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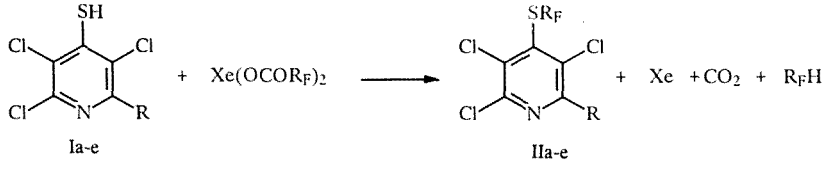
REACTION OF POLYHALOPYRIDINES 4.* REACTION OF MERCAPTOPOLYCHLOROPYRIDINES WITH FLUORINE-CONTAINING XENON COMPOUNDS

A. M. Sipyagin, I. A. Pomytkin, S. V. Pal'tsun, and N. N. Aleinikov

A method has been developed for the perfluoroalkylation of mercaptopolychloropyridines by the thermolysis of xenon(II) perfluoroalkanecarboxylates, obtained by the reaction of xenon difluoride and aperfluoroalkanecarboxylic acids, in the presence of the appropriate thiol. Perfluoroalkylthio derivatives of polychloropyridines have been synthesized. The fluorosulfonyl derivatives of tetrachloropyriidne and of tetrachloropyridine N-oxide were obtained by the action of XeF_2 on mercaptotetrachloropyridine dissolved in aqueous HF.

It is known that polyhalopyridines are stable to the action of such reactive reagents as mineral acids, oxidizing agents, and halogenating agents [2]. Their mercapto derivatives may be interesting models for investigating the reaction of the thiol group with highly reactive fluorine-containing reagents such as xenon difluoride, which occurs with retention of the pyridine ring.

We reported recently on the possibility of alkylating thiols with the aid of xenon compounds [3]. Results are given in the present work of investigations on the reactions of mercaptopolychloropyridines (I) with fluorine-containing reagents obtained from compounds of Xe(II). We have shown that decomposition of xenon beisperfluoroalkanecarboxylates in the presence of thiols (I) leads to the perfluoroalkylation of the latter. The xenon bisperfluoroalkanecarboxylates are obtained previously (method A) or *in situ* (method B). The perfluoroalkylthiopolychloropyridines (IIa-e) were formed in yields of 45-60% (method A) or 36.5-85% (method B).



Ia-e IIa-e

IIa,d,e $R_F = CF_3$; II b C_2F_5; II c C_3F_7; I, II a-e R = Cl; I, II d CCl_3; I, II e CN

Compounds (IIa-c,e) are liquids at room temperature and crystallize readily on storage in the cold. Compound (IId) is a white crystalline substance. The structures of compounds (IIa-e) were confirmed with the aid of NMR spectroscopy and mass spectrometry. The CF_3S group in compounds (IIa,d,e) is displayed in the ^{19}F NMR spectra as a singlet near 38 ppm (Table 1) and in the ^{13}C NMR spectra as a quartet at 128 ppm, the J_{CF} constant being 313 Hz (Table 2). The introduction of trifluoromethyl groups into the molecules of the initial thiols (I) leads to a significant change in the ^{13}C chemical shifts of the pyridine ring carbon atoms. A significant displacement of the signals of the $C_{(4)}$ atom of 9-10 ppm towards high field and of the $C_{(3)}$ and $C_{(5)}$ atoms of 9-12 ppm towards low field is observed. Compound (IIb) is characterized in the ^{19}F NMR spectrum by the presence of a pair of signals with values of chemical shifts corresponding to the perfluoroethyl group and there are three

*For Communication 3 see [1].

