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POLYHALOAROMATICS. PART I. 4,5,6,7-TETRACHLORO-1,1,3,3-TETRAFLUORO-1,3-DIHYDROISOBENZOFURAN AND RELATED COMPOUNDS FROM THE REACTION OF TETRACHLOROPHTHALIC ANHYDRIDE WITH SULPHUR TETRAFLUORIDE

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SUMMARY

Fluorination of tetrachlorophthalic anhydride 1 or tetrachlorophthalic acid hemihydrate 4 with an excess of sulphur tetrafluoride provides an efficient one-step synthesis of 4,5,6,7-tetrachloro-1,1,3,3-tetrafluoro-1,3-dihydroisobenzofuran 2. 3,4,5,6-Tetrachloro-2-(trifluoromethyl)benzoyl fluoride 3 is formed as a side product. A method for the quantitative removal of fluoride 3 and its isolation as 3,4,5,6-tetrachloro-2-(trifluoromethyl)benzoic acid 6 has been developed. The reduced SF_4 to 1 ratio gives a mixture of 2 and 4,5,6,7-tetrachloro-3,3-difluoro-3-hydroisobenzofuranone 5.

INTRODUCTION

Tetrachlorophthalic anhydride 1 is a versatile, commercially available inexpensive intermediate with many applications [1]. Regarding fluoroderivatives, the anhydride was used as starting material for a three-step synthesis of tetrafluorophthalic acid [2] and for a four-step synthesis of tetrafluorophthalonitrile [3] with overall yields 18% and 33%, respectively. More recently, a high yield conversion of tetrachlorophthaloyl dichloride to tetrafluorophthaloyl difluoride, i.e. the crucial step on the way from anhydride 1 to tetra-

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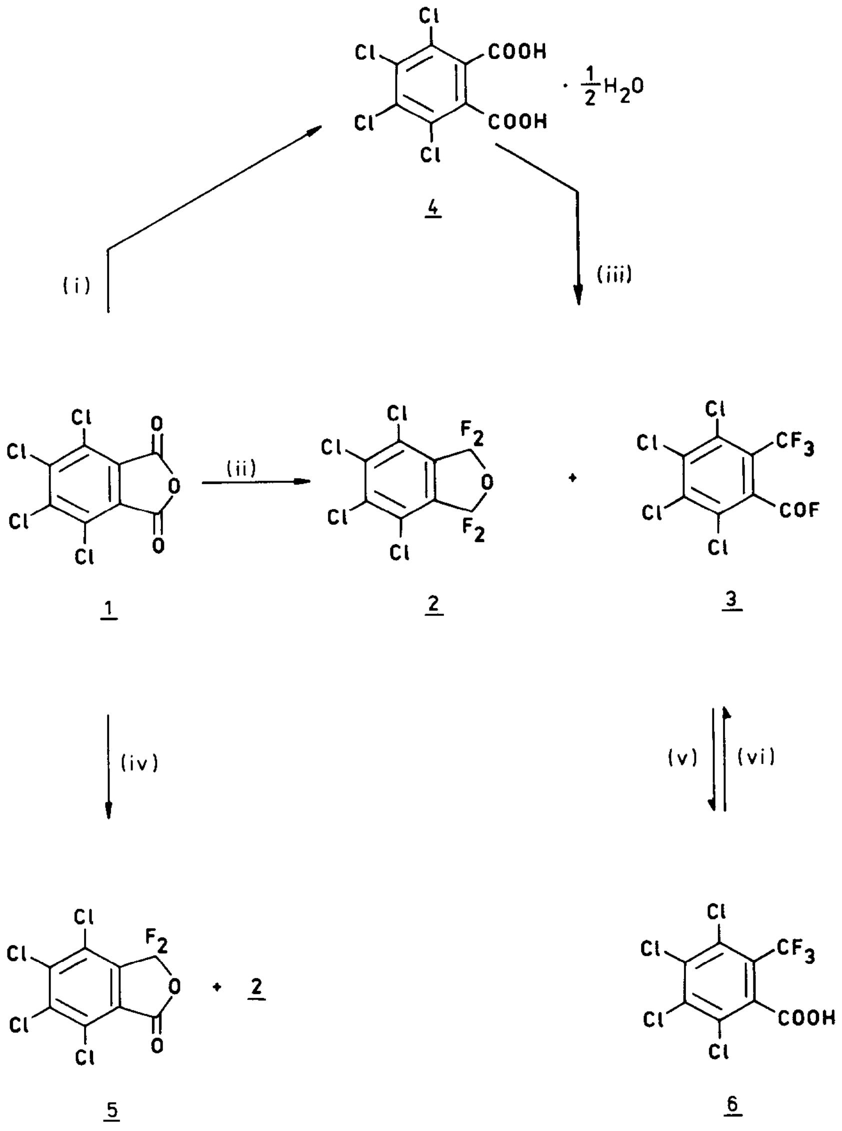
fluorophthalic acid, has been patented [4]. Anhydride 1 was also converted to 4,5,6,7-tetrachloro-1,1,3,3-tetrafluoro-1,3-dihydroisobenzofuran 2 in a two-step process involving chlorination with phosphorus pentachloride followed by fluorination with antimony trifluoride [5].

