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HALOGENATION OF TRIFLUOROMETHOXY AND BIS(TRIFLUOROMETHOXY)BENZENE

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ABSTRACT

Controlled chlorination of trifluoromethoxybenzene produced the mono-, di-, tri-, and tetrachloro derivatives. Two isomers were detected at each level of substitution. Exhaustive chlorination and bromination of 1,3- and 1,4-bis(trifluoromethoxy)-benzene yielded isomeric mixtures of only the disubstituted bis(trifluoromethoxy)benzenes. No hydrolysis of the -OCF_3 group was detected in any halogenations. The configuration of all the products was determined by ^1H and ^{19}F nmr. A through-space hydrogen-fluorine coupling of 0.7 - 1.3Hz between the -OCF_3 substituent and the ortho proton was observed in all the halogenated products. The polychlorinated derivatives all exhibited good thermal stability at 200°-250°.

INTRODUCTION

Aromatics containing a trifluoromethoxy substituent have been reported to possess good thermal stability as well as a chemical inertness to oxidation, reduction and hydrolysis. These properties are necessary requirements for stable fluids commonly used in high temperature applications such as in transformers and Rankine Cycle engines. In addition to having chemical and thermal stability, these fluids should be useful over a wide temperature and liquid range, i.e. they are liquids at low temperatures. The unsubstituted trifluoromethoxy-and bis(trifluoromethoxy)benzenes possess these properties but suffer from wide application use because of their low boiling points (<130°). Ideally, although not necessarily, boiling points of >150° are desired for high temperature use.

Our main interest in these compounds was the preparation of potentially stable fluids containing one or two $-OCF_3$ groups with high boiling points and low freezing points. This was accomplished by the successive replacement of hydrogen with either chlorine or bromine, of the aromatic nucleus. In determining the configuration of these halo derivatives a noticeable "through-space" H-F coupling between the $-OCF_3$ group and the ortho phenyl hydrogen was observed and analyzed.

RESULTS AND DISCUSSION

Chlorination of Trifluoromethoxybenzene

Neat trifluoromethoxybenzene (1) was chlorinated to its mono-, di-, tri-, and tetrachloro isomers in stages using excess chlorine with catalytic amounts of $SbCl_3$ at 50°-100°. The time-product profile was monitored by gc and gc/ms to obtain suitable reaction conditions (Scheme I) for preparation of all the polychloro derivatives. The products were isolated and purified by fractional distillation of mixtures containing small amounts of the higher or lower molecular weight products. Product configurations and isomer distributions (Table I) were determined by ^{1}H and ^{19}F nmr (Table II).