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TABLE 1. ^{13}C NMR Spectra of Compounds I, IIa, d, e

Compound	$C_{(2)}$	$C_{(3)}$	$C_{(4)}$	$C_{(5)}$	$C_{(6)}$	CF_3	Other groups
Ia	145,6	126,1	149,8	126,1	145,6	—	—
IIa	147,1	137,4	137,2	137,4	147,1	128,2 q J_{CF} = 313 Hz	—
Id	144,8	126,0	149,9	129,4	152,3	—	95,4 (CCl_3)
IId	145,4	136,4	139,3	140,7	150,6	128,1 q J_{CF} = 313 Hz	94,5 (CCl_3)
Ie	128,9	130,8	148,1	131,2	149,4	—	113,3 (CN)
IIe	130,6	141,8	137,4	143,8	150,0	128,0 q J_{CF} = 313 Hz	113,3 (CN)

TABLE 2. Mass, ^{19}F NMR, and IR Spectra of Compounds IIa-e

Compound	Mass spectrum, m/z (I_{rel}, %)	^{19}F NMR (δ, ppm)	IR spectrum (ν, cm^{-1})
IIa	315 (100) M^+, 296 (4) $[M - F]^+$, 280 (6) $[M - Cl]^+$, 246 (6) $[M - CF_3]^+$, 211 (66) $[M - CF_3—Cl]^+$, 69 (75)	38,5 (s, CF_3)	1498 (pyridine), 1316, 1220, 1192, 1154, 1080 (CF_3, C—F)
IIb	365 (76) M^+, 346 (2) $[M - F]^+$, 296 (41) $[M - CF_3]^+$, 246 (9) $[M - C_2F_5]^+$, 211 (100) $[M - C_2F_5—Cl]^+$, 119 (60) $[C_2F_5]^+$, 69 (45)	-6,2 (2F, br.s CF_3), -11,1 (2F, br.s , CF_2)	1500 (pyridine), 1330, 1315, 1220, 1195, 1155, 1110, 1085 (CF_3, C—F)
IIc	415 (100) M^+, 296 (41) $[M - C_2F_5]^+$, 246 (13) $[M - C_3F_7]^+$, 211 (62,5) $[M - C_3F_7—Cl]^+$, 169 (20) $[C_3F_7]^+$, 69 (40)	-2,8 (3F, J = 9 Hz CF_3), -6,8 (2F, J = =9 Hz., -46,8 (2F, br.s , CF_2)	1502 (pyridine), 1336, 1318, 1220, 1070, 1035 (CF_3, CF_2, C—F)
IId	397 (15) M^+, 378 (2,5) $[M - F]^+$, 362 (100) $[M - Cl]^+$, 328 (4) $[M - CF_3]^+$, 293 (37) $[M - CF_3—Cl]^+$, 258 (56) $[M - CF_3—2Cl]^+$, 69 (74)	38,5 (s, CF_3)	1535, 1525, 1500 (pyridine), 1340, 1320, 1220, 1185, 1160, 1115, 1088 (CF_3, C—F)
IIe	306 (100) M^+, 237 (7) $[M - CF_3]^+$, 202 (70) $[M - CF_3—Cl]^+$, 176 (20) $[M - CF_3—Cl—CN]^+$, 69 (93)	38,2 (s, CF_3)	2225 (C≡N), 1502 (pyridine), 1346, 1320, 1245, 1220, 1190, 1112, 1088 (CF_3, C—F)

signals for the perfluoropropyl group in the spectrum of (IIc). Intense molecular ion peaks were observed in the mass spectra of compounds (IIa-e), the main directions of decomposition being elimination of $[C_nF_{n+1}]^+$ and $Cl^\cdot$ fragments in various order (Table 2).

The pathways of the conversions may be represented as follows. The perfluoroalkyl radicals formed on thermolysis of xenon bisperfluoroalkanecarboxylates react by free radical replacement of the hydrogen on the sulfur atom of the mercaptopolychloropyridine R'SH (where R' is a polychloropyridine) with the generation of a R'S moiety which then recombines with $R_F^\cdot$ radicals to form the perfluoroalkyl derivatives $R'SR_F$.

$$Xe(OCOR_F)_2 \longrightarrow Xe + 2CO_2 + 2R_F^\cdot$$
$$R'SH + R_F^\cdot \longrightarrow R'S^\cdot + R_FH$$
$$R'S^\cdot + R_F^\cdot \longrightarrow R'SR_F$$

The reaction is accompanied by a side reaction forming the disulfide R'SSR' which was isolated from the reaction mixture in all experimentals.

