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Perfluorinated Compounds

Convenient Access to Trifluoromethanol**

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Dedicated to Professor George Olah on the occasion of his 80th birthday

With the exception of *cyclo*-C_4F_7OH,[1] alcohols possessing a fluorine atom on the α-carbon atom are unstable and undergo facile HF elimination. Therefore, it is not surprising that the most simple perfluorinated alcohol, trifluoromethanol (CF_3OH), was synthesized by Seppelt only in 1977.[2] His synthesis of CF_3OH involved the reaction of a positively and a negatively polarized chlorine ligand at −120 °C [Eq. (1)].

$$CF_3OCl + HCl \rightarrow CF_3OH + Cl_2 \tag{1}$$

The fact that the thermally unstable CF_3OCl is not readily available and had to be prepared from ClF and $Cs^+[CF_3O]^-$, which in turn had to be prepared from CsF and COF_2, discouraged further synthetic work with this interesting compound. In spite of great academic and commercial interest in -OCF_3 substituted compounds, these have been prepared exclusively by relatively cumbersome methods, such as the replacement of the doubly bonded oxygen atom in acyl fluorides by SF_4 or halogen-exchange reactions using HF at elevated temperatures and pressures and long reaction times.[3] A literature survey showed that out of 128 citations found by SciFinder for CF_3OH, only the original synthesis reports,[2] an unsuccessful attempt to protonate CF_3OH in HF/SbF_5,[4] a measurement of its UV spectrum,[5] and a study of its photoionization[6] involved the actual bulk synthesis or handling of CF_3OH. Therefore, it was of great interest to find a more convenient access to this interesting compound to make it readily available for general syntheses.

During a previous study we found that an excess of COF_2 reacts with the strong Lewis acids SbF_5 and AsF_5 to form oxygen-bridged, donor–acceptor adducts.[7,8] However, when anhydrous HF was used as a solvent in these reactions, very different products were obtained. This surprising result prompted us to study the interaction of anhydrous HF with COF_2 in more detail. It was found that anhydrous HF and COF_2 are in equilibrium with CF_3OH [Eq. (2)].

$$COF_2 + HF \overset{K_1}{\rightleftharpoons} CF_3OH \tag{2}$$

Equation (2) constitutes a direct polar addition of HF across the C=O bond with the δ^+ hydrogen and the δ^- fluorine atoms of HF adding to the δ^- oxygen and δ^+ carbon atoms of the carbonyl group, respectively. Such addition reactions are well known. For example, Olah and Pavlath reported in 1953 that HF adds across the C=O bond of formaldehyde, but were unable to isolate and characterize the pure monofluoromethanol.[9] In subsequent papers, Olah and Mateescu[10] and Minkwitz et al.[11] successfully stabilized this alcohol by protonation in super acids and identified the resulting $FCH_2OH_2^+$ ion in solution by multinuclear NMR spectroscopy. Similarly, Andreades and England successfully added HF across the C=O bond of hexafluorocyclobutanone.[1]

We have studied the equilibrium in Equation (2) by variable-temperature ^{19}F NMR spectroscopy. In the temperature range from −45 to 25 °C the percentage of CF_3OH increased from about 21 % at −45 °C to a maximum of about 33 % at −5 °C and then dropped off again rather sharply to about 20 % at 25 °C (Figure 1). This kind of temperature dependence was rather unexpected because the unimolecular dissociation of CF_3OH to COF_2 and HF has been calculated to be endothermic ($\Delta H \approx 7\ \mathrm{kcal\,mol^{-1}}$),[12] and, therefore, the formation of CF_3OH should be favored by a decrease in temperature. The shape of the temperature-dependence curve of Equation (2) implies that more than one equilibrium reaction is involved. A plausible explanation for the observed curve shape is that the concentration of monomeric HF is also governed by a temperature-dependent equilibrium between monomeric and oligomeric HF [Eq. (3)].

