1,2,4-triazoline-3,5-dione and 4-(3-chlorophenyl)-1,2,4-triazoline-3,5-dione appear to be new compounds.

The five different 4-aryl-1,2,4-triazoline-3,5-diones (2 where G = 3-ClC_6H_4, 4-ClC_6H_4, H, 4-$CH_3C_6H_4$, and 4-$CH_3OC_6H_4$) were synthesized via the following general procedure.[29] *N*-Bromosuccinimide (20 mmol) was added to an ice-cold suspension of urazoles (10 mmol) in 150 mL of CH_2Cl_2. After being stirred for 20 min, the resulting red solution was extracted five times with water. The CH_2Cl_2 layer was then dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting solution was chilled to −10 °C (freezer) overnight and gave pink to dark red crystals of the various triazolinediones. The yield (%), melting point, ^1H NMR, and elemental analyses are as follows: (a) **4-phenyl-1,2,4-triazoline-3,5-dione**, red solid, (82%); mp 169–180 °C (dec at lower temperature) (lit.[28b] mp 165–175 °C); ^1H NMR ($CDCl_3$) δ 7.41–7.60 (m, 5 H, aryl protons); (b) **4-(4-methoxyphenyl)-1,2,4-triazoline-3,5-dione**, brick red solid, (80%); mp 130–131 °C dec (lit.[30] mp 130–131 °C); ^1H NMR ($CDCl_3$) δ 3.85 (s, 3 H, CH_3), 7.0 (d, 2 H, *m*-H), 7.35 (d, 2 H, *o*-H); (c) **4-(4-chlorophenyl)-1,2,4-triazoline-3,5-dione**, cherry red crystals, (60%); mp 131–133 °C (expanded) (lit.[29] mp 130–132 °C); ^1H NMR ($CDCl_3$) δ 7.4 (d, 2 H, m-H), 7.55 (d, 2 H, m-H); (d) **4-(4-methylphenyl)-1,2,4-triazoline-3,4-dione**, deep purple crystals, (82%); mp 160–168 °C (dec before melting); ^1H NMR ($CDCl_3$) δ 2.4 (s, 3 H, CH_3), 7.3 (m, 4 H, aryl protons). Anal. Calcd for $C_9H_7N_3O_2$: C, 57.14; H, 3.70; N, 22.22. Found: C, 57.20; H, 3.75; N, 22.29;[31] (e) **4-(3-chlorophenyl)-1,2,4-triazoline-3,5-dione**, red crystals (70%); mp 109–110 °C (with dec); ^1H NMR ($CDCl_3$) δ 7.4–7.55 (m, 4 H, aryl protons). Anal. Calcd for $C_8H_4N_3O_2Cl$: C, 45.93; H, 1.91; N, 20.10; Cl, 16.75. Found: C, 45.91; H, 1.92; N, 19.96; Cl, 16.97.[31]

Acidity Determinations. An overlapping indicator method identical to that described previously[3b] was utilized to acquire the acidity data listed in Table I. The acidity constants for the neutral urazoles have been published previously; these pK_a's are thought to be accurate to less than 0.1 pK_a unit (0.1 kcal/mol).[5] The 4-phenylurazole monoanion was equilibrated against 9-[*p*-(methylsulfonyl)phenyl]xanthene, 1,1,3-triphenylpropene, 9-*tert*-butylfluorene, and iminostilbene (pK_{H-A}'s for these indicators are 24.4, 25.6, 24.3, and 26.1, respectively),[3b] while the 4-methylurazole monoanion was equilibrated against 1,1,3-triphenylpropene, 9-(*m*-chlorophenyl)xanthene, and iminostilbene (pK_{H-A}'s for these indicators are 25.6, 26.6, and 26.1, respectively).[3b] The internal agreement for the data collected when measuring pK_a's for the 4-phenylurazole monoanion and 4-methylurazole monoanion is such that the uncertainties in the pK_a's for these species are ca. 0.2 pK_a units (0.3 kcal/mol).

Redox Determinations. Dimethyl sulfoxide electrochemistry: 0.1 M $Et_4N^+BF_4^-$ electrolyte; Pt working and Ag/AgI reference electrodes (ferrocene/ferrocenium = +0.875 V as internal standard, values corrected to NHE_{aq} by subtracting 0.125 V). In the argonated electrochemical cell, the substrates were present in 1–2 mmol concentrations. The E_{ox} values in Table I are the anodic peak potentials as reported by a BAS 100A electrochemical analyzer, are the averages of several runs for each compound, and are reproducible to ≤25 mV (ca. 0.5 kcal/mol). The $E_{1/2}$ values in Table I are the midpoints between the anodic and cathodic CV waves for the reversible redox reactions in question. Cyclic voltammetry sweep rate: 0.1 V/s, except where indicated.

