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OXIDATION OF PERFLUOROAROMATICS

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SUMMARY

3,4,5,6-Tetrafluoro-2-nitroaniline (I), 2,3,5,6-tetrafluoro-4-nitroaniline (IV) and 2,5,6-trifluoro-4-nitro-1,3-phenylenediamine (VI) react with nitrous acid to give 3,4,5-trifluoro-6-nitro-1,2-diazo-oxide (III), 3,5,6-trifluoro-4-nitro-1,2-diazo-oxide (V) and 5-fluoro-6-nitro-bis-1,2:3,4-diazo-oxide (VII), respectively. Reduction of the diazo-oxide (III) with hypophosphorous acid gives 4,5,6-trifluoro-3-nitrophenol (VIII). Treatment of 2,3,4,6-tetrafluoroacetanilide with nitric acid affords trifluoro-*p*-benzoquinone (X), the reduction of which gives trifluorohydroquinone (XI). Proton and fluorine chemical shifts and coupling constants of the new compounds are reported.

INTRODUCTION

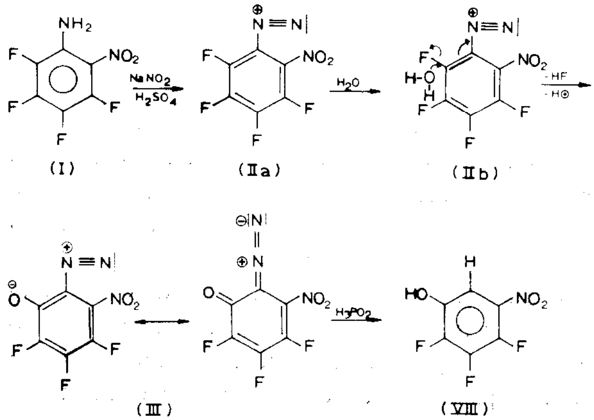
Perfluorobenzene and some of its derivatives undergo oxidation to perfluoro-*p*-benzoquinone (fluoranil)[1,2]. Low to medium yields show that the reaction is accompanied by the breaking down of the aromatic ring. Indeed, perfluorophenol gives difluoromaleic acid on oxidation with peroxyacetic acid; this material is also obtained by oxidation of fluoranil with the same reagent[3].

Being interested in the preparation of fluoronitromaleic acid, we tried to oxidize pentafluoronitrobenzene. Under the conditions which convert hexafluorobenzene to fluoranil—refluxing with fuming nitric acid—pentafluoronitrobenzene was partly recovered unchanged and partly degraded to fluorine-free fragments, mainly oxalic acid. Perfluoro-*o*-nitrophenol oxidized by dilute nitric acid gave a complex mixture of fluorinated and fluorine-free dicarboxylic acids. Similar results were obtained from the oxidation of the same compound with peroxyacetic acid.

Since *p*-benzoquinone is readily obtained by oxidation of aniline, we turned our attention to perfluoro-*o*-nitroaniline which we expected to give trifluoronitro-*p*-benzoquinone, a potential precursor of fluoronitromaleic acid. To our surprise, the reaction of 3,4,5,6-tetrafluoro-2-nitroaniline (I) with potassium dichromate and sulfuric acid as well as with nitric acid took an entirely different course.

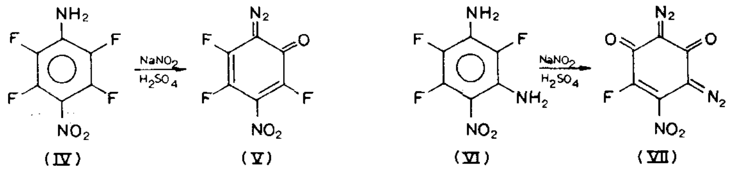
The product was a yellow compound of empirical formula $C_6F_3N_3O_3$. The infrared spectrum showed a fairly rare peak at 4.7 μ, and the NMR spectrum showed three different fluorines. The compound proved to be 3,4,5-trifluoro-6-nitro-1,2-diazo-oxide (III) as confirmed by another, more straightforward, synthesis from the same starting material and nitrous acid. Its formation can be interpreted as follows:

