Chemistry of 2-(Trifluoromethyl)-2-hydroxy-3,3,3-trifluoropropionitrile

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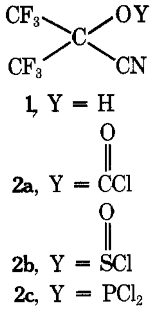
Pyrolysis of either 1-cyano-1-(trifluoromethyl)-2,2,2-trifluoroethyl chloroformate (**2a**) in an inert atmosphere, or bis[1-cyano-1-(trifluoromethyl)-2,2,2-trifluoroethyl] sulfite (**6**) in an atmosphere of $SOCl_2$ leads to 2-(trifluoromethyl)-2-chloro-3,3,3-trifluoropropionitrile (**9**), which is a potential precursor to perfluoromethyacrylonitrile. Since the sulfite **6** is readily prepared from the cyanohydrin of hexafluoroacetone, the described procedure provides access to perfluoromethacrylic acid derivatives from hexafluoroacetone. Thermal decomposition of sulfite **6** in an inert atmosphere leads to perfluorinated tertiary alkyl derivatives not otherwise available. Possible mechanisms for these reactions are discussed.

When hexafluoroacetone reacts with a nucleophile such as HCN, adducts of type **1** are formed. Substitution of the hydroxy group in cyanohydrin **1** by a halide ion might provide access to bis(trifluoromethyl)ketene and perfluoromethacrylic acid which are now available only from extremely toxic[1] perfluoroisobutene.[2] Unfortunately, owing to the electronic and steric effects, such a nucleophilic substitution is ruled out. It was therefore decided to study the thermal decomposition of chloroformate **2a**, chlorosulfite **2b**, and dichlorophosphite **2c**.



1, Y = H

2a, Y = $\overset{O}{\overset{\|}{C}}Cl$

2b, Y = $\overset{O}{\overset{\|}{S}}Cl$

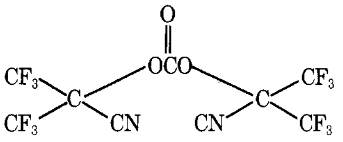
2c, Y = PCl_2

Results and Discussion

Reaction of Cyanohydrin 1 with Phosgene, Thionyl Chloride, and Phosphorus Trichloride. Cyanohydrin **1** [pK_a (OH) = 4.1][7] failed to react with either of the above chlorides, while methyl 2-hydroxy-2-(trifluoromethyl)-3,3,3-trifluoropropionate (**3**) [pK_a (OH) = 7.7][3] did react partially with $SOCl_2$ and quantitatively with PCl_3. Therefore, it can be concluded that any alcohol with pK_a ~ 6 or lower will not react with phosgene, thionyl chloride, and phosphorus trichloride if no base is present.

Addition of the sodium salt of cyanohydrin **1** to an excess of phosgene in ether at −60 °C yielded a mixture of chloroformate **2a** and a smaller amount of carbonate **4**. The products could be separated by distillation. An attempt to prepare chlorosulfite **2b** and dichlorophosphite **2c** in a similar way using excess thionyl chloride or phosphorus trichloride gave quantitative yields of sulfite **6** and phosphite **5** even at −70 °C.

A possible reason for the difference in the reactivity of phosgene as compared with thionyl chloride and phosphorus trichloride may be based on two effects: (a) the anion of cyanohydrin **1** is more strongly electron withdrawing and, therefore, a better leaving group than chloride ion; (b) the oxygen of the cyanohydrin **1** is capable of more extensive $(p \rightarrow d)_\pi$ dative bonding to sulfur and phosphorus than chlorine. If the first chloride ion in phosgene is displaced by cyanohydrin anion, any further substitution will only exchange one cyanohydrin anion for another one. Therefore, the major product is the chloroformate **2a**. In the case of thionyl chloride or phosphorus trichloride, the introduction of the cyanohydrin group into the molecule will increase the reactivity of the molecule toward further nucleophilic substitution. However, cyanohydrin becomes a poorer leaving group than chlorine since the strength of the O–S or O–P bonds is increased by $(p \rightarrow d)_\pi$ dative bonding. Therefore, the second chlorine will be replaced more readily than the first chlorine in $SOCl_2$ or PCl_3. As a result only sulfite **6** and phosphite **5** are isolated even if an excess of $SOCl_2$ or PCl_3 is present.