The aim of the present work was to elaborate a simple one-step synthesis of chlorofluoro-dihydroisobenzofuran 2 by fluorination of tetrachlorophthalic anhydride 1 with sulphur tetrafluoride. Compound 2 has been deemed as useful intermediate for a number of chlorofluoro- and perfluoroaromatics.

RESULTS AND DISCUSSION

Tetrachlorophthalic anhydride 1, although resistant to sulphur tetrafluoride alone, undergoes fluorination with a mixture of sulphur tetrafluoride and anhydrous hydrogen fluoride at the temperature over 130°C, preferably, at 190 - 200°C. When an excess of the fluorinating mixture was used, fluorination of both carbonyl groups in 1 occurred to give high yield of the required 4,5,6,7-tetrachloro-1,1,3,3-tetrafluoro-1,3-dihydroisobenzofuran 2. This product, after washing with aqueous potassium hydroxide and crystallisation with hot methanol, gave satisfactory elemental analysis and its melting point was close to the reported one [5]. However, the IR spectrum exhibited a sharp absorption at 1860 cm^{-1} of medium intensity, thus suggesting the presence of certain amount of an acid fluoride. Indeed, this fluoride was isolated by the column chromatography on silica-gel and then identified as 3,4,5,6-tetrachloro-2-(trifluoromethyl)benzoyl fluoride 3. The amount of isolated 3 was 7% of the total weight of the crude product. Neither tetrachlorophthaloyl difluoride nor 3,4,5,6-tetrachloro-1,2-bis(trifluoromethyl)benzene were found.

Compound 2 (also contaminated with 3) was obtained in equally good yield by fluorination of tetrachlorophthalic acid hemihydrate 4, which can be readily prepared by refluxing the anhydride in water [6]. In the reaction with the acid hemihydrate, the required amount of hydrogen fluoride is formed *in situ* by the reaction of sulphur tetrafluoride with water and with hydroxyl groups of the acid. This



SCHEME 1.

Reagents and reaction conditions: (i) H_2O, reflux; (ii) SF_4/HF, 190-200°C; (iii) SF_4, 190-200°C; (iv) SF_4/HF, 190-200°C; (v) AcONa/AcOH, reflux; (vi) SF_4/HF, 20°C or 190-200°C.

allows handling of anhydrous hydrogen fluoride to be avoided, but sufficiently more sulphur tetrafluoride should be used.

The decreased ratio of sulphur tetrafluoride to anhydride 1 resulted in incomplete fluorination to give a mixture of compound 2 and 4,5,6,7-tetrachloro-3,3-difluoro-3-hydroisobenzofuranone 5, the latter being the predominant product. Compounds 2 and 5 were easily separated due to a difference in solubility of these compounds in n-pentane.

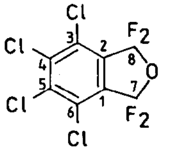
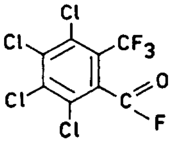
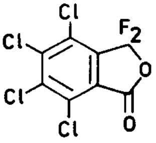
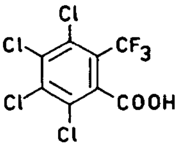
Acid fluoride 3 is difficult to remove from the main product 2 by usual procedures like washing with alkaline solutions. Crystallisation from hot methanol also did not remove 3. We have found that fluoride 3 may be quantitatively removed by refluxing the crude product with a solution of sodium acetate in acetic acid. Pouring of the resultant homogeneous solution into water gave a precipitate of compound 2 and addition of hydrochloric acid to the aqueous solution precipitated 3,4,5,6-tetrachloro-2-(trifluoromethyl)benzoic acid 6.