TABLE I

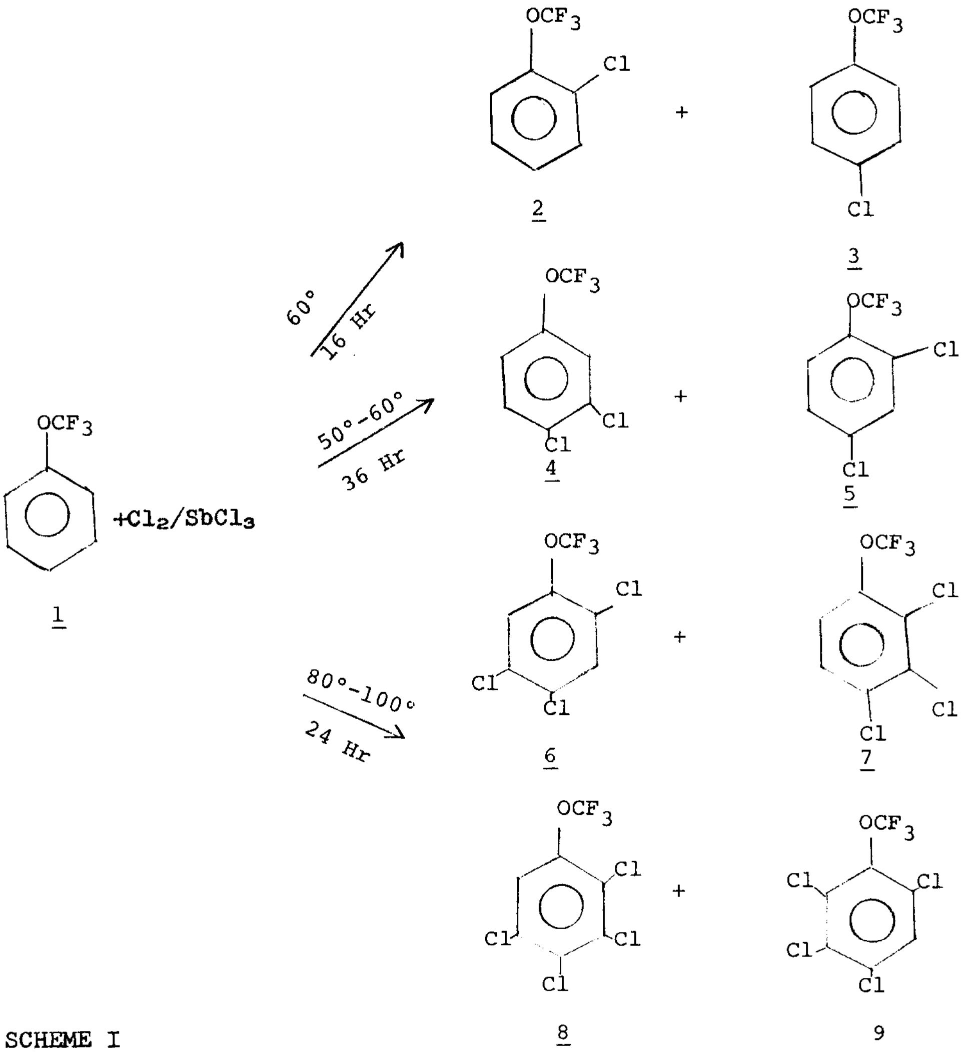
CHLORINATION OF 1 TO POLYCHLOROTRIFLUOROMETHOXYBENZENES

Products[a]	Reaction Conditions		Yield[b]	Isomer Distribution[c]	
	Temp., °C	Time, Hr.	%	(Product)	
2 + 3	60	16	67	17(2)	83(3)
4 + 5	50-60	36	41	95(4)	5(5)
6 + 7	80-100	24	62	10(6)	90(7)
8 + 9			8	89(8)	11(9)

[a] Isolated as mixtures

[b] By-products in most cases consisted of higher and lower boiling polychloro derivatives of 1 with respect to the desired product.

The initial electrophilic chlorination of 1 to a mixture of 2 and 3 in 67% yield was accomplished using a long reaction time (16 hr) at 60° in order to minimize formation of the dihalo products. The isomer distribution of the monochloro derivatives was 83:17 -para: ortho similar to that observed for the ionic[2] and free-radical[3] chlorination of anisole. Extending the reaction time to 36 hrs at 60° under similar chlorination conditions produced a mixture of both the di- and trichlorotrifluoromethoxybenzene with the latter predominating. Fractionation of this mixture produced a pure sample (>98% by gc) of the dichloro product which consisted



SCHEME I

of two isomers (4 and 5) in a 95:5 distribution, respectively. The tri- and tetrachlorotrifluoromethoxybenzenes required higher temperatures (80°-100°) and a 24 hr. reaction time. The only products detected (i.e. <1%) were a mixture of the tri and tetrachloro derivatives. Again as in the case of the mono and dichloro products, two isomers were detected by ^{19}F nmr for both the tri- and tetrachloro products (Table I). No attempt was made to optimize their individual yield. No detectable (gc) formation of the pentachloro isomer was observed. The trichloro isomers 6 and 7 were easily separated from 8 and 9 by careful fractional distillation at atmospheric pressure. No hydrolysis of the ether group was observed in any of the chlorinations, in direct contrast to the facile ether cleavage of anisole by strong acids.