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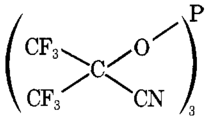

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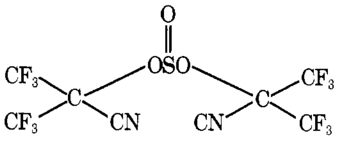

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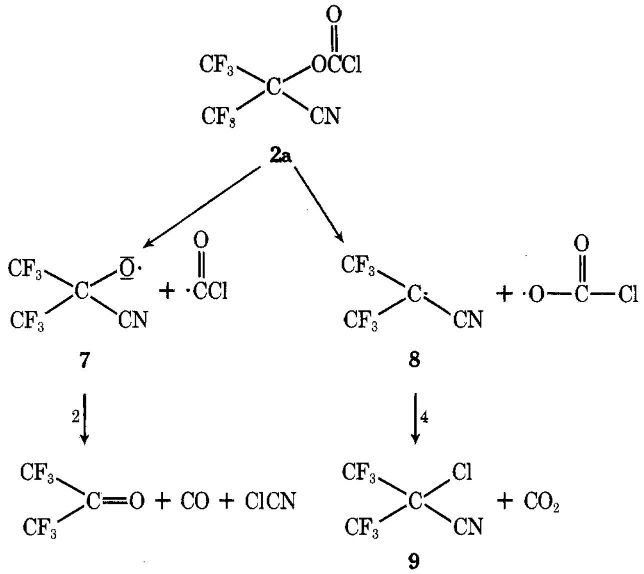
Pyrolysis of Chloroformate 2a. Chloroformate **2a** was pyrolyzed in a flow reactor. A conversion of 40% was achieved only at a temperature of 500 °C and contact time of 51 s. The gaseous products were separated by gas chromatography and identified by infrared and mass spectrometry. The main components were hexafluoroacetone and cyanogen chloride. The minor components were the desired 2-chloro-2-(trifluoromethyl)-3,3,3-trifluoropropionitrile (**9**) and carbon dioxide. The products can be accounted for by two reaction pathways (Scheme I).

The products are formed either by the decomposition of radical **7** (step 2) or by the combination of radicals in step 4.

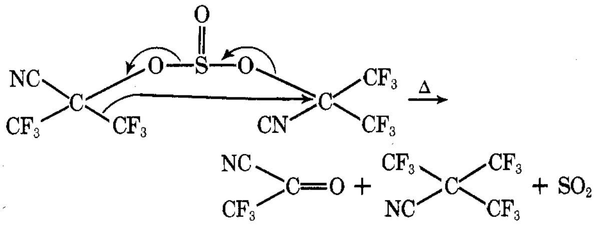
The extremely high temperature required for thermolysis of chloroformate **2a** and the predominant formation of hexafluoroacetone led to the conclusion that in the chloroformate **2a** the strength of the >C–OCOCl bond was greater than the strength of the >CO–COCl bond. In order to avoid formation of hexafluoroacetone, a group Y in **1** with more electron-withdrawing power must be employed. Sulfite **6** was expected to fulfill the requirement.

Pyrolysis of Sulfite 6. Pyrolysis of sulfite **6** was studied at temperatures of 290–410 °C. As before, gaseous products were separated by gas chromatography and analyzed by infrared and mass spectra. The following compounds were identified: hexafluoroacetone, sulfur dioxide, equal molar quantities of perfluoropivalonitrile (**10**) and 2-oxo-3,3,3-trifluoropropionitrile (**11**), and traces of trifluoroacetonitrile and trifluoroacetyl fluoride. The pyrolysis products are stable to 500 °C and are primary products.

