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REACTIONS OF POLYHALOPYRIDINES
6.* SYNTHESIS OF THE ISOMERIC TRIFLUOROMETHYL-TETRACHLOROPYRIDINES

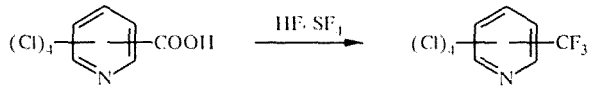
A. M. Sipyagin and B. V. Kunchenko

α, β, γ-Trifluoromethyltetrachloropyridines are obtained by the fluorination of the isomeric tetrachloropyridinecarboxylic acids with SF_4 in the presence of HF. Fluorination of the carboxylic acids proceeds more readily than in the case of unsubstituted pyridinecarboxylic acids.

The chlorinated trifluoropyridines are important intermediates in the synthesis of modern highly effective agrochemical preparations. The main methods of obtaining such compounds are described in the patent literature and reduce to replacement of the chlorine atoms of a trichloromethyl group by fluorine under the action of hydrogen fluoride or antimony trichloride, gas phase or liquid phase chlorination of trifluoromethyl derivatives of pyridine [1, 2], or fluorination of chlorine substituted pyridinecarboxylic acids with sulfur tetrafluoride [3]. The only tetrachloro derivative of trifluoromethylpyridine described is 2-trifluoromethyl-3,4,5,6-tetrachloropyridine (IIa), which was formed on fluorination of heptachloro-2-picoline with antimony trifluoride-dichloride [4]. The other isomers are as yet unknown.

The synthesis of the isomeric 3-trifluoromethyl-2,4,5,6- (IIb) and 4-trifluoromethyl-2,3,5,6-tetrachloropyridines (IIc), and also of compound (IIa), is described in the present paper. The compounds are possible synthons for obtaining a whole series of new chemical compounds.

Since heptachloro-3- and -4-picolines are unknown or are available with difficulty [1], we used the fluorination of pyridinecarboxylic acids with sulfur tetrafluoride for the synthesis of compounds (II). Tetrachloropicolinic (Ia), tetrachloronicotinic (Ib), and tetrachloroisonicotinic (Ic) acids were selected as starting materials, they were obtained by the hydrolysis of the corresponding tetrachlorocyanopyridines [5].



I a-c II a-c

The fluorination of acids (I) was effected with a mixture of sulfur tetrafluoride and hydrogen fluoride with molar ratios of reactants (Ia-c):SF_4:HF = 1:5:25 at various temperatures.

It was shown that for complete conversion of the carboxyl group into trifluoromethyl it was quite sufficient to maintain the reaction mixture in an autoclave at 60-70°C for 7-10 h. A further increase in temperature activated exchange of the pyridine ring chlorine atoms by fluorine and leads to a reduction in the yield of compound (II) (Table 1). The presence of products containing fluorine atoms in the pyridine nucleus was detected by the appearance of the appropriate signals in the ^{19}F NMR spectra, for example at −14 ppm ($F_{(2)}$ [16]) when fluorinating compound (Ib) at temperatures above 70°C. It must be noted that the number of fluorine atom signals in the spectra gradually grew as the temperature of the process was increased.

*For Communication 5 see [9].

Institute of Chemical Physics, Chernogolovka, Russian Academy of Sciences, Chernogolovka 142432. Odessa Polytechnic Institute, Odessa 270044. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 5, pp. 657-659, May, 1994. Original article submitted March 15, 1994.

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TABLE 1. Dependence of Yield of Compounds (IIa, b) on the Fluorination Temperature

Expt. No.	Starting material	T, °C	Heating time, h	Reaction product	Yield, %
1	Ia	65	7	IIa	84
2	Ia	100	7	IIb	76
3	Ia	180-190	7	IIa	12
4	Ib	65	7	IIb	92
5	Ib	100	7	IIb	31
6	Ib	150	7	IIb	8
7	Ib	200	20	IIb	0

TABLE 2. ^{13}C and ^{19}F NMR Spectra of Compounds (IIa-c) (δ, ppm)