Nitrous acid converts (I) to the 3,4,5,6-tetrafluoro-2-nitrobenzenediazonium ion (IIa) in which the *para* and *ortho* positions are activated for nucleophilic displacement of fluorine by water (IIb). Loss of a proton then gives (III). Formation of diazo-oxides is general in the diazotization of *o*- and *p*-aminophenols, *e.g.*, tetrafluoro-*o*- and -*p*-aminophenol[4]. In our case, it was preceded by displacement of fluorine. This reaction was observed during diazotization of 3,4,6-trifluoro-2-nitroaniline[5] and 4-fluoro-3-nitroaniline[6]. Of the two possible positions for nucleophilic displacement of fluorine, the position *ortho* to the diazo group seems to be preferred to the *para* position. NMR and mass spectrometric data for the diazo-oxide are consistent with structure (III), and hypophosphorous acid reduction of the diazo-oxide to (VIII) provided additional evidence for this structure. The structure of (VIII) was determined primarily by NMR spectroscopy (Table 1). The reported coupling constants are quite consistent with structure (VIII) and are totally inconsistent with the structure of 2,5,6-trifluoro-3-nitrophenol which would have been the product of the reduction of a *para*-diazo-oxide.

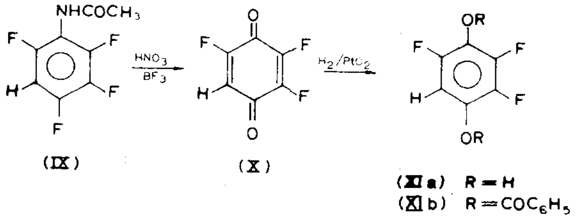


Formation of the diazo-oxide by treatment of (I) with nitric acid or dichromate is more difficult to rationalize. In the case of nitric acid, it is possible that some reduction to nitrous acid takes place providing *in situ* generation of this reagent. For the case of the dichromate experiments, loss of the nitro group by nucleophilic substitution in the acidic reaction medium would provide a source of nitrous acid. The fact that yields of diazo-oxide were never greater than 50% is consistent with this hypothesis. However, no by-products were ever found.

Two other diazo-oxides were also prepared by nitrous acid treatment of the corresponding amines. 2,3,5,6-Tetrafluoro-4-nitroaniline (IV) gave 3,5,6-trifluoro-4-nitro-1,2-diazo-oxide (V) and 2,5,6-trifluoro-4-nitro-1,3-phenylenediamine (VI) gave 5-fluoro-6-nitro-bis-1,2:3,4-diazo-oxide (VII).



In order to conclude our study of the oxidation of perfluoronitroanilines, we intended to oxidize 2,4,5,6-tetrafluoro-3-nitroaniline. To prepare this compound, we nitrated 2,3,4,6-tetrafluoroacetanilide (IX) according to a procedure for the preparation of 3,4,6-trifluoro-2-nitroaniline[5]. This technique however failed entirely, and the unchanged starting compound (IX) was recovered. Under more forcing conditions described for the preparation of pentafluoronitrobenzene[7], *viz.* the use of fuming nitric acid in sulfolane and boron trifluoride as a catalyst, the reaction took an irregular course *, and oxidation rather than nitration occurred to give trifluoro-*p*-benzoquinone (X). Hydrogenation of (X) gave trifluorohydroquinone (XIa) which was characterized as the dibenzoate (XIb).



EXPERIMENTAL

Melting points are not corrected. Infrared spectra were measured on a Beckman 5A spectrophotometer. Proton and fluorine NMR spectra were obtained on a JEOL PFT-100 spectrometer at 100 and 94 MHz, respectively. Mass spectra were obtained on a Hitachi–Perkin–Elmer RMU-7 spectrometer. Physical constants, analytical and spectral data are listed in Table 1.

3,4,5,6-Tetrafluoro-2-nitroaniline (I), 2,3,5,6-tetrafluoro-4-nitroaniline (IV) and 2,5,6-trifluoro-4-nitro-1,3-phenylenediamine (VI) were prepared as described in the literature[8] except that chromatographic separation was carried out on silica

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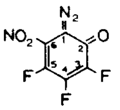
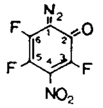
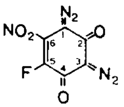
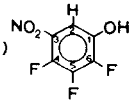
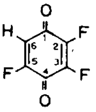
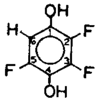
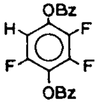
* A similar anomaly was observed during the treatment of 1,2,4,5-tetrafluorobenzene with fuming sulfuric and fuming nitric acid when 2,5-difluoro-*p*-benzoquinone was obtained in lieu of a nitro compound[5].