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Fluorinated Tertiary Alcohols and Alkoxides from Nucleophilic Trifluoromethylation of Carbonyl Compounds

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$(CH_3)_3SiCF_3$ reacts with fluoro ketones in the presence of excess KF in CH_3CN to produce alkoxides derived from formal addition of CF_3^- to the carbonyl carbon. These alkoxides may be isolated as such or acidified to the corresponding alcohols. Ketones to which this technique was applied include $(CF_3)_2C{=}O$, $CF_3C(O)CF_2Cl$, $CF_3C(O)CF_2H$, and $[(CF_3)_2CF]_2C{=}O$. The last compound reacts with replacement of one of its perfluoroisopropyl groups by CF_3. With 2 equiv of TMS–CF_3, the acid fluorides RC(O)F (R = CF_3CF_2, *n*-C_3F_7, *n*-C_7F_{15}) yield products of the form $RC(CF_3)_2OX$ (X = K, H) due to both substitution and addition of CF_3 at the carbonyl. Similarly, $F_2C{=}O$ with 3 equiv of TMS–CF_3 provides a novel and high-yield synthesis of the perfluoro-*tert*-butoxide group. Phosgene does not appear to react directly with the TMS–CF_3/KF system, but is converted first to $F_2C{=}O$. The intermediate ketone $CF_3CF_2C(O)CF_3$ is observed in reactions of equimolar amounts of $CF_3CF_2C(O)F$ and TMS–CF_3.

Introduction

During an investigation into the chemistry of fluorine-containing hypohalites, we developed a need for highly-fluorinated tertiary alcohols and their alkoxides, especially $(CF_3)_3COH$ and $(CF_3)_3COM$. Perfluoro-*tert*-butyl alcohol is very expensive even when it can be found and is subject to severe availability problems. While we had developed a method for the preparation of certain longer-chain alcohols via ring-opening of fluorinated oxetanes with HF/SbF_5,[1] this and related superacid reactions[2] proved to be of limited generality. $(CF_3)_3COH$ can in fact be obtained using such a ring-opening approach,[3,4] but the cyclic precursor in this case is the epoxide of the extremely toxic[5,6] perfluoroisobutene, $(CF_3)_2C{=}CF_2$. Other known

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routes rely on reactions using hexafluoroacetone, either through halogen exchange of the low-yield intermediate $CCl_3C(CF_3)_2OH$ with SbF_5[7-10] or via another low-yield reaction of $(CF_3)_2C{=}O$ with CsF[11] requiring a complicated workup. Other methods[12-15] are known which, like the ring-opening route, are based on $(CF_3)_2C{=}CF_2$.

Work has appeared[16] by Olah et al. in which $(CH_3)_3SiCF_3$ was used to prepare alcohols containing the trifluoromethyl group from hydrocarbon aldehydes and ketones. These reactions, initiated by a catalytic amount of F^-, $(CH_3)_3CO^-$, or Me_3SiO^- produce trimethylsilyl ether derivatives which can be converted in most cases to the alcohol by acid hydrolysis. Recent Hoechst patents[17] similarly describe reactions of $RR'C{=}O$ with perfluoroalkyl silicon compounds, but R and R′ did not both contain fluorine. One example of the conversion of an acid chloride to an intermediate trifluoromethyl ketone has appeared.[16b] In other related work, TMS–CF_3 has recently been used to prepare aryl trifluoromethyl sulfones from sulfonyl fluorides[18] and can also react with nonfluorinated oxalates[19] and quinones[20,21] to give alcohols or their intermediates in reactions catalyzed by F^- or other bases. $C_6F_5SiMe_3$ in the presence of CsF has been shown to effect replacement of fluorine in fluoro olefins[22,23] and imines.[24] The $C_6F_5SiMe_3$/CsF system also replaces aromatic fluorines in perfluorotoluene but is claimed to undergo no reaction with acid fluorides.[25] Substitution has also been achieved in perfluoroaromatics[26] using TMS–CF_3 with $(Me_2N)_3S^+$ $(CH_3)_3SiF_2^-$. In the case of benzaldehyde, $C_6F_5SiMe_3$ with KF reacts in a fashion similar to that described by Olah[16] for TMS–CF_3, leading to $Ph(C_6F_5)CH$–OTMS.[27] In the absence of KF the reaction requires a temperature of 170 °C.[28] Other nucleophiles, such as CN^-, in place of F^- cause $C_6F_5SiMe_3$ to react with ketones to produce silyl enol ethers resulting from abstraction of α-hydrogen by $C_6F_5^-$.[29-31] Metal fluoride-induced reactions of carbonyl compounds with other electronegatively-substituted aryltrimethylsilanes have also been investigated.[32] The general use of organosilicon compounds with nucleophilic catalysts has been reviewed.[33]