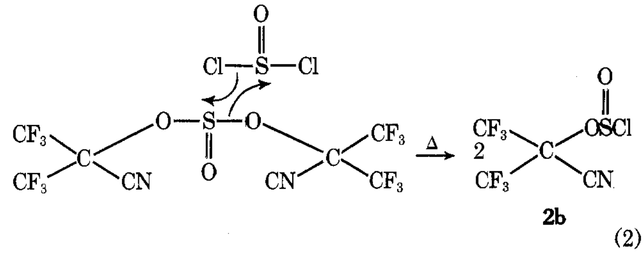
Scheme I



The formation of the main products in pyrolysis of sulfite **6** can be explained either by a radical mechanism (Scheme II) similar to that suggested for pyrolysis of chloroformate **2a** or by a concerted mechanism (eq 1).


(1)

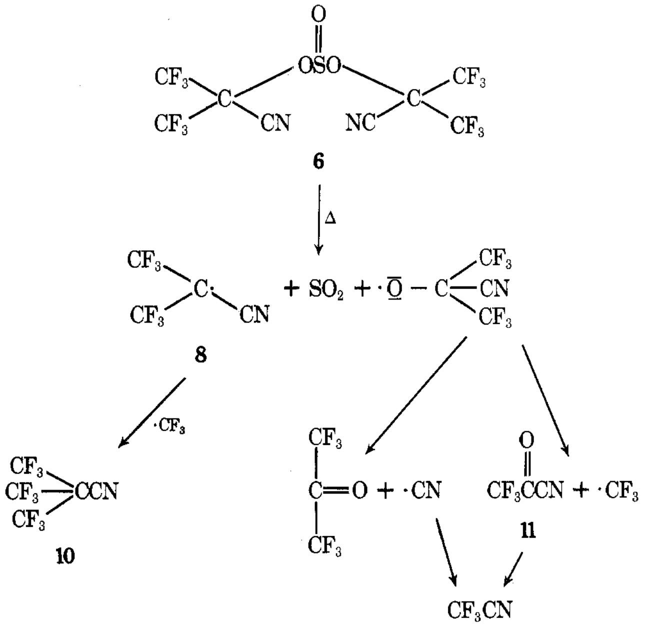
In order to distinguish between the two possible mechanisms, sulfite **6** was pyrolyzed in an excess of thionyl chloride. Thionyl chloride may react with sulfite **6** via a four-center mechanism (eq 2) and form chlorosulfite **2b** at temperatures lower than that necessary for pyrolysis of sulfite **6**. Chlorosulfite **2b** would then decompose immediately to


(2)

nitrile **9** via radical **8**. If thionyl chloride does not react with sulfite **6** at temperatures below 300 °C, it will be decomposed[4] into SO_2, SCl_2, Cl_2, and other fragments. Chlorine will then function as a trap for radical **8** (Scheme II). A large excess of thionyl chloride would then give only nitrile **9** and no perfluoropivalonitrile **10**. If the concerted mechanism (eq 1) is the main reaction path for pyrolysis of sulfite **6**, then no, or a very small amount of, nitrile **9** would be expected to form at temperatures above 300 °C.

When a mixture of sulfite **6** and an excess of thionyl chloride was pyrolyzed at temperatures below 300 °C, the sulfite **6** was recovered unchanged. However, substantial decomposition of thionyl chloride to a mixture of sulfur dioxide, sulfur dichloride, and chlorine was observed. When the same mixture of sulfite **6** and thionyl chloride was subjected to pyrolysis at temperatures above 300 °C, hexafluoroacetone, sulfur dioxide, and 2-chloro-2-(trifluoromethyl)-3,3,3-trifluoropropionitrile (**9**) were the main products.

Scheme II



Since the thermolysis of sulfite **6** in an excess of thionyl chloride does not occur at temperatures lower than that required for pyrolysis of the same sulfite in an inert atmosphere, the chlorosulfite **2b** can be excluded as the intermediate. No perfluoropivalonitrile was formed in the presence of thionyl chloride; therefore, the concerted mechanism (eq 1) is ruled out and we conclude that the radical path (Scheme II) is responsible for the product formation.