TABLE 1

PHYSICAL CONSTANTS OF SOME DIAZO-OXIDES AND RELATED COMPOUNDS

Compound	Formula	M.p./°C	IR maxima/μm	Analysis: Found (calcd.)			
				C	H	F	N
(III)		153–155.5 (decomp.)	4.70, 6.12, 6.90, 7.28, 7.54, 7.70, 8.62, 9.22, 9.51, 9.97	32.70 (32.90)	0.07 (0)	26.50 (26.00)	19.05 (19.20)
(V)		86–89 (decomp.)	4.70, 6.15, 7.41, 7.85, 9.65, 9.90			26.36 (26.02)	
(VII)		118–119 (decomp.)	4.73, 7.10, 7.45, 7.56, 9.80			9.18 (8.45)	
(VIII)		78.5–79.5	2.81, 3.23, 6.18, 6.71, 7.22, 7.45, 7.62, 7.86, 8.12, 8.57, 9.00, 9.66, 10.88, 11.55, 14.49	37.36 (37.30)	1.11 (1.04)	30.24 (29.50)	6.83 (7.25)
(X)		148–149 (sealed capillary)	5.88, 5.94, 6.10, 7.46, 7.58, 7.72, 8.61, 9.57, 10.57, 11.48, 14.90	43.92 (44.45)	0.72 (0.62)	35.54 (35.16)	
(XIa)		129.5–131	2.80, 6.17, 6.73, 7.52, 7.85, 8.20, 8.33, 8.73, 9.58, 9.70, 10.60, 10.82				
(XIb)		134–135		64.77 (64.52)	3.45 (2.98)		

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[a] Spectra were determined in deuterochloroform, concentration 0.02–0.03 g (0.5 cm^3)$^{-1}$.

[b] Proton shifts are downfield from TMS. Fluorine shifts are downfield from hexafluorobenzene.

Mass spectrum/*m*/*e* (intensity)	NMR spectral data[a]	
	Chemical shifts/ppm[b]	Coupling constants/Hz
219(66), 193(2), 191(2), 145(73), 133(24), 117(100), 105(24), 100(6), 98(24), 95(7), 93(40), 86(7), 79(16), 74(5), 71(24)	$\Phi_{3(\text{or } 5)}$: 22.4 Φ_4: 19.6 $\Phi_{5(\text{or } 3)}$: 24.8	*J*(3,4) or *J*(4,5): 18.0 *J*(3,5): 8.5[c] *J*(4,5) or *J*(3,4): 12.1
219(33), 191(20), 145(23), 133(17), 117(100), 105(25), 98(23), 95(19), 93(33), 86(9), 79(15), 74(10), 71(18)	Φ_a: —2.2[d] Φ_b: 22.1 Φ_c: 25.5	*J*(a,b): 16.7 *J*(a,c): 11.1 *J*(b,c): 15.5
225(92), 181(3), 169(5), 151(39), 131(5), 119(6), 111(6), 95(100), 83(38), 73(10), 71(42)	Φ_5: 29.3	
193(33), 163(7), 147(25), 135(25), 119(100), 99(55), 93(40), 87(32), 80(18), 79(13), 75(58), 74(12), 71(13)	δ_2: 7.62 Φ_4: 14.6 Φ_5: 9.0 Φ_6: 15.8	*J*(2,4): 6.8 *J*(4,5): 21.3 *J*(2,5): 2.5 *J*(4,6): 7.6 *J*(2,6): 8.4 *J*(5,6): 19.7
162(100), 134(10), 115(5), 106(65), 91(7), 90(17), 87(5), 75(14), 72(15), 71(13)	δ_6: 6.45 Φ_2: 24.8 Φ_3: 18.4 Φ_5: 49.6	*J*(2,6): 6.0 *J*(2,3): 5.5 *J*(3,6): 0.9 *J*(2,5): 2.1 *J*(5,6): 8.2 *J*(3,5): 0.3
164(100), 144(2), 135(2), 116(15), 115(2), 106(2), 91(2), 88(24), 87(7), 82(3), 71(3)	δ_6: 6.54 Φ_2: —4.2 Φ_3: 5.1 Φ_5: 22.2	*J*(2,6): 7.7 *J*(2,3): 21.2 *J*(3,6): 2.5 *J*(2,5): 9.8 *J*(5,6): 11.4 *J*(3,5): 6.0

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[c] In trifluoroacetic acid, compound (III) gave an ABX pattern. Analysis of the spectrum showed that the sign of *J*(3,5) (8.5 Hz) was opposite to that of *J*(3,4) (18.0 Hz).