$$n\,HF \overset{K_2}{\rightleftharpoons} (HF)_n \tag{3}$$

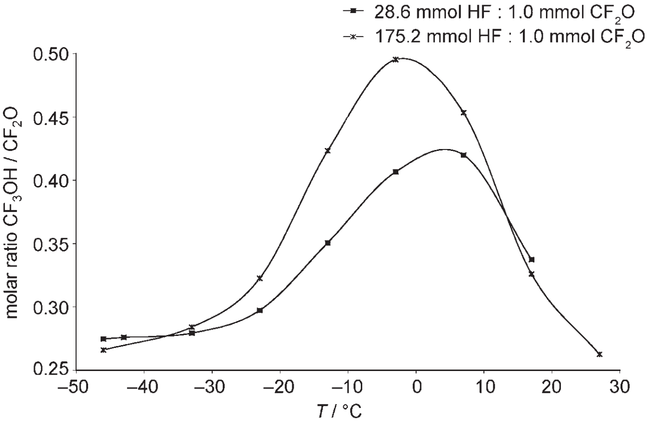

Figure 1. Temperature dependence of the $COF_2 + HF \rightleftharpoons CF_3OH$ equilibrium measured by area integration of the corresponding ^{19}F NMR signals for two different mole ratios of HF/COF_2.

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It is well known that HF forms oligomeric ring and chain structures in the liquid phase, and even in the gas phase at elevated pressures.[13] Combining Equations (2) and (3) shows that the absolute concentration of CF_3OH increases, as expected, with increasing concentrations of COF_2 and monomeric HF [Figure 2 and Eq. (4)] and that the mole ratio of

$$[CF_3OH] = K_1[COF_2][HF] = K_1[COF_2]^n\sqrt{\frac{[(HF)_n]}{K_2}} \qquad (4)$$

CF_3OH to COF_2 increases with increasing dilution, and decreases if K_2 dominates at the lower temperatures [Eq. (4)].

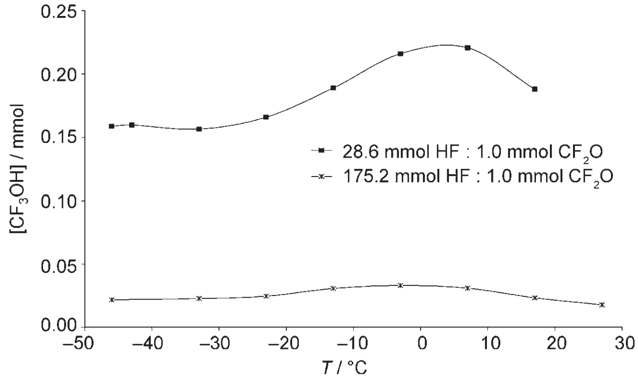

Figure 2. Temperature dependence of the absolute concentrations of CF_3OH measured by area integration of the ^{19}F NMR signals of HF and CF_3OH for two different mole ratios of HF/COF_2.

Therefore, the CF_3OH/COF_2 ratio is higher in dilute solution, although the absolute CF_3OH concentration becomes lower. To a lesser extent, the CF_3OH concentration is also influenced by the solubility of COF_2 in liquid HF. To minimize this effect, the NMR equilibrium measurements were carried out with a large excess of COF_2 and a minimum of ullage above the liquid phase.

The reversal of the slope of the CF_3OH concentration curve at about $-5\,^{\circ}C$, accompanied by a sharp decline in CF_3OH concentration at higher temperatures is attributed to the thermal decomposition of CF_3OH[2] becoming the dominating effect. On the basis of previous calculations, which showed that the energy barrier for intramolecular HF elimination is very high,[12] this decomposition is most likely not unimolecular, but either involves a dimer or oligomer or is catalyzed by traces of H_2O,[12] HF, or active surfaces. The equilibrium in Equation (2) was also approached from the CF_3OH side by treating $Cs^+CF_3O^-$ with a large excess of liquid HF [Eq. (5)].

$$Cs^+CF_3O^- + 2\,HF \rightarrow Cs^+HF_2^- + CF_3OH \qquad (5)$$

It was found that the equilibrium in Equation (2) was rapidly established and the COF_2/CF_3OH ratio was comparable to that obtained when it was approached from the COF_2/HF side. The experimental determination of individual rate constants for the different equilibria was not feasible because of the complexity of the system.

A second major issue was the determination of the exact nature of the CF_3OH species present in liquid HF. Because gaseous oligomeric HF is a stronger acid than monomeric HF[14] or HN_3,[15] HN_3 is completely protonated in liquid HF [Eq. (6)].[16]

$$n\,HF + HN_3 \rightleftharpoons H_2N_3^+HF_2^- \cdot (n-2)\,HF \qquad (6)$$

Although the gas-phase acidity of CF_3OH is somewhat higher[17,18] than that of HN_3, polymeric liquid HF is more acidic than either monomeric HF or CF_3OH (see Table 1). Therefore, the possibility had to be considered that in liquid HF trifluoromethanol might also be protonated.