Also, since the R_FSiR_3[34] or $C_6F_5SiR_3$ transfer agents are synthesized from R_FX[17,35] or C_6F_5X[36,37] (X = Br, I) and $P(NR_2'')_3$ using R_3SiCl or R_3SiBr to trap the R_F group in a stable form, others have chosen to bypass formation of the organosilicon transfer agent and perform perfluoroalkyations with the $R_FX/P(NR_2'')_3$ mixture directly. This approach has been used to substitute R_F for F in fluoroolefins and perfluorotoluene.[38] The chlorine of aroyl chlorides may also be replaced to give $ArC(O)R_F$.[39]

We wish to report that TMS–CF_3 can be employed to generate tertiary alkoxides and alcohols by nucleophilic trifluoromethylation of a variety of fluoro ketones and acid fluorides in the presence of F^-. Besides an extension of scope, this investigation reflects departures from existing applications necessitated by differences between the chemistry of highly fluorinated ketones and alkoxides and their nonfluorinated analogues. Among other successes, the chemistry of TMS–CF_3 has provided a simple, high-yield synthesis of $(CF_3)_3COH$ from either $(CF_3)_2C{=}O$ or $F_2C{=}O$. This probably represents the best overall route to this alcohol to date.[40]

Experimental Section

General. Infrared spectra were recorded in glass cells of 10-cm pathlength; KCl or AgCl windows were attached with Halocarbon 1500 wax. NMR spectra were acquired at 200.13 MHz for ^1H and 188.31 MHz for ^{19}F. Chemical shifts are reported relative to $Si(CH_3)_4$ or $CFCl_3$ with shifts upfield from these designated as negative. Tetramethylsilane was usually omitted from ^1H samples, and the reference was actually set on the residual ^1H resonance of the deuterated solvent. Mass spectra were recorded on a Hewlett-Packard 5985B spectrometer. Both EI (70 eV) and $CI(CH_4)$ spectra were run at samples introduced by direct gas insertion.

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Volatile materials were manipulated on a glass vacuum line fitted with glass-Teflon stopcocks; amounts of volatiles were determined by PVT measurements using a Wallace & Tiernan Series 1500 differential pressure gauge. All trap-to-trap fractionations were performed under dynamic vacuum.

The reaction vessel for each run consisted of a 100-mL glass flask with a glass–Teflon stopcock attached through an Ace-Thred O-ring seal. The body of the flask was modified by the addition of a side arm fitted with a Teflon-faced silicone septum through which liquids could be added or withdrawn via syringe, without compromising the ability of the system to hold vacuum after removal of the needle. The reactors contained a Teflon-coated magnetic stirbar.

Purity of new compounds was determined by ^{19}F NMR and also by ^{1}H NMR as appropriate. Known compounds were identified by NMR and comparison with literature values.

Starting Materials. Anhydrous $(CF_3)_2C{=}O$, $[(CF_3)_2CF]_2{=}O$, $F_2C{=}O$, NaF, $(n\text{-}Bu)_4N^+F^-{\cdot}3H_2O$, anhydrous HCl, concd H_2SO_4, concd aqueous HCl, and 18-crown-6 were obtained from commercial sources and used as received. The solvents CH_3CN, Et_2O, and 2-methoxyethyl ether (diglyme) were anhydrous grade and also were used as received; they were transferred by syringe. Authentic samples of $(CF_3)_3COH$ were purchased from PCR, Inc. pentafluorochloroacetane was purified before use by vacuum trap-to-trap distillation through traps cooled to −70, −111, and −196 °C; the material collecting at −111 °C was retained for use. Phosgene was similarly distilled through −46, −126 and −196 °C traps, and the −126 °C fraction was used. Potassium fluoride and CsF were melted in a platinum dish and then ground to a fine powder under nitrogen in a ball mill. The KF and CsF were subsequently stored and handled in a nitrogen-filled drybox. (Trifluoromethyl)trimethylsilane[35] and authentic samples of $CF_3CF_2C(CF_3)_2OH$[1] were prepared by literature methods. $CF_3C(O)CF_2H$ was prepared from $CF_3C(O)CF_2Cl$.[41] $CF_3CF_2C(O)F$ was produced by fluorination of $CF_3CF_2C(O)Cl$ with SbF_3. Perfluorobutanoyl fluoride and $CF_3(CF_2)_6C(O)F$ were prepared from the respective acid chlorides using a large excess of NaF in sulfolane at 80 °C for 14 h. Sodium perfluoro-*tert*-butoxide was obtained by reacting commercial $(CF_3)_3COH$ with NaH in Et_2O.[42]