$$2\ R'S^\cdot \longrightarrow R'SSR'$$

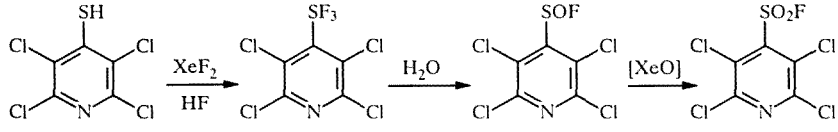
It was established during the investigations that an increase in the acceptor properties of the substituent R in the initial thiol (I) reduces the nucleophilicity of the thiol group and correspondingly the yield of perfluoroalkylation product. Method A is perferred for trifluoromethylation enabling higher yields of the desired products (IIa, d, e) to be achieved, compounds (IId, e) are formed in trace quantities by method B. the use of this method enables the direct perfluoroalkylation of thils to be broadened significantly, extending it to compounds sensitive to nucleophilic replacement of the group.

TABLE 3. Main Characteristics of Compounds IIa-e

Compound	Empirical formula	Preparative method	n_D^{20}	Mp, °C	Yield, %
IIa	$C_6Cl_4F_3NS$	A B	1,5605	—	66 36
IIb	$C_7Cl_4F_5NS$	B	1,5210	—	85
IIc	$C_8Cl_4F_7NS$	B	1,4968	—	85
IId	$C_7Cl_6F_3NS$	A	—	59-61	45
IIe	$C_7Cl_3F_3N_2S$	A	1,5615	—	50

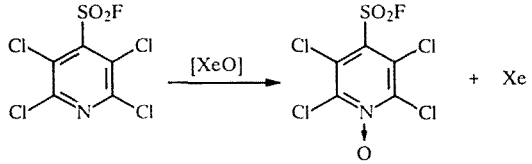
The next direction of our investigations was a study of the reaction of the thiols (I) with XeF_2 in aqueous HF, the aim being the fluorination and oxidation of the mercapto group with the aid of XeF_2. In this HF is the solvent, a component of the fluorinating agent, but the presence of water molecules is necessary to generate the oxidizing agent, the [XeO] particle. Two compounds were isolated from the reaction mixture on keeping a mixture of thiol (Ia) and XeF_2 in HF solution at 0-5°C for 1 h. These were 2,3,5,6-tetrachloro-4-fluorosulfonylpyridine (V) and its N-oxide (VI). The reaction is accompanied by the oxidation of the initial thiol to di-(2,3,5,6-tetrachloro-4-pyridyl) disulfide.

There are three signals of pyridine carbons in the ^{13}C NMR spectra of compounds (V) and (VI), which is characteristic for tetrachloropyridines substituted at position 4 [4]. The $C_{(4)}$ signal is displayed in both cases as a doublet with $^2J_{CF}$ equal to 2.1 Hz [compound (V)] and 1.7 Hz [compound (VI)]. By comparing the spectra of compounds (V) and (VI) it is seen that several carbon atom signals of the N-oxide are displaced significantly towards high field, viz. $C_{(5)}$ and $C_{(6)}$ by 10.5 ppm and $C_{(4)}$ by 5 ppm, the position of the $C_{(3)}$ and $C_{(5)}$ signals being almost unchanged. In the ^{19}F spectrum the fluorine atom of the fluorosulfonyl group is displayed as a singlet at 54.7 ppm. Intense molecular ions were observed in the mass spectra of compounds (V) and (VI). The presence of an $[M-O]^+$ ion on fragmentation of M^+ is a characteristic of the N-oxide. The general direction of decomposition of the sulfonyl fluorides (V) and (VI) is elimination of SO_2 and SO_2F.



Ia III IV V

The formation of a fluorosulfonyl fragment probably occurs by the following route. Initially the thiol group is fluorinated by XeF_2 in the presence of HF to the SF_2 derivative (III) which is hydrolyzed readily to the sulfoxide (IV) [5]. The latter may be converted to compound (V) by oxidation by the [XeO] moiety which is formed on hydrolysis of XeF_2 (the energy of the Xe−O bond is 7 kcal/mole which corresponds to weakly bound atomic oxygen [6]).