The ^{1}H nmr of hydrogens ortho to the $-OCF_3$ group in compounds 2 through 9 appeared as quartets with J_{H-F} = 0.71-1.3Hz which in some cases was split further by an adjacent or para hydrogen (Table II). The coupling constants and chemical shifts of these hydrogens where the spectrum was complex were determined by fluorine decoupling. The ^{19}F nmr spectra of the $-OCF_3$ group in compounds 2 through 9 exhibited either a singlet, doublet, or triplet depending on the number of ortho hydrogens. No meta or para coupling of hydrogen with the $-OCF_3$ group was detected. The magnitude of J_{H-F} in 2-9 was not greatly affected by the increasing chlorine substitution. The H-F coupling in 2 through 9 is best explained by a through-space coupling mechanism.[4] The observed H-F coupling of 0.7-1.3Hz in these derivatives suggests, based on Myhre's work,[5] that the H-F internuclear distance is in fact ca. 3Å, indicative of a perpendicular conformation of the aromatic ring with the trifluoromethoxy carbon.

Halogenation of 1,4-Bis(trifluoromethoxy)benzene

Chlorination of neat 1,4-bis(trifluoromethoxy)benzene (10) was carried out in a similar fashion as that described for 1.

TABLE II

PHYSICAL AND SPECTRAL PROPERTIES OF POLYHALOGENATED MONO- AND BIS(TRIFLUOROMETHOXY)BENZENES

Structure	Mp, °C[a,e]	Bp, °C[d,e]	n_D^t (°C)[e]	$^1H_{NMR}$, δ[b]	$^{19}F_{NMR}$, δ[c]
2[1,6,7]				7.11(s), 7.05(m)	58.8(t,J_{HF} ~1Hz)
	-63	145	1.4322(24.5)		
3[1,7]				complex	58.4(d,J_{HF} = 1.3Hz)
4				complex	58.7(t,J_{HF} = 0.7Hz)
	-58	173	1.4611(24.5)		
5				complex	58.8(d,J_{HF} = 1.3Hz)
6				7.43(d, meta OCF_3 J = 0.4Hz)^d, 7.35	59.2(d)
	-25	205	1.4868(24.5)	(quartet of d, J_{HF} = 1.3Hz)	
7				7.12(d, ortho OCF_3)^d, 7.28 (d, meta OCF_3, J = 9.0Hz)	58.6(d, J_{HF} = 1.3Hz)
8				7.34 (quartet, J_{HF} = 1.3 Hz)	57.0(d)
	+5	215	1.5102(24.5)		
9				7.41(s)	56.6(s)
11				7.46(quartet, J_{HF} = 1.4Hz)	58.9(d)
	-32	174	1.4219(22)		
12				7.29(s)^d	58.8(unsymm t)
13				7.59(q, J_{HF} = 1.2Hz)	58.6(d)
	+20	198	1.4570(24.5)		
14				7.32(q)	59.9(dd)
16				7.55(d, J = 0.4Hz)^d	59.2(d, J_{HF} = 1.2Hz)
	-35	178	1.4190(22)	7.37(d)	
17				7.38(d, J = 9.2Hz)^d	58.6(d, J_{HF} = 1.2Hz),
				7.00 (q)	56.6(s)
18	-10	200	-	8.05(s), 7.49(septet)	58.6 (d, J_{HF} = 1.3Hz)

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[a] DTA measurement.

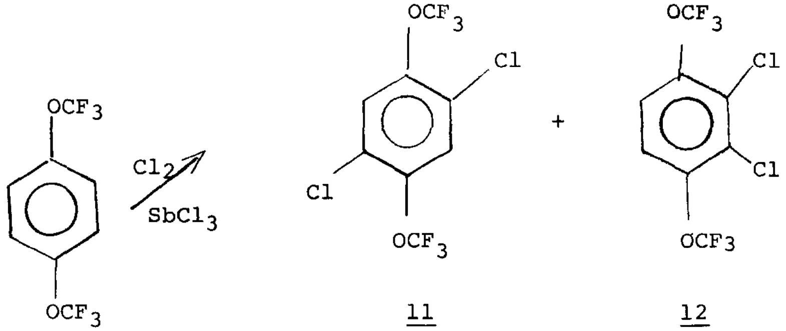
[b] Recorded in neat solution and expressed in ppm downfield from internal TMS.