Experimental Section

Gas chromatography was carried out on a 6 ft × 0.25 in. column packed with 207 QF-1 on Chromosorb W at ambient temperature. All mass spectra were obtained on A. E. I. MS 902 using 70 eV electron energy. Interpretation was aided by high-resolution accurate mass measurement.

Sodium Salt of Cyanohydrin 1. The salt was prepared by a procedure similar to that described by Filler and Schure.[3] Sodium cyanide (270 g, 5.5 mol) was suspended in ether (2.5 l.) in a 5-l. flask fitted with a manometer, a mechanical stirrer, and a gas inlet tube. The flask was evacuated until ether started to boil. Hexafluoroacetone was introduced until a pressure of 740 mmHg was achieved. The stirrer was started and the pressure kept constant by adjusting the valve on the container of hexafluoroacetone. When the required amount of hexafluoroacetone (900 g, 5.42 mol) was consumed, the rate of hexafluoroacetone uptake dropped to zero. The solvent was evaporated under vacuum, leaving behind the product (1170 g, 5.42 mol).

2-Hydroxy-2-(trifluoromethyl)-3,3,3-trifluoropropionitrile. The sodium salt of cyanohydrin **1** (53.8 g, 0.25 mol) was suspended in ether (200 ml). Dry HCl (9.1 g, 0.25 mol) was introduced with simultaneous external cooling by ice. The salts were filtered off and the mixture distilled on a 30 TP column. The product, bp 108 °C (lit.[5] 107.5 °C), was obtained in a quantitative yield.

Chloroformate 2a. The synthesis and isolation were carried out in an argon atmosphere. A solution of phosgene (100 g, 1 mol) in ether (400 ml) was cooled to −60 °C and the sodium salt of cyanohydrin **1** (100 g, 0.465 mol) was added in 10 min with vigorous stirring. The stirring was continued for 2 h at −60 °C. The reaction mixture was allowed to warm to room temperature and the salts were filtered off. At this moment the ir showed only one C═O band at 5.5 μ which corresponds to chloroformate **2a**. Distillation of the filtrate afforded three fractions. The first fraction, bp 84 °C (32.1 g), corresponds to chloroformate **2a**: ir 4.4 (w, CN), 5.5 μ (s, C═O); mass spectrum *m/e* 255 ($C_5ClF_6NO_2$) and 220 ($C_5F_6NO_2$). The second fraction (17.2 g), bp 90–125 °C, is a mixture of chloroformate **2a**, cyanohydrin **1**, and carbonate **4**. The third fraction (49.9 g), bp 127–128 °C, mp 48–49 °C, corresponds to carbonate **4**, ir 4.45 (CN, m) and 5.45 μ (C═O, s). Both chloroformate **2a** and carbonate **4** are hygroscopic and if not stored under inert atmosphere they are hydrolyzed to cyanohydrin **1**.

Sulfite 6. A solution of thionyl chloride (100 ml) in ether (300 ml) was cooled under argon to −60 °C. The sodium salt of cyanohydrin 1 (100 g, 0.465 mol) was added slowly with vigorous stirring. The stirring was continued for 2 h at −60 °C. The reaction mixture was allowed to warm to room temperature. The salts formed were filtered under argon and the filtrate was distilled. Only sulfite **6** (61 g, 60%), bp 139–141 °C, was obtained, ir 4.42 (m, CN), 7.8–8.2 μ [vs, COS(O)OC]. Hydrolysis with 1 equiv of water gave 1 equiv of SO_2 and 2 equiv of cyanohydrin **1**.

[1-(Trifluoromethyl)-1-methylcarboxy-2,2,2-trifluoroethyloxy]dichlorophosphite. A mixture of methyl 2-hydroxy-2-(trifluoromethyl)-3,3,3-trifluoropropionate (19.0 g) and phosphorus trichloride (24.5 g) was refluxed and the disappearance of the O–H bond was followed by ir. After 25 h, the excess of PCl_3 was removed by distillation and the product (quantitative yield) distilled at 171–173°C: ir 3.38 (s, C–H), 5.65 μ (s, C=O); MS *m/e* 326 ($C_5H_3Cl_2F_6O_3P$), 291 ($C_5H_3ClF_6O_3P$), 256 ($C_5H_3F_6O_3P$), 189 ($C_5H_2F_5O_2$).