Table 1: Observed (values listed with error bars) and calculated (values listed without error bars) gas-phase acidities of CF_3OH and related acids.

acid	ΔG° [kcal mol^{-1}]	Ref.
$(HF)_3$	304.0	[14]
HI	309.3 ± 0.2	[a]
CF_3OH	323.0 ± 1.6	[17]
$(HF)_2$	326.1	[14]
HCl	328.10 ± 0.10	[a]
HN_3	337.9 ± 2.3	[a]
HF	365.50 ± 0.2	[a]

[a] Data from NIST Standard Reference Database 69, March 1998 Release: *NIST Chemistry WebBook* (data compiled by J. E. Bartmess).

This issue was settled by recording the ^{13}C and ^{19}F NMR spectra of HF solutions of CF_3OH and $[CF_3OH_2]^+[SbF_6]^-$ and comparing them with those previously reported[2] for neat CF_3OH. It was found that the chemical shifts of all three systems were, within experimental error, identical (see Table 2). Because one would predict that on protonation of CF_3OH the carbon and the fluorine nuclei should become more deshielded, the chemical shifts for these species were calculated by theoretical methods (see Table 2). The calculated ^{19}F chemical shifts were in excellent agreement with those observed for neat CF_3OH[2] and the closely related species CF_3OCH_3 and $[CF_3O(CH_3)_2]^+$[19] and, indeed, predicted significant deshielding on protonation. The calculated corresponding ^{13}C chemical shifts for the trifluoromethyl

Table 2: Observed ^{19}F and ^{13}C NMR data for CF_3OH and related compounds. Values calculated at the MP2/6-311++G(2d,2p) level are given in parentheses.

	δ ^{19}F obsd (calcd) [ppm]	δ ^{13}C obsd (calcd) [ppm]	$^1J_{13C-19F}$ [Hz]
neat CF_3OH[a]	−54.5 (−59.9)	118 (131.4)	256
CF_3OH in HF	−57.8	120.4	254
$CF_3OH_2^+SbF_6^-$ in HF	−58.4 (−41.1)	116.8 (136.4)	277
CF_3OCH_3[b]	−65.6 (−68.3)	CF_3 123.7 (132.6), CH_3 53.7 (56.3)	252.3
$CF_3OHCH_3^+SbF_6^-$ in HF	−63.7 (−59.1)	CF_3 118.2 (132.5), CH_3 (78.9)	281
$CF_3O(CH_3)_2^+SbF_6^-$ in HF[b]	−66.9 (−67.9)	CF_3 120.7 (132.8), CH_3 80.2 (81.0)	287.0

[a] Data from reference [2]. [b] Data from reference [19].

groups of the unprotonated species were about 12 ± 2 ppm lower than those observed and also showed some, albeit smaller, deshielding on protonation.

These findings presented a dilemma because either the experimental or the calculated shifts had to be seriously flawed and, therefore, it was impossible to decide on the basis of the chemical shift data alone whether CF_3OH in liquid HF is protonated or not. Fortunately, the one-bond ^{13}C-^{19}F coupling constants were found to be significantly different for CF_3OH ($^1J_{13C,19F} = 255 \pm 1$ Hz) and $CF_3OH_2^+$ ($^1J_{13C,19F} = 277 \pm 1$ Hz). This difference is in accord with our expectations that on protonation, the covalent character and s-orbital contribution to the C–F bond should increase, resulting in stronger coupling. Because the $^1J_{13C,19F}$ coupling constant for CF_3OH in liquid HF was observed to be 254 Hz, it can be concluded that 1) CF_3OH is not protonated in liquid HF and 2) coupling constants provide a much better criterion than chemical shifts for distinguishing between protonated and unprotonated species. Additional support for the conclusion that CF_3OH in HF solution is unprotonated comes from the reaction of $CsCF_3O$ with HF. The formation of HF_2^- as a by-product in Equation (5) reduces the acidity of the HF solvent, thereby rendering protonation of CF_3OH less likely. In agreement with the spectra of the neat $CF_3OH/COF_2/HF$ system, the $^1J_{13C,19F}$ coupling constant was observed to be 254 Hz.