Acid 6, by treatment with sulphur tetrafluoride at 20 - 40°C, was converted back to fluoride 3, thus giving a proof to the identity of the latter. Attempted fluorination of acid 6 to the corresponding bis(trifluoromethyl) derivative failed; treatment with an excess of sulphur tetrafluoride and anhydrous hydrogen fluoride at 200°C also gave fluoride 3 as the only product. This is in accord with earlier observations [7,8] that sterically crowded ***ortho***-trifluoromethyl substituted aryloyl fluorides, even under extreme conditions, do not react further with sulphur tetrafluoride. This also explains the lack of the bis(trifluoromethyl) derivative amongst the products of the fluorination of anhydride 1 or acid 4.

The molecular compositions of the products were obtained from elemental analyses and mass spectra and their structures were confirmed by ^{19}F and ^{13}C NMR spectroscopy (Table 1). The chemical shifts of the fluorine signals of the CF_2 and CF_3 groups of compounds 2 and 5, and 3 and 6, respectively, are in agreement with those previously reported for similar compounds [7,8]. The presence of the COF group in 3 has been evidenced by a singlet at -53.6 ppm (downfield from

TABLE 1

^{19}F and ^{13}C NMR data for compounds 2 - 6.

Compound	Chemical shift		Coupling const.
	Nucleus	δ (ppm)*	J (Hz)
 2	F-7,F-8	71.8 (s)	
	C-7,C-8	123.8 (tt)	^1J(C-F) = 261.4 and ^3J(C-F) = 3.5
	C-3,C-6	128.0 (s)	
	C-1,C-2	130.3 (t)	^2J(C-F) = 31.0
	C-4,C-5	139.4 (s)	
 3	F-7(COF)	-53.6 (s)	
	F-8(CF_3)	59.4 (s)	
	C-8	120.9 (q)	^1J(C-F) = 275.0
	C-2	125.9 (q)	^2J(C-F) = 33.0
	C-1	128.0 (d)	^2J(C-F) = 70.0
	C-3,C-6	130.2 and 132.7 (s)	
	C-4,C-5	138.5 and 138.6 (s)	
	C-7	152.3 (d)	^1J(C-F) = 355.0
 5	F-8	80.7 (s)	
	C-8	122.5 (t)	^1J(C-F) = 259.4
	C-3,C-6	125.2 and 128.5 (s)	
	C-1	132.1 (s)	
	C-2	136.3 (t)	^2J(C-F) = 28.6
	C-4,C-5	140.1 and 141.7 (s)	
	C-7	157.8 (s)	
**  6	F-8	59.0 (s)	
	C-8	121.3 (q)	^1J(C-F) = 275.5
	C-2	125.7 (q)	^2J(C-F) = 32.5
	C-1	130.0 (s)	
	C-3,C-6	131.8 and 132.4 (s)	
	C-4,C-5	137.3 and 138.2 (s)	
	C-7	168.8 (s)	

* From internal CCl_3F for the ^{19}F (positive upfield) and from internal TMS for the ^{13}C spectra. ** ^{1}H NMR: δ(OH) = 10.7 ppm (TMS).

CCl_3F). Unequivocal evidence for the presence of the CF_2 and CF_3 groups came from the ^{13}C NMR spectra which showed intense triplets or quartets with the characteristic large carbon-to-fluorine coupling constants. In the case of compound 2, a coupling of the C-7 and C-8 carbons to the opposite CF_2 group fluorines was observed. The assignment of signals of the aromatic ring carbons was done by the comparison with the data reported for tetrachlorophthalic acid and tetrachlorophthalic anhydride [9].

EXPERIMENTAL

Melting points are uncorrected. ^{19}F and ^{13}C NMR spectra were recorded with a Brucker WM 250 PT or Brucker MSL 300 spectrometers. Mass spectra were obtained with a Finnigan 8200 spectrometer at 70 eV; the ^{35}Cl ions are quoted only but the isotope ions of appropriate intensities were present. IR spectra were measured with a Beckmann Acculab instrument.

Starting materials:

Sulphur tetrafluoride was prepared in this laboratory as described previously [10]. Tetrachlorophthalic anhydride was pure grade laboratory reagent (Fluka A.G.). Hydrogen fluoride was commercial product. n-Pentane and n-hexane were purified by standard procedure.

Preparation of 4,5,6,7-tetrachloro-1,1,3,3-tetrafluoro-1,3-dihydro--isobenzofuran 2.

(a) From tetrachlorophthalic anhydride 1.