[c] Recorded in neat solution and expressed in ppm upfield from internal $CFCl_3$.

[d] Fluorine decoupled spectrum.

[e] For isomeric mixture.

Exhaustive chlorination of 10 at 100° for 3 days resulted in a 48% yield of only the dichloro products 11 and 12 in a 87:13 distribution. No detectable trichloro isomer was found (*via* gc).

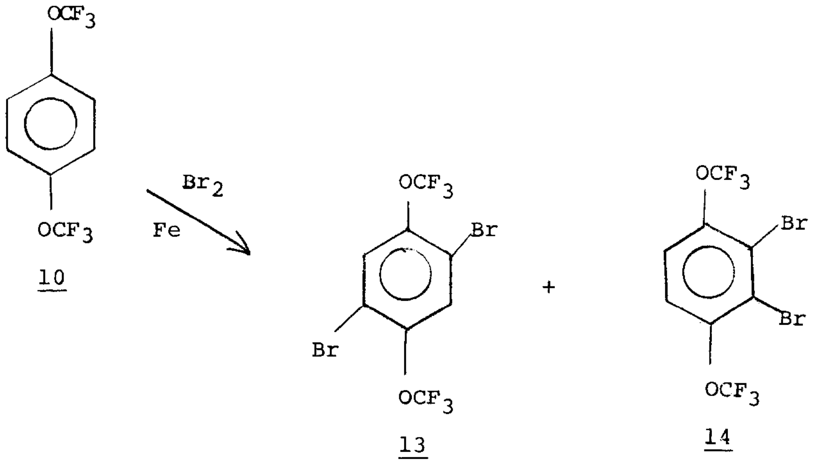


10 11 12

The configuration of the major isomer 11 was deduced from its ^1H nmr spectrum which consisted of a quartet and a doublet with J_{H-F} = 1.4Hz. The minor isomer was assigned the structure 12 on the basis of its ^1H, ^{19}F, and ^{13}C satellite spectra. The ^1H nmr spectrum of 12 appeared as an unresolved septet and upon ^{19}F spin decoupling collapsed to yield a singlet at $\delta 7.46$. The ^{13}C satellite spectrum of neat 12 showed two weak absorptions with $J_{^{13}C-H}$ = 169.2Hz and a calculated J_{H-H} = 9.4Hz indicative of ortho hydrogen coupling. The hydrogens in 11 are more shielded because of the neighboring inductive effect of chlorine. In 12 the chemical shifts are almost identical to those of 10 (i.e., $\delta 7.23$) indicating the absence of an ortho chlorine atom. The orientation of substitution in 11 and 12 is similar to that observed in the chlorination of 1,4-dimethoxybenzene.[8]

Based on the above results we felt it worthwhile to re-examine[1] the bromination of 10 in light of the formation of 11 and

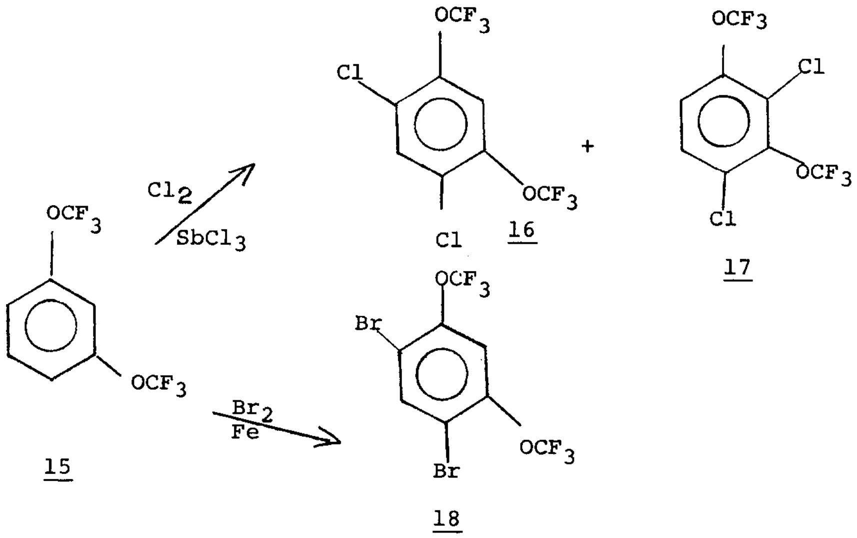
12 from 10. Exhaustive bromination of 10 at 100° for 2 days produced a mixture of the dibromo products 13 and 14 in 31% yield. (Table II). The distribution of 13 and 14 was 98:8.