Pyrolysis. The thermal decomposition of chloroformate **2a** and sulfite **6** was studied in a quartz flow reactor either empty (230 ml) or filled with quartz chips. The empty volume of the reactor was 100 ml. The flow of carrier gas (argon) was 0.5 ml/s. The compounds **2a, 6,** or a mixture of **6** and thionyl chloride were added from a syringe driven by a motor at a constant speed. The products were collected in a trap cooled by a dry ice–acetone mixture at ~−80 °C.

Chloroformate 2a. When chloroformate **2a** (5.0 g) was allowed to react for 15 min at 400 °C, the chloroformate **2a** was recovered unchanged. Under the same conditions, at 500 °C, 3 g (60%) of chloroformate **2a** was recovered. The gaseous compounds were separated into two fractions and then analyzed by gas chromatography. The major fraction (1.2 g) contained hexafluoroacetone: ir 5.5 (m, C=O), 7.5 (m), 7.8–8.3 (vs), 10.35 (s), 12.9 (w), 14.0 μ (s); mass spectra *m/e* 166 (C_3F_6O), 147 (C_3F_5O), and CO_2; ir 2.7 (doublet, m), 4.3 μ (s). The second fraction (0.6 g) contained mainly 2-chloro-2-(trifluoromethyl)-3,3,3-trifluoropropionitrile as shown by GC: ir 4.4 (m, CN), 7.8 (vs), 8.10 (vs), 9.3 (s), 10.55 (s), 13.3 (m), 14.0 μ (s); and mass spectra *m/e* 192 (C_4F_5NCl), 157 (C_4F_5N), 142 (C_3F_3NCl), 123 (C_3F_2NCl). Cyanogen chloride was also present in small quantities, ir 4.6 μ (CN).

Sulfite 6. The thermolysis of sulfite was studied at temperatures of 290–410 °C. As an example the experiment carried out at 330 ± 10 °C in a reactor filled with glass chips is described in detail. Pyrolysis of 17.2 g of sulfite **6** yielded 16.5 g of a mixture from which 12.7 g (73.6% conversion) was volatile products with boiling points lower than 30 °C. The residue (3.8 g) was shown by GC and ir to be the starting sulfite **6.** A small portion of the volatile product was separated by GC into six fractions. Each fraction was collected in an ir cell and analyzed by ir and mass spectrometry. The following components were identified. Trifluoroacetyl fluoride: ir 5.25 (s, C=O), 7.55 (m), 8.0 (s), 8.3 (s), 9.15 μ (s). Trifluoroacetonitrile: ir 4.45 (m, CN), 8.3 μ (vs). Hexafluoroacetone: ir and mass spectrum as above. Perfluoropivalonitrile: ir 4.7 (s, CN), 8.1 (m), 8.7 (s), 9.0 (s), 10.1 μ (m); mass spectrum *m/e* 245 (C_5F_9N). Sulfur dioxide: ir 4.0 (w), 4.3 (vs), 7.3–7.6 (vs), 8.6 (s), 8.8 μ (s); mass spectrum *m/e* 64 (SO_2). 2-Oxo-3,3,3-trifluoropropionitrile: ir 4.55 (m, CN), 5.67 (s, C=O), 7.7 (m), 7.9 (m), 8.15 (vs), 8.45 (vs), 9.85 μ (vs); mass spectrum *m/e* 123 (C_3F_3NO), 104 (C_3F_2NO), 97 (C_2F_3O), 54 (C_2NO). The unused volatile material (10.4 g) was bubbled through distilled water. Pure perfluoropivalonitrile (4.4 g, 71.2%) was isolated, as shown by GC and mass spectra.