The anhydride (60 g, 0.21 mole) was placed in a 250 ml stainless steel autoclave, then cold (ca.-10°C) liquid anhydrous hydrogen fluoride (10 ml, 0.5 mole) was added and the autoclave was quickly closed. After cooling in a acetone-dry ice bath, the autoclave was evacuated and sulphur tetrafluoride (80 g, 0.74 mole) was condensed in it. The charged autoclave was heated in a rocking muffle furnace at 190 - 200°C for 16 hours. After completion of the reaction the autoclave was allowed to cool to ambient temperature and the gases (SOF_2, SF_4, HF) were let off. The white solid product was thoroughly removed from the autoclave*, mixed with anhydrous sodium acetate (10 g, 0.12mole)and acetic acid (50 ml),refluxed for one hour and poured into water (400 ml). The resultant precipitate was filtered off and dissolved in n-pentane (300 ml), and the water solution was extracted with n-pentane (100 ml). The combined n-pentane solutions were filtered, washed with 5% aqueous sodium carbonate, and evaporated to give a product melting at 84-86.5°C (62 g, 89.5%). Recrystallisation from methanol (100 ml) gave pure 4,5,6,7-tetrachloro-1,1,3,3-tetrafluoro-1,3-dihydroisobenzofuran 2 (53 g) as white crystals; m.p. 86.5-87°C (ref. [5], m.p. 86-86.5°C) (Found: C, 29.2; Cl, 42.9; F, 23.1%. $C_8Cl_4F_4O$ requires: C, 29.1; Cl, 43.0; F, 23.05%); MS: m/z 328(60%)M^+, 330(100)M^+(^{37}Cl), 309(10)M^+-F, 281(82)M^+-COF, 227(15), 211(13); IR (nujol): ν(aromat)= 1595 cm^{-1} (m). The product possesses the characteristic smell of chloroaromatics.

(b) From tetrachlorophthalic acid hemihydrate 3.

Freshly prepared tetrachlorophthalic acid hemihydrate [6] (17.5 g, 0.056 mole) and sulphur tetrafluoride (50 g, 0.46 mole) were heated at 190 - 200°C for 16 hours. The crude product was mixed with sodium acetate (3 g, 0.036 mole) and acetic acid (15 ml) and worked up as in (a) to give a product melting at 83-86°C (16.5 g, 89.3%). Recrystallisation from methanol (30 ml) gave pure compound 2 (13 g); m.p. 86-87°C.

Isolation of 3,4,5,6-tetrachloro-2-(trifluoromethyl)benzoyl fluoride 3 (nc).

The crude product (2 g) of the reaction of anhydride 1 with sulphur tetrafluoride was subjected to column chromatography on silica (95 g, 200 mesh) using n-pentane/diethyl ether (99 : 1 v/v) as eluant. Two fractions were collected. The first fraction contained

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* *In the first experiment, the crude product was dissolved in n-pentane, the solution was washed with 5% aqueous potassium hydroxide, followed by water. The residue obtained after removal of the solvent (67 g) was recrystallised from methanol (130 ml) to give a product (56.3 g, 81%) which showed satisfactory elemental analysis (m.p. 83-85°C). This material, as shown by the IR spectroscopy, was contaminated with acid fluoride 3.*

compound 2 (1.85 g), and evaporation of the second fraction gave 3,4,5,6-tetrachloro-2-(trifluoromethyl)benzoyl fluoride 3 (140 mg); m.p. 62-63°C (Found: C, 28.9; Cl, 43.1; F, 23.1%. $C_8Cl_4F_4O$ requires: C, 29.1; Cl, 43.0; F, 23.05%); MS: m/z 328(70%)M^+, 330(100)M^+(^{37}Cl), 300(30)M^+-CO, 281(30)M^+-COF, 265(34)M^+-Cl-CO, 69(8)CF_3^+. IR(nujol): ν(aromat) = 1540 cm^{-1} (m), ν(C=O) = 1860 cm^{-1} (s).

Preparation of 4,5,6,7-tetrachloro-3,3-difluoro-3-hydroisobenzofuranone 5 (nc).

Tetrachlorophthalic anhydride 1 (23 g, 0.08 mole), anhydrous hydrogen fluoride (5 ml, 0.25 mole), and sulphur tetrafluoride (15 g, 0.14 mole) were reacted in a 100 ml autoclave at 190-200°C for 16 h. The product was washed off the autoclave with n-pentane (200 ml), the undissolved crystalline solid was filtered off and washed with n-pentane (50 ml) to give crude compound 5 (13.7 g, 55.6%). This material was dissolved in refluxing n-hexane (250 ml), the hot solution was filtered (2.2 g remained undissolved), then the solvent was partially distilled off (ca. 100 ml) until first crystals appeared, and the residue was left for crystallisation to give pure 4,5,6,7-tetrachloro-3,3-difluoro-3-hydroisobenzofuranone 5 (9.2 g) as white odourless crystals; m.p. 136-138°C (Found: C, 31.7; Cl, 46.1; F, 12.5%. $C_8Cl_4F_2O_2$ requires: C, 31.2; Cl, 46.1; F, 12.35%); MS: m/z 306(17%) M^+, 306(100)M^+(^{37}Cl), 278(14)M^+-CO, 259(58)M^+-COF, 240(15)M^+-CF_2O, 212(20)$C_6Cl_4^+$; IR(nujol): ν(aromat) = 1580 cm^{-1} (m), ν(C=O) = 1830 cm^{-1} (vs).

