give ether **4**. The irreversibility of the formation of isomer **6** is evidently due to the fact that it requires elimination of the fluoride ion from a very stable group $-CF_2-$, and the reaction which occurs is the acid-catalyzed elimination of the nitrite ion (cf. ref. 15) to give the benzenium ion **12** with the alkoxy group in the non-resonant *meta* position which diminishes its stability and, consequently, slows down its formation relative to ion **11**. The subsequent capture of ion **12** by hydrogen fluoride yields the diene **10** (Scheme 3).

In view of reversibility of the formation of diene **7**, the product composition during the nitrofluorination of ether **4** may differ from the kinetically controlled regioselectivity of nitronium cation addition to the substrate because of the higher content of **6**, whose formation is virtually irreversible. This conclusion may be extended to other cases of polyfluoroarene nitrofluorination involving nitronium cation attack *para* to a non-fluorine substituent which efficiently stabilizes the carbocationic π-system and yielding polyfluorinated dihydroarenes with this substituent *ipso* to the fluorine. The latter characteristic of such dienes provides the possibility of acid-catalyzed heterolysis of the $C-F$ bond. The irreversible character of formation of polyfluorinated dihydroarenes containing $-CF_2--$ fragment evidently arises from the increased strength of the geminal $C-F$ bonds [16, 17] and is in line with previous results regarding the nitrofluorination of 1-*H*-heptafluoronaphthalene [18].

Thermolysis of nitrodiene **6** or its mixture with isomer **7** gives respectively 2-difluoromethoxy-3,4,4,5,6-pentafluorocyclohexa-2,5-dien-1-one (**13**) or its mixture with 4-difluoromethoxy-2,3,4,5,6-pentafluorocyclohexa-2,5-dien-1-

Scheme 3.

| 6,13 | X = $OCHF_2$, Y = F |
| 7,14 | X = F, Y = $OCHF_2$ |
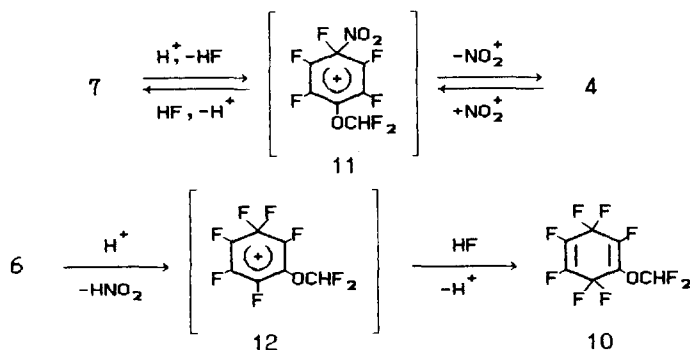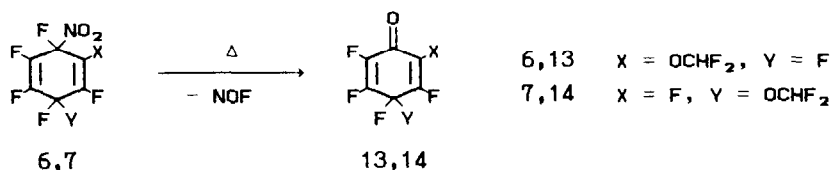
Scheme 4.

one (14), due to the transformation of the $-CFNO_2-$ fragment into the carbonyl group (Scheme 4) [19].

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