***Caution*!** Many of the fluoro ketones and tertiary alcohols involved in this work are very toxic. Also, we have found the conversion of the tertiary alkoxides to alcohols with sulfuric acid to be very exothermic; cooling of larger-scale reactions is recommended.

Exploratory NMR Experiments. Reactions designed to be run in NMR tubes were assembled by loading the fluoride source, if used, into a 5-mm NMR tube and determining the amount on an analytical balance. The tube was then attached to the vacuum line, and the volatile components (e.g., TMS–CF_3, $(CF_3)_2C{=}O$, reference, solvent) were added by vacuum transfer with the tube cooled to −196 °C. The liquid nitrogen bath was removed, and the tube was filled with dry N_2, removed from the vacuum line, capped, and warmed to room temperature.

Preparative-Scale Reactions. Preparation of $(CF_3)_3COH$ from $(CF_3)_2C{=}O$. Potassium fluoride (0.16 g, 2.8 mmol) was loaded into the reactor (see above), the reactor was evacuated, and 4.0 mL of CH_3CN was added by syringe. After the reactor was cooled to −196 °C, $(CF_3)_2C{=}O$ (3.50 mmol) and TMS–CF_3 (2.19 mmol) were condensed in and the reactor was placed in a −40 °C $CFCl_3$ bath to warm on its own. Stirring was begun as soon as the reaction mixtured melted (mp CH_3CN −48 °C). After 9 h the bath was removed and stirring was continued at 18 °C for another 3 h. A sample of the reaction mixture showed no remaining TMS–CF_3 by NMR. The solvent and other volatile materials were removed by vacuum pumping for 3 h at 18 °C, leaving a white solid. Concd H_2SO_4 (3 mL) was injected at 18 °C; it reacted exothermically with effervescence. The resulting colorless solution was subjected to dynamic vacuum for 1 h at 18 °C and the volatiles were collected in a liquid nitrogen trap on the vacuum line. The crude volatile product was fractionated through traps cooled to −50, −85, and −196 °C. $(CF_3)_3COH$ (2.00 mmol, 91.3% yield based on TMS–CF_3) was found in the −85 °C trap and was identified by its IR, ^{1}H and ^{19}F NMR, and mass spectra.

From $F_2C{=}O$. In the same manner as above, KF (0.44 g, 7.6 mmol), COF_2 (2.10 mmol), TMS–CF_3 (6.66 mmol), and 4.0 mL of CH_3CN were combined and the reaction mixture was stirred as it warmed from −40 °C to room temperature over 18 h. The solvent and other volatiles were then removed from the slightly yellow solution by pumping for 5 h at 22 °C. The volatiles collected in a −196 °C trap were fractionated and consisted of CH_3CN, TMS–F, and 0.12 mmol of CF_3H by IR. Concentrated H_2SO_4 (4.0 mL) was injected into the reactor cooled in an ice bath, and after 15 min, the resulting volatile products were collected in a liquid nitrogen trap by pumping on the reactor at 22 °C for 45 min. Fractionation of the crude product through traps at −46, −100, and −196 °C gave $(CF_3)_3COH$ (1.6 mmol, 77.1% yield) in the −100 °C trap.

Attempted Preparation from $Cl_2C{=}O$. Similarly, KF (0.47 g, 8.1 mmol), $COCl_2$ (2.02 mmol), and TMS–CF_3 (6.74 mmol) were combined in 4.0 mL of CH_3CN. After reaction the mixture consisted of CH_3CN, unreacted TMS–CF_3 (6.40 mmol), $COCl_2$, (0.37 mmol), and COF_2 (1.56 mmol).