Having demonstrated that CF_2O and HF are in equilibrium with CF_3OH with useful CF_3OH concentrations as high as 33 mol %, it remained to be shown that this equilibrium can be exploited for synthetic purposes. Continuous removal of CF_3OH by reaction with a suitable reagent shifts the equilibrium in Equation (2) all the way to the right and allows trapping of the CF_3OH in the form of useful derivatives. We have demonstrated this approach by conversion of the CF_3OH into either trifluoromethyloxonium MF_6^- (M = Sb or As) salts [see above and Eq. (7)] or ethers,

$$CF_3OH + HF + MF_5 \rightarrow CF_3OH_2^+MF_6^- \qquad (7)$$

such as CF_3OCH_3 (E143A), which are of significant interest as potential chlorofluorocarbon replacements with low ozone depletion potentials [Eq. (8)].

$$CF_3OH + CH_3F \rightarrow CF_3OCH_3 + HF \qquad (8)$$

The syntheses of numerous higher α-fluoro alcohols and the generality of the ether formation have also been demonstrated in our laboratory, but are not included herein because of the large amount of data and the space limitations. In addition to the ether synthesis, the convenient access to trifluoromethanol is expected to have also significant industrial interest for other applications, such as trifluoromethoxy-substituted compounds for pharmaceuticals and liquid-crystal materials.[3] More details on the reaction chemistry of CF_3OH, the stability and barriers to HF elimination in fluoro alcohols, and the syntheses of higher α-fluoro alcohols and their reaction chemistry will be published in separate papers.

In conclusion, the $COF_2 + HF \rightleftharpoons CF_3OH$ equilibrium provides a convenient one-step access to trifluoromethanol from inexpensive and readily available bulk chemicals. It is expected to transform CF_3OH from an exotic laboratory curiosity into a generally useful reagent of significant interest for the syntheses of commercially interesting products.

Experimental Section

Caution! Carbonyl fluoride is a toxic gas (24 h $LC_{50} = 370$ ppm)[20] and should be handled with care. Anhydrous HF can cause severe burns and contact with the skin must be avoided.

Materials and apparatus: All reactions were carried out in either teflon-FEP NMR tubes or ampules that were closed by stainless steel valves. Volatile materials were handled in a stainless steel/teflon-FEP vacuum line.[21] All reaction vessels were passivated with ClF_3 prior to use. HF was dried by storage over BiF_5.[22] Carbonyl fluoride (PCR Research Chemicals) was purified by fractional condensation prior to use. The NMR spectra were recorded either on Varian Unity 300 MHz or Bruker AMX-500 NMR instruments by using 5-mm variable-temperature broad-band probes and TMS and $CFCl_3$ as external references. The mole ratios of HF and CF_3OH were determined by area integration of the corresponding NMR signals. The absolute concentrations of CF_3OH were determined by integration of the areas of the CF_3OH and HF NMR signals and weighing of the HF used. Nonvolatile materials were handled in the dry nitrogen atmosphere of a glove box.

Preparation of solutions of CF_3OH in HF: In a typical experiment, anhydrous HF (3 mL) and COF_2 (5 mmol) were condensed on the vacuum line at −196 °C into a prepassivated, 5-inch o.d. teflon-FEP ampule, which was closed by a stainless steel valve. The mixture was warmed to 0 °C and rapidly equilibrated to a solution containing COF_2 and CF_3OH in a mole ratio of about 2.5:1. These solutions were stable at room temperature. Complete conversion of COF_2 into CF_3OH could be achieved by the addition of a third component, such as a strong Lewis acid or CH_3F in the presence of a suitable catalyst, which reacted quantitatively with the CF_3OH and shifted the $COF_2 \rightleftharpoons CF_3OH$ equilibrium all the way to the side of CF_3OH.

Theoretical methods: Theoretical calculations were carried out by using the B3LYP density functional method[23] and a 6-311++G(2p,2d)[24] basis set. Optimized geometries and isotropic NMR shieldings were calculated by the GIAO-MBPT(2) approach,[25] which employs the gauge-including atomic orbital (GIAO) solution to the gauge-invariance problem.[26] Chemical shifts were obtained by referencing these shieldings to those of the standard reference compounds TMS and $CFCl_3$, which were computed at the same level of theory.