The combined n-pentane solutions (from the first filtration were condensed to ca. 70 ml, filtered from a precipitate (2 g), and then evaporated to give crude compound 2 (8 g, 30%, contaminated with 3).

Isolation of 3,4,5,6-tetrachloro-2-(trifluoromethyl)benzoic acid 6 (nc).

The water solution, obtained by pouring into water a mixture of the crude product of the reaction of anhydride 1 with SF_4, sodium acetate, and acetic acid, and filtering off the solid material, was evaporated to ca. 150 ml, filtered, and acidified with concentrated hydrochloric acid (10 ml). The white precipitate was filtered off, washed with small amount of cold water and dried at ambient temperature to give 3,4,5,6-tetrachloro-2-(trifluoromethyl)benzoic acid 6 (5.6 g, 8.1%); m.p. 179-181°C (Found: C, 29.0; Cl, 43.3; F, 17.2%. $C_8HCl_4F_3O_2$ requires: C, 29.3; Cl, 43.25; F, 17.4%); IR (CCl_4): ν(aromat) = 1540 cm^{-1} (s), ν(C=O) = 1730 cm^{-1} (vs).

By following the above procedure, acid 6 (1 g, 5.5%) was also isolated from the product of the fluorination of tetrachlorophthalic acid hemihydrate 4.

Reactions of 3,4,5,6-tetrachloro-2-(trifluoromethyl)benzoic acid 6 with sulphur tetrafluoride

(a) The acid (1.1 g, 3.35 mmole) and sulphur tetrafluoride (10 g, 93 mmole) were reacted at 40°C for 2 hours followed by 16 hours at 20°C. The product was dissolved in n-hexane (20 ml), dry sodium fluoride (1 g) was added, and the solution was left for 18 hours (removal of HF). Evaporation of the solvent gave 3,4,5,6-tetrachloro-2-(trifluoromethyl)benzoyl fluoride 3 (1 g, 90.5%) (elemental analysis, m.p., and spectral data were identical with those obtained for compound 3 isolated by the column chromatography).

(b) The acid (3.9 g, 12 mmole), water (0.5 ml, 28 mmole), and sulphur tetrafluoride (18 g, 166 mole) were reacted at 190 - 200°C for 17 hours. The product was dissolved in n-hexane (40 ml), the solution was washed with water and evaporated. The residue was identified by spectral means as 3,4,5,6-tetrachloro-2-(trifluoromethyl)benzoyl fluoride 3 (3.5 g, 89%).

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REFERENCES

1 F.E.Lawlor, Ind.Eng.Chem., **39** (1947) 1419.

2 V.M.Vlasov, G.F.Grebenshchikova, A.Ya.Lvova, and G.G.Yakobson, in I.L.Knunyants and G.G.Yakobson (Ed.), 'Sintezy ftororganicheskhih Soedinenii', Moscow (1973) 171.

3 I.L.Knunyants and G.G.Yakobson (Ed.), 'Sintezy ftororganicheskhih Soedinenii. Monomery i Promezhutochnoye Produkty', Moscow (1977) 189, and references therein.

4 P.J.V.Cleare and A.T.Costello, Brit.Pat., 2 146 635 (1983); Eur.Pat., 0 140 482.

5 R.V.Belinskaya and L.M.Yagupolskii, Zh.Obshch.Khim., **38** (1968) 1726.

6 F.E.Lawlor, Ind.Eng.Chem., **39** (1947) 1424.

7 L.M.Yagupolskii, A.I.Burmakov, L.A.Alekseeva, and B.V.Kunshenko, Zh.Org.Khim., **9** (1973) 689.

8 B.V.Kunshenko, L.A.Alekseeva, and L.M.Yagupolskii, Zh.Org.Khim., **9** (1973) 1954.

9 M.J.Fifolt, S.A.Sojka, and R.A.Wolfe, J.Org.Chem., **47** (1982) 148.

10 W.Dmowski and R.Koliński, Pol.J.Chem., **47** (1973) 1211.