$(CF_3)_3CO^-K^+$. Hexafluoroacetone (3.63 mmol) and TMS–CF_3 (2.21 mmol) were condensed at −196 °C onto a mixture of KF (0.22 g, 3.8 mmol) in 4.0 mL of CH_3CN. The reactor was placed in an EtOH bath at −25 °C and stirred as it warmed to 20 °C over 16 h. The volatiles were removed by pumping under high vacuum for 1 h, leaving a white powder which was then extracted into three 10-mL portions of Et_2O. Removal of the ether under vacuum permitted isolation of $(CF_3)_3CO^-K^+$[42] (0.55 g, 90.8% yield), identified by its ^{19}F NMR (acetone-d_6, singlet at −76.0 ppm).

$CClF_2C(CF_3)_2OH$. Chloropentafluoroacetone (3.50 mmol), KF (0.14 g, 2.4 mmol), and TMS–CF_3 (2.19 mmol) reacted in 4.0 mL of CH_3CN upon warming from −40 to 19 °C over 18 h. Evacuation for 5 h at 19 °C gave a yellow-white solid, to which was added 4.0 mL of concd H_2SO_4. The crude product was collected in a trap cooled in liquid nitrogen by pumping at 19 °C. Trap-to-trap distillation through traps cooled to −35, −70, and −196 °C gave the alcohol (1.94 mmol, 88.6% yield) in the −70 °C trap. IR, ^{19}F/^{1}H NMR, and mass spectra were consistent with this known compound.[7,8,10]

$CClF_2C(CF_3)_2O^-K^+$. On the same scale as above, $CF_3C(O)CF_2Cl$ gave a white powder, $CF_2ClC(CF_3)_2O^-K^+$ (0.54 g, 83.0% yield) which was characterized by its ^{19}F NMR spectrum: $CF_2{}^AClC(CF_3)_2{}^BO^-K^+$ (acetone-d_6) δ A −60.4 (2 F, sept), B −74.0 (6F, t) ppm; J_{AB} = 10.5 Hz. The sodium salt has been previously reported.[42]

$CHF_2C(CF_3)_2OH$ and $CF_3C(O)CF_2C(CF_3)(CF_2H)(OH)$. As above, $CF_3C(O)CF_2H$ (2.40 mmol) was combined with TMS–CF_3 and KF in CH_3CN at −196 °C. Fractionation of the volatile material after treatment with concd H_2SO_4, through traps cooled to −60, −80, and −196 °C gave $CHF_2C(CF_3)_2OH$ (0.41 mmol, 17.8%) in the −80 °C trap. Further fractionation of the material initially trapped at −60 °C through traps at −25 and −196 °C gave $CF_3C(O)CF_2C(CF_3)(CF_2H)(OH)$ (0.32 mmol) in the −25 °C trap.

The new compound $CHF_2C(CF_3)_2OH$ was characterized as follows: IR (3 Torr) 3617 (ν_{OH}, sharp, m), 3002 (ν_{CH}, w) cm^{-1}; NMR $H^ACF_2{}^BC(CF_3)_2{}^COH^D$ ($CDCl_3$) δ ^{19}F B −132.7 (2 F, d-sept), C −74.7 (6 F, t-d) ppm; δ ^{1}H A 6.09 (1 H, t-sept), D 3.41 (1 H, br s) ppm; $J_{AB} = 52.7$, $J_{AC} = 0.9$, $J_{BC} = 9.2$, $J_{AD} = J_{BD} = J_{CD} = 0$ Hz; m/z [EI] 179 $(M - HF - F)^+$, [CI] 219 $(MH)^+$.

The other product was identified by IR, ^{19}F/^{1}H NMR, and MS as $CF_3C(O)CF_2C(CF_3)(CF_2H)(OH)$, a known compound arising from dimerization of $CF_3C(O)CF_2H$ or its isomer $CF_3C(OH){=}CF_2$ in reactions with bases followed by acidification.[43,44]

$[(CF_3)_2CF]C(CF_3)_2OH$. Potassium fluoride (0.20 g, 3.4 mmol), 18-crown-6 (262.2 mg, 0.99 mmol), and 5.0 mL of diethyl ether were loaded into the reaction vessel, and then 3.00 mmol of $[(CF_3)_2CF]_2C{=}O$ and 3.30 mmol of TMS–CF_3 were condensed in at −196 °C. The reaction mixture was stirred for 30 min in a −10 °C bath followed by 11.5 h additional stirring at 20 °C, giving

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a yellow solution. Volatiles were removed under vacuum at 20 °C and 5.0 mL of concd H_2SO_4 was added to the remaining yellow-white solid. Crude product was collected by pumping at 20 °C through a trap cooled to −196 °C. Fractionation through traps at −40, −60, and −196 °C gave the known compound[45,46] $[(CF_3)_2CF]C(CF_3)_2OH$ (0.35 mmol, 21.2%) in the −60 °C trap.