Compound	$C_{(2)}$	$C_{(3)}$	$C_{(4)}$	$C_{(5)}$	$C_{(6)}$	CF_3	
						^{13}C	^{19}F
Pentachloropyridine	146,2	129,7	144,7	129,7	146,2	—	—
IIa	142,6 q, J_{CF} = 36,1 Hz	129,4	145,8	134,2	147,4	119,8 q, J_{CF} = =274,3 Hz	10,9
IIb	146,3	123,2 q, J_{CF} = =43,5 Hz	145,6	131,0	151,6	121,0 q, J_{CF} = =276,5 Hz	20,3
IIc	148,0	128,5	137,3 q, J_{CF} = 31,8 Hz	128,5	148,0	120,7 q, J_{CF} = =277,2 Hz	19,3

TABLE 3. Ratio of Reactants, Conditions of Carrying Out the Synthesis, Yields, and Characteristics of Compounds (IIa-c)

Reactants			Reaction condition		Reaction prouct	Yield, %	Mp or Bp
Starting material	SF_4, g	HF, ml	Time, h	T, °C			
Ia	6...7	5	7	60...65	IIa	84	Mp 36...37 °C
Ib	6...7	5	7	60...65	IIb	92	Mp 31...32 °C
Ic	6...7	5	10	60...70	IIc	60	Bp 132...134 °C (30 mm Hg) n_D^{20} = 1.5450

More severe conditions, 120°C for 8 h, are given in the literature for the fluorination of pyridine-carboxylic acids [7] and of monochloropyridinecarboxylic acids [3] with a mixture of SF_4 and HF. Consequently the presence of four chlorine atoms in the pyridinecarboxylic acid molecule facilitates significantly the conversion of the carboxyl group into trifluoromethyl, which is in agreement with the general rules for the fluorination of aromatic carboxylic acids. Electron-accepting substituents in the benzene ring increase the positive charge on the carboxyl group carbon atom, and as a result increase the yield of the corresponding benzotrifluoride derivatives [8].

Compounds (IIa, b) are white, low-melting crystalline substances but compound (IIc) is a colorless liquid. They are all soluble in organic solvents. The structures of the isomers (IIa-c) were confirmed with the aid of physicochemical methods but the data of NMR spectra for carbon and fluorine nuclei (Table 2) were the most informative. For example, in the ^{13}C spectra of compounds (II) a significant displacement (of 3.6-7 ppm), compared to that of pentachloropyridine, towards high field was observed for the signals of carbon atoms linked to the CF_3 group and a displacement of approximately 5 ppm towards low field was observed for the signals of the carbon atoms located in the para position relative to the substituent. The isomers (IIa-c) have significant differences in the position of the signal of the carbon atom linked to the CF_3 group, which is displayed as a quartet with coupling constant $^2J_{CF}$ = 31.8-43.5 Hz. The trifluoromethyl group gives a quartet at 119.8-121 ppm with coupling constant J_{CF} equal approximately to 275 Hz. It must be noted that the CF_3 signal of isomer (IIb) is at higher field and that of (IIa) at lower, an intermediate position being observed for (IIc). A similar regularity in peak positions is retained in the ^{19}F NMR spectra.

The use of sulfur tetrafluoride in a medium of hydrogen fluoride as a fluorinating agent has afforded a preparative synthesis of the isomeric tetrachloro-trifluoromethylpyridines. These compounds may be used as synthons to open prospects for the synthesis of a wide spectrum of pyridine derivatives.

EXPERIMENTAL

The NMR spectra of compounds were recorded in $CDCl_3$ solution on a Bruker AC 200 instrument with an operating frequency of 188 MHz (^{19}F) and 50 MHz (^{13}C), internal standard was TMS, external standard was trifluoroacetic acid. The GLC analyses were carried out on a PAKhV 07 chromatograph with a catharometer detector. The column (300 × 6 mm) was packed with 15% Silicone FS-1265 on Chromosorb W (AW-DMCS) 60-80 mesh. Carrier gas was helium. Separation temperature was 130°C.

Synthesis of Tetrachlorotrifluoromethylpyridines (IIa-c) ($C_6Cl_4F_3N$) (general procedure). Tetrachloropyridine-carboxylic acid, sulfur tetrafluoride, and anhydrous hydrogen fluoride were loaded into a stainless steel autoclave of capacity 100 ml. The autoclave was sealed, heated, and maintained for several hours. After cooling, the gaseous products were removed, passed through a 30% solution of potassium hydroxide, the reaction mixture was poured onto ice, the solution neutralized with sodium bicarbonate solution, and steam distilled. The products were extracted with ether, the extracts dried over sodium sulfate, and the ether evaporated. The conditions of carrying out the reaction, yields, and characteristics of compounds (IIa-c) are given in Table 3.

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