V VI

The presence of [XeO] in the reaction mixture may also explain the oxidation of part of the compound (V) formed to the N-oxide (VI).

In conclusion it should be noted that the use of xenon difluoride in reactions with mercapto derivatives of polychloropyridines provides new methods of perfluoroalkylation and fluorooxidation of thiol groups, and also of the oxidation of polychloropyridine to the N-oxide. The latter method is unique in that it enables the use of 90-95% hydrogen peroxide, which is usually used for this purpose [2], to be avoided.

EXPERIMENTAL

The IR spectra of compounds were measured with a Specord M-80 instrument in chloroform or in a liquid film. The NMR spectra were recorded in $CDCl_3$ solution with a Bruker AC-200 instrument with an operating frequency of 200 MHz

(^{1}H), 188 MHz (^{19}F), or 50 MHz (^{13}C), internal standard was TMS, external standard was trifluoroacetic acid (^{19}F). The mass spectral measurements were performed on a Finnigan 4021 instrument (direct insertion, ionization energy 70 eV).

Perfluoroalkylation of Polychloropyridine Mercapto Derivatives (I). Method A. An equimolar quantity of the initial compound (I) was added below −5°C to a stirred suspension of xenon bistrifluoroacetate, obtained by mixing stoichiometric quantities of xenon difluoride and trifluoroacetic acid in dichloromethane. The reaction mixture was stirred while heating spontaneously to 5-12°C. The end of the reaction was determined by the end of gas evolution.

Method B. Xenon difluoride (two equivalents) was added in portions to a suspension of the starting material (I) in a four−fold excess of the appropriate perfluorocarboxylic acid. The end of the reaction was determined by the end of gas evolution. The reaction mixture obtained by methods A or B was evaporated in vacuum and the residue chromatographed on silica gel, the eluent being a mixture of hexane−benzene (9:1), or hexane−benzene (3:1) for IIe). The characteristics of compounds (IIa-e) are given in Table 3.

Reaction of 2,3,5,6-Tetrachloro-4-mercaptopyridine (Ia) with Xenon Difluoride in Aqueous HF. 2,3,5,6-Tetrachloro-4-mercaptopyridien (Ia) (5 g: 0.02 mole) was dissolved with stirring in hydrogen fluoride (30 ml). water (1.5 ml) was added anmd then XeF_2 (14 g: 0.0828 mole) in portions with cooling to 0°C. After adding all the reactant the reaction mixture was maintained under cooling for a further hour, and then at room temperature in an open vessel. The HF was evaporated, the residue was washed with water, extracted with chloroform, the organic layer was dried, and evaporated. The residue was chromatographed on a column of silica gel (eluent was benzene). Two products were obtained. Compound (V) was eluted first [a white solid substance (1.5 g) was obtained] and then compound (VI) (0.5 g), also a white crystalline substance.

2,3,5,6-Tetrachloro-4-fluorosulfonylpyridine (V, $C_5Cl_4FNO_2S$). Yield was 25% of mp 56-57 °C (lit. 57-58.5°C [7]). ^{13}C NMR: 128.86 ($C_{(3)}$, $C_{(5)}$); 140.10 ($C_{(2)}$, $C_{(6)}$); 149.44 ppm (d $^2J_{CF}$ = 2.06 Hz, $C_{(4)}$). Mass spectrum, *m/z* (I_{rel}, %): 297 (76) M^+, 233 (4) $[M-SO_2]^+$, 214 (40) $[M-SO_2F]^+$.

2,3,5,6-Tetrachloro-4-fluorosulfonylpyridine N-Oxide (VI, $C_5Cl_4FNO_3S$). Yield was 8% of mp 203-205°C. ^{13}C NMR: 129.54 ($C_{(3)}$, $C_{(5)}$); 129.57 ($C_{(2)}$, $C_{(6)}$); 144.18 ppm (d, $^2J_{CF}$ = 1.71 Hz, $C_{(4)}$). Mass spectrum, *m/z* (I_{rel}, %): 313 (100) M^+, 297 (17) $[M-O]^+$, 283 (2) $[M-NO]^+$, 250 (59) $[MH-SO_2]$, 214 (7) $[M-O-SO_2F]^+$.

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