Mixture of Sulfite 6 and Thionyl Chloride. The pyrolysis of sulfite **6** in the presence of an excess of thionyl chloride was studied at 400, 350, and 300 °C. At 400 and 350 °C the sulfite conversion was complete. As an example the run at 300 °C is described in detail. In 15 min a mixture of sulfite **6** (11.0 g, 0.025 mol) and thionyl chloride (8.3 g, 0.069 mol) was passed through the reactor. The products (18.0 g) were trapped at −70 °C. The gaseous products (9.2 g) were separated by distillation. The residue (8.8 g) was a mixture of thionyl chloride and sulfite **6.** The gaseous materials were separated by GC into three major peaks of about equimolar quantities and one minor peak (~5% of the third fraction). The fractions were collected in gas infrared cells and analyzed by infrared and mass spectroscopy. The first fraction was shown to be hexafluoroacetone. The second fraction was sulfur dioxide. The third fraction corresponded to 2-chloro-2-(trifluoromethyl)-3,3,3-trifluoropropionitrile (**9**). Hexafluoroacetone and the nitrile **9** were present in a molar ratio of 1:0.84.

Perfluoropivalamide. A crude mixture of products (29.0 g) from pyrolysis of sulfite **6** at 400 °C was introduced into a flask containing 140 ml of concentrated sulfuric acid and heated to 130 °C. The flask was equipped with a dry ice condenser. Reflux was continued for 8 h while the bath was kept at 150 °C. The volatile portions were collected (19.5 g) and analyzed by ir after separation by GC. The volatile portions contained unreacted perfluoropivalonitrile, sulfur dioxide, and traces of trifluoroacetyl fluoride. Hexafluoroacetone and 2-oxo-3,3,3-trifluoropropionitrile were consumed. The residual sulfuric acid solution was distilled, affording 0.5 g of colorless crystals: mp 139 °C; mass spectrum *m/e* 263 ($C_5H_2F_9NO$), 179 (C_4HF_6O), 113 (C_3F_4H), 112 (C_3F_4), 92 (C_2F_2NO), 91 (C_3HF_2O). Both the melting point of 139 °C (lit.[6] mp 138 °C) and the mass spectrum correspond to perfluoropivalamide.

2-Chloro-2-(trifluoromethyl)-3,3,3-trifluoropropionic Acid. The crude volatile products (7.6 g) from pyrolysis of a mixture of thionyl chloride and sulfite **6** were added to concentrated sulfuric acid (80 ml) in a stainless steel container. The reaction mixture was stirred and heated to 180 °C for 30 min. The volatile portions (2.2 g) were collected and shown by GC to contain the unreacted 2-chloro-2-(trifluoromethyl)-3,3,3-trifluoropropionitrile, small amounts of sulfur dioxide, and traces of hexafluoroacetone. Distillation of the residual sulfuric acid yielded hygroscopic, colorless crystals (2.1 g): bp 138–140 °C; mp 67–70 °C; MS *m/e* 186 (C_3HClF_6), 44 (CO_2); 4.30 mequiv CO_2H/g (theory 4.34 mequiv CO_2H/g).

Acknowledgment. We wish to thank E. McCarthy for his assistance with mass spectral measurement and chromatographic separations.

Registry No.—**1**, 677-77-0; **1** Na salt, 6737-59-3; **2a,** 58249-77-7; **2b,** 58249-78-8; **3,** 7594-51-6; **4,** 58249-79-9; **6,** 58249-80-2; **9,** 15056-76-5; **10,** 58249-81-3; **11,** 5882-04-2; sodium cyanide, 143-33-9; hexafluoroacetone, 684-16-2; [1-(trifluoromethyl)-1-methylcarboxy-2,2,2-trifluoroethoxy]dichlorophosphite, 58249-82-4; phosphorus trichloride, 7719-12-2; trifluoroacetyl fluoride, 354-34-7; trifluoroacetonitrile, 353-85-5; sulfur dioxide, 7446-09-5.

References and Notes

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(7) The pK_a value was obtained from extrapolation of the pK_a vs. $\Sigma\sigma$ plot using pK_a values for fluorinated tertiary alcohols.[3]