With the exception of the chemical shifts, the ^{1}H and ^{19}F nmr spectra as well as its ^{19}F spin decoupled spectrum showed a splitting pattern similar to that of 11 and 12. The ^{13}C satellite spectrum of 14 again yielded $J_{^{13}C\text{-}H}$ = 170Hz and an ortho $J_{H\text{-}H}$ coupling of 9.0Hz. In the previously reported bromination of 10, only the 2,5 dibromo isomer (13) was detected. Its ^{1}H and ^{19}F nmr splitting pattern were identical to that of 13.

Halogenation of 1,3-Bis(trifluoromethoxy)benzene

Chlorination of neat, 1,3-bis(trifluoromethoxy)benzene (15) to the dichloro derivatives 16 and 17 in 74% yield required a shorter reaction time (10 hr) at 100°.



The major isomer, 16, was identified as the 4,6-isomer, based on the fluorine decoupled ^1H nmr spectrum. The 2 and 5 hydrogens appeared as doublets at $\delta 7.37$ and $\delta 7.55$, respectively, with J_{H-H} = 0.4Hz. The ^{19}F nmr spectrum showed a doublet at δ 59.2 with J_{H-F} = 1.2Hz. The ^1H nmr of the minor isomer with ^{19}F irradiation displayed a doublet at δ 7.38 and a quadruplet at 7.00 with J_{H-H} = 9.2Hz. These data coupled with the ^{19}F nmr spectrum indicated the isomer 17.

Bromination of 15 in a similar fashion as that described for 10 yielded the 4,6-dibromo isomer, 18, as the only detectable dibromo product in 82% yield (Table II). The ^1H and ^{19}F nmr spectra of 18 were similar to those of 16. The effect of bromine vs. chlorine on the hydrogens in position 5 of 18 was shown by a pronounced downfield shift of 0.50 ppm. The absence of any detectable minor dibromo isomer suggests a possible steric inhibition by the flanking trifluoromethoxy on the 2 position. The trifluoromethoxy groups of 10 and 13 in these halogenations were resistant to hydrolysis contrary to observations on resorcinol ethers.[7]

Thermal Stability Studies

As an integral part of our study on the halo and polyhalo derivatives of 1, 10 and 15, we investigated the thermal stability of these compounds. Compounds 1, 10 and 15 have good thermal stability in the presence of SS at temperatures <500°[1]. At higher temperatures (550-570°), a significant amount of degradation occurs (5 to 10%), and at 625° the extent of decomposition approaches 30-40 The formation of carbon monoxide, carbon dioxide and fluorobenzene derivatives becomes significant at these higher temperatures. For transformer fluids long term stability at temperatures of 130° and above in the presence of metals (copper, steel, aluminum, etc.) are highly desirable. In Rankine cycle engines, the vaporization so in the Carnot cycle represents the highest operating temperature which is typically about 125° above the normal boiling point. All of the polychloro derivatives prepared showed good thermal stability in a Pyrex® vessel at 250° up to 30-50 days in the absence of air. At higher temperatures (i.e., 350°) their stability dropped sharply In the presence of metals such as aluminum, stainless steel and 101 steel, their stability was also diminished. The monochloro derivatives of 1 (2 and 3) showed good stability at 300° for 100 days in Pyrex® and 1018 steel. In the presence of aluminum they totally degraded at 300° after 17 days. This was true of all the polyhalo compounds in the presence of aluminum. Similar results were observe with stainless steel but to a lesser extent (50 days at 300°).