[d] Assignment of the NMR parameters of compound (V) to specific positions within the molecule was not attempted.

gel. Benzene elution gave first 54% of (I) and then 28% of (IV). Ether elution gave 4.6% of (VI). The 2,3,4,6-tetrafluoroaniline used was a commercial product (Columbia Organic Chemical).

Preparation of 3,4,5-trifluoro-6-nitro-1,2-diazo-oxide (III)

(a) By oxidation with potassium dichromate

3,4,5,6-Tetrafluoro-2-nitroaniline (I) (2.1 g, 0.01 mol) was partly dissolved in a mixture consisting of 32 cm^3 of water and 7.8 cm^3 of concentrated sulfuric acid. Finely powdered potassium dichromate (3 g, 0.01 mol) was added in small portions to the stirred mixture over a period of 1 h. Carbon tetrachloride was added (10 cm^3) and the mixture was stirred at room temperature for a further 16 h. Another 10 cm^3 of carbon tetrachloride was then added to dissolve the yellow precipitate which had formed, the organic layer separated from the dark-green aqueous layer and the latter further extracted with three 10 cm^3 portions of chloroform. The combined organic solutions were dried with magnesium sulfate and evaporated to dryness *in vacuo* to give 2 g of a yellow crystalline residue. Chromatography over 60 g of silica gel and elution with benzene recovered 0.5 g (24%) of starting material (I) whereas elution with chloroform afforded 0.55 g (33%) of glistening orange crystals of 3,4,5-trifluoro-6-nitro-1,2-diazo-oxide (III), m.p. 153–154 °C (decomp.) after recrystallization from ethanol.

(b) By oxidation with nitric acid

3,4,5,6-Tetrafluoro-2-nitroaniline (I) (1.3 g, 0.0062 mol) was stirred with a mixture consisting of 5 cm^3 of concentrated nitric acid and 5 cm^3 of water and heated in a Teflon beaker at 65–75 °C for 1 h. The dark-orange residue was diluted with 5 cm^3 of water which precipitated bright yellow crystals. Evaporation in a dish at room temperature yielded 1.0 g (74%) of crude 3,4,5-trifluoro-6-nitro-1,2-diazo-oxide (III) which, after recrystallization from carbon tetrachloride or ethanol, gave the pure product, m.p. 153–154 °C (decomp.), identical with that prepared by oxidation with potassium dichromate (no depression of mixed melting point).

(c) By diazotization with nitrous acid

3,4,5,6-Tetrafluoro-2-nitroaniline (I) (4.2 g, 0.02 mol) was dissolved in 42 cm^3 of 70% sulfuric acid, the solution cooled and 1.6 g (0.022 mol) of finely powdered sodium nitrite added in portions over a period of 15 min at temperatures in the range −15 °C to −12 °C. The mixture was stirred for a further 2 h at 10–20 °C and then extracted with 50 cm^3 of dichloromethane. The aqueous layer was diluted with 20 cm^3 of water and extracted with four 30 cm^3 portions of dichloromethane. The combined extracts were washed with 5 cm^3 of water, dried with anhydrous magnesium sulfate and evaporated *in vacuo* at room temperature to give 4 g (91%) of 3,4,5-trifluoro-6-nitro-1,2-diazo-oxide (III), m.p. 153–155.5 °C (decomp.), identical with the compounds prepared by oxidation with potassium dichromate and nitric acid.

Preparation of 3,5,6-trifluoro-4-nitro-1,2-diazo-oxide (V)

A solution consisting of 1.0 g (0.0048 mol) of 2,3,5,6-tetrafluoro-4-nitroaniline (IV) in 10 cm^3 of 70% sulfuric acid was stirred and cooled to −5 °C to 0 °C and then treated with 0.5 g (0.007 mol) of sodium nitrite added in portions over a period of 10 min. After 1 h, the resulting yellow-brown reaction mixture was extracted with dichloromethane. Evaporation of the extract at room temperature gave 0.7 g (67%) of orange-brown crystals which, after recrystallization from 2 cm^3 of chloroform, afforded dark brown prisms of (V), m.p. 86–89 °C (decomp.). The compound was unstable and decomposed slowly even at room temperature.

Preparation of 5-fluoro-6-nitro-bis-1,2:3,4-diazo-oxide (VII)

A solution consisting of 0.4 g (0.0019 mol) of 2,5,6-trifluoro-4-nitro-1,3-phenylenediamine (VI) in 4 cm^3 of 70% sulfuric acid was treated with 0.4 g (0.0058 mol) of sodium nitrite as above. Extraction of the reaction mixture diluted with an equal volume of water with dichloromethane and evaporation of the extract to dryness *in vacuo* at room temperature gave 0.3 g (69%) of orange crystals of (VII), m.p. 118–119 °C (decomp.) (after recrystallization from chloroform).