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[1] S. Andreades, D. C. England, *J. Am. Chem. Soc.* **1961**, *83*, 4670.
[2] a) K. Seppelt, *Angew. Chem.* **1977**, *89*, 325; *Angew. Chem. Int. Ed. Engl.* **1977**, *16*, 322; b) G. Kloeter, K. Seppelt, *J. Am. Chem. Soc.* **1979**, *101*, 347.
[3] P. Kirsch, *Modern Fluoroorganic Chemistry*, Wiley-VCH, Weinheim, **2004**.
[4] R. Minkwitz, D. Konikowski, *Z. Anorg. Allg. Chem.* **1995**, *621*, 2055.
[5] L. T. Molina, M. J. Molina, *Geophys. Res. Lett.* **1996**, *23*, 563.

[6] R. L. Asher, E. H. Appelman, J. L. Tilson, M. Litorja, J. Berkowitz, B. Ruscic, *J. Chem. Phys.* **1997**, *106*, 9111.

[7] K. O. Christe, B. Hoge, J. A. Boatz, G. K. S. Prakash, G. A. Olah, J. A. Sheehy, *Inorg. Chem.* **1999**, *38*, 3132.

[8] B. Hoge, J. A. Boatz, J. Hegge, K. O. Christe, *Inorg. Chem.* **1999**, *38*, 3143.

[9] G. A. Olah, A. Pavlath, *Acta Chim. Acad. Sci. Hung.* **1953**, *3*, 203.

[10] G. A. Olah, G. D. Mateescu, *J. Am. Chem. Soc.* **1971**, *93*, 781.

[11] R. Minkwitz, S. Schneider, H. Preut, *Angew. Chem.* **1998**, *110*, 510; *Angew. Chem. Int. Ed.* **1998**, *37*, 494.

[12] W. F. Schneider, T. J. Wallington, R. E. Huie, *J. Phys. Chem.* **1996**, *100*, 6097, and references therein.

[13] a) N. N. Greenwood, A. Earnshaw, *Chemistry of the Elements, 2nd ed.*, Butterworth-Heinemann, Oxford, **1998**, chap. 17; b) Holleman-Wiberg, *Inorganic Chemistry*, Academic Press, **2001**, p. 61.

[14] W. D. Chandler, K. E. Johnson, J. L. E. Campbell, *Inorg. Chem.* **1995**, *34*, 4943.

[15] Y. Fu, L. Liu, R.-Q. Li, R. Liu, Q-X. Guo, *J. Am. Chem. Soc.* **2004**, *126*, 814, and references therein.

[16] W. W. Wilson, K. O. Christe, A. Vij, R. Haiges, Paper B-O-03, presented at the 14th European Symposium on Fluorine Chemistry, 11–16th July, **2004**, Poznan, Poland.

[17] L. G. Huey, E. J. Dunlea, C. J. Howard, *J. Phys. Chem.* **1996**, *100*, 6504.

[18] R. Notario, O. Castano, J. L. M. Abboud, *Chem. Phys. Lett.* **1996**, *263*, 367.

[19] R. Minkwitz, S. Reinemann, R. Seelbinder, D. Konokowski, H. Hartl, I. Bruedigam, J. Hegge, B. Hoge, J. A. Sheehy, K. O. Christe, *Inorg. Chem.* **2001**, *40*, 4404.

[20] D. L. Scheel, W. C. Lane, W. E. Coleman, *Am. Ind. Hyg. Assoc. J.* **1968**, *29*, 41.

[21] K. O. Christe, W. W. Wilson, C. J. Schack, R. D. Wilson, *Inorg. Synth.* **1986**, *24*, 39.

[22] K. O. Christe, W. W. Wilson, C. J. Schack, *J. Fluorine Chem.* **1978**, *11*, 71.

[23] A. D. Becke, *J. Chem. Phys.* **1993**, *98*, 5648.

[24] M. J. Frisch, J. A. Pople, J. S. Binkley, *J. Chem. Phys.* **1984**, *80*, 3265.

[25] J. Gauss, *Chem. Phys. Lett.* **1992**, *191*, 614.

[26] R. Ditchfield, *Mol. Phys.* **1974**, *27*, 789.