At 350°, which was considered a break point for thermal stability for stable fluid applications, few of the polychloro derivatives survived. Solids were observed with 4 and 5, 6 a and 8 and 9 in Pyrex® and 1018 steel vessels. In contrast to 2 an 3, monochlorobenzene and chloropentafluorobenzene show decomposition at 382° after 5 and 6 days, respectively. Hexachlorobenzene is however very stable, but the partially chlorinated benzenes do not have this exceptional stability. Chloro- and dichlorobenzene are less stable than benzene. The thermal stability of compounds 2 through 9 appeared to decrease with increasing chlorine substitution presumably by the increased propensity to eliminate HCl. Addition of metal oxide bases has been shown to minimize some of this thermal degradation. An unknown factor in these studies is the relative stability of the individual isomers (i.e., stability of 2 vs. 3). The trend in stability with increasing chlorine substitution could thus be masked by the individual isomer's inherent thermal stability. The dichloro derivative of 15 exhibited excellent heat stability at 280° for 100 days whereas the dichloro derivative of 10 was only fair under the same conditions.

EXPERIMENTAL SECTION

Melting and boiling points were measured by DTA. Proton and fluorine nmr spectra were recorded on Varian Associates A56/60, A60, and HA100 nmr spectrophotometers, respectively, using neat solutions. Gas chromatography/mass spectral analyses were performed on a Du Pont 21492 GC/MS Instrument coupled to a 21094 data system. Glpc analyses of the polyhalogenated trifluoromethoxy and bis(trifluoromethoxy)benzenes were carried out using a F&M TCGC Model 700 equipped with a 6 ft x 0.25 in SS column packed with 20% Triton X305 on 60/80 mesh Chrom W (non-acid washed). Satisfactory analytical data were reported for all new compounds listed in Table I. Compounds in Table I were also characterized by infrared and ultraviolet spectra.

Trifluoromethoxy- and 1,3- and 1,4-bis(trifluoromethoxy)-benzene were prepared in 73%, 90%, and 69% yield, respectively.[1] Bromination of 10 was carried out as described by Sheppard.[1]

General Procedure for the Chlorination of 1, 10 and 15

Chlorination of 1, 10 and 15 were carried out by sparging an intimate mixture of the appropriate trifluoromethoxybenzene and $SbCl_3$ (4 wt %) with undiluted chlorine (40cc/min) for the given length of time at the given reaction temperature. GC analysis of the product on the above GC column indicated the time required for the desired extent of chlorination. The cooled solution was then added slowly tothe ice water. The mixture was filtered to remove the insoluble antimon salts. The filtrate was extracted with ether, washed with saturated $NaHCO_3$, then saturated NaCl, and dried. The product(s) were isolate and purified by fractional distillation from P_2O_5 on a 38 cm spinnin band column of "Teflon" fluorocarbon resin.

Bromination of 1,3-Bis(trifluoromethoxy)benzene

A mixture of 75 g (0.30 mole) 15 and 5 g (0.09 g. atom) iro powder was heated to 100° followed by slow addition of 40 ml (0.72 mole) bromine. After heating at 100° for 18 hr, an additional 15 ml (0.27 mole) bromine was added at 100° followed by heating an additional 18 hr. The organic layer was decanted into 300 ml pentane and the mixture washed with 6 N HCl (2 x 75 ml), 10% $NaHSO_3$ (2 x 75 ml) and dried over anhydrous $MgSO_4$. After removal of drying agent and solvent, the residue was distilled on a 6" Vigreux column to yield 98 g (82%) of 1,3-bis(trifluoromethoxy)-4,6-dibromobenzene (18), bp 113°-114° (41 torr).

ELEMENTAL ANALYSIS OF COMPOUNDS SUMMARIZED IN TABLE I

	Theoretical			Observed		
Structure	C	H	F	C	H	F
2,3	42.81	2.05		42.85	1.91	
4,5	36.04	1.31		36.28	1.56	
6,7	31.67	0.76		31.53	0.94	
8,9	28.04	0.34		28.49	0.57	
11,12	30.50	0.64	36.19	30.84	0.92	36.22
13,14	30.50	0.64	36.19	30.75	0.91	36.54
16,17	23.79	0.50		24.12	0.63	
18	23.79	0.50		23.88	0.83	

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