Preparation of 4,5,6-trifluoro-3-nitrophenol (VIII)

3,4,5-Trifluoro-6-nitro-1,2-diazo-oxide (III) (2.0 g, 0.0092 mol) was stirred with 15 cm^3 of 50% hypophosphorous acid at room temperature. Use of a smaller amount of hypophosphorous acid resulted in lower yields. During the first hour the temperature rose to 35 °C. The red-brown mixture was stirred for 8 h, then extracted with four 25 cm^3 portions of benzene, the aqueous layer diluted with 20 cm^3 of water and the solution extracted further with three 25 cm^3 portions of benzene. The combined benzene extracts were washed with 5 cm^3 of water, dried with anhydrous magnesium sulfate and evaporated to dryness *in vacuo* at 40 °C. The residue (1.3 g, 73.5%) was recrystallized from carbon tetrachloride to give 0.7 g (40%) of yellow needles of (VIII), m.p. 78.5–79.5 °C (after recrystallization from carbon tetrachloride). The compound dissolved in an aqueous solution of ferric chloride to produce a dark-red colored solution.

*Preparation of 2,3,5-trifluoro-*p*-benzoquinone (X)*

A solution consisting of 6 cm^3 (0.125 mol) of white fuming nitric acid in 24 cm^3 of sulfolane was cooled to 0 °C and saturated with boron trifluoride over a period of 15 min. During this time the temperature rose to 55 °C and was reduced to 10 °C by cooling with a Dry Ice/acetone bath. 2,3,4,6-Tetrafluoroacetanilide (IX) (16.3 g, 0.079 mol), prepared from commercial 2,3,4,6-tetrafluoroaniline according to the method described in the literature[9], was added portionwise to the stirred solution over a period of 75 min at 10–30 °C. The resulting brown solution was warmed in a water bath. At 55 °C a sudden vigorous reaction commenced resulting in a temperature rise to *ca.* 150 °C. After cooling, the dark-brown reaction mixture was diluted with 200 cm^3 of ice and water and extracted with three 100 cm^3 portions of benzene and with 50 cm^3 of dichloromethane. After treatment with sodium hydroxide, the aqueous layer was found not to contain any amine. The combined extracts were washed with 10 cm^3 of water, dried with anhydrous magnesium sulfate and evaporated *in vacuo*. The dark-brown residue (18 g) was chromatographed over 250 g of silica gel. Benzene elution (1200 cm^3) gave only 1.6 g (12.5%) of bright yellow crystals of trifluoro-*p*-benzoquinone, m.p. after sublimation 148–149 °C (sealed capillary).

Preparation of 2,3,5-trifluorohydroquinone (XIa)

A solution consisting of 0.4 g (0.0025 mol) of 2,3,5-trifluoro-*p*-benzoquinone in 15 cm^3 of absolute ethanol was hydrogenated over 0.1 g of platinum oxide at room temperature and atmospheric pressure for 30 min. Filtration and evaporation of the colorless filtrate *in vacuo* at room temperature gave 0.35 g (86.5%) of 2,3,5-trifluorohydroquinone, m.p. 129.5–131 °C (after vacuum sublimation). The compound is immediately oxidized with ferric chloride in aqueous solution to the original trifluoro-*p*-benzoquinone.

Preparation of 2,3,5-trifluorohydroquinone dibenzoate (XIb)

This compound was prepared from 0.16 g of (XIa) and 0.3 cm^3 of benzoyl chloride in 2 cm^3 of 2 mol l^{-1} sodium hydroxide solution. It melted at 134–135 °C (after recrystallization from ethanol) while a mixed melting point with (XIa) occurred below 110 °C.

Compounds (X), (XIa) and (XIb) exhibit some properties different from those listed in the literature[10]. The quinone (X) was stable but not hygroscopic and could be sublimed *in vacuo* as well as at atmospheric pressure without decomposition. The hydroquinone (XIa) exhibited a m.p. of 129.5–131 °C (depending on the rate of heating) (the literature value is 112–113 °C) and the dibenzoate (XIb) melted at 134–135 °C (the literature value is 80 °C).

The fluorine coupling constants of quinone (X) appear unusually small, and we intend to prepare some other quinones in order to investigate this matter further. On the other hand, the coupling constants of the hydroquinone (XIa) are very close to predicted values[11].

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