$CF_3(CF_2)_6C(CF_3)_2O^-K^+$. Potassium fluoride (0.53 g, 9.1 mmol) and 6.0 mL of CH_3CN were loaded into a 250-mL glass reactor, and 3.17 mmol perfluorooctanoyl fluoride and 7.34 mmol TMS–CF_3 were added by vacuum transfer as above. The reactor was warmed slowly with stirring from −25 to 20 °C (16 h). The volatiles were then removed from the brown solution by pumping through a trap at −196 °C with intermittent heating of the reactor with a heating mantle or heat gun. The remaining brown powder was extracted with three 10-mL portions of Et_2O. The ether was removed on a rotary evaporator followed by high vacuum (4 h) to give $CF_3(CF_2)_6C(CF_3)_2O^-K^+$ (0.19 g, 10.4%). The new compound was characterized by its ^{19}F NMR spectrum: $CF_3{}^ACF_2{}^BCF_2{}^CCF_2{}^DCF_2{}^ECF_2{}^FCF_2{}^GC(CF_3{}^H)_2O^-K^+$ (acetone-d_6) δ A −80.6 (3 F, t-t), B −125.7 (2 F, m), C −122.2 (2 F, br s), D −121.3 (2 F, br s), E −120.5 (2 F, br s), F −118.8 (2 F, br s), G −114.4 (2 F, br s), H −73.8 (6 F, br s) ppm; $J_{AC} = 10.2$, $J_{AD} = 2.5$, $J_{BD} = 14.2$, $J_{HG} = 11.1$, $J_{HF} = 8.5$ Hz. A COZY ^{19}F NMR experiment supported the above assignments.

The volatile material removed contained a substantial amount of unreacted $TMSCF_3$ (~3.0 mmol) and a heavy oil along with the solvent. The oil appeared by ^{19}F NMR to consist of a mixture of the ester $CF_3(CF_2)_6C(CF_3)_2OC(O)(CF_2)_6CF_3$ (major) and another unknown compound. After removal of the solvent, the mixture could not be separated and no further characterization was attempted.

$CF_3(CF_2)_6C(CF_3)_2COH$. To a sample of $CF_3(CF_2)_6C(CF_3)_2COK$ (0.17 g) prepared as above was added 0.4 mL of concd H_2SO_4. After standing at 22 °C for 1 h, the volatile materials were collected under dynamic vacuum in a −196 °C trap and found to be a trace of SiF_4 and TMSF and the new alcohol $CF_3(CF_2)_6C(CF_3)_2OH$ (0.15 g, 94%): IR (~2 Torr) 3609 cm^{-1} (OH, w); NMR $CF_3{}^ACF_2{}^BCF_2{}^CCF_2{}^DCF_2{}^ECF_2{}^FCF_2{}^GC(CF_2{}^H)_2OH^I$ ($CDCl_3$) δ A −81.3 (t,t), B −126.6 (br s), C −123.2 (br s), D −123.1 (br s), E −122.3 (br s), F −120.5 (br s), G −115.2 (br s), H −72.6 (t, t), I 3.6 (s) ppm; $J_{AC} = 10.0$, $J_{AD} = 2.5$, $J_{HG} = 11.4$, $J_{HF} = 9.3$ Hz; *m/z* [CI] 537 (MH^+).

$CF_3CF_2CF_2C(CF_3)_2O^-K^+$. Heptafluorobutanoyl fluoride (2.00 mmol) and 4.69 mmol of TMS–CF_3 were allowed to react as above. The solvent and other volatiles were removed by pumping with occasionall gentle heating with a heat gun. The remaining brown powder was extracted with three 10-mL portions of Et_2O and treated as in the previous reaction to give $CF_3CF_2CF_2C(CF_3)_2O^-K^+$ (0.55 g, 73.5%), which was characterized by its ^{19}F NMR spectrum: $CF_3{}^ACF_2{}^BCF_2{}^C(CF_3)_2{}^DO^-K^+$ (acetone-d_6) δ A −80.1 (3 F, t), B −123.3 (2 F, m), C −115.4 (2 F, m), D −74.4 (6 F, br t) ppm; $J_{AC} = 11.7$, $J_{BC} = 4.3$, $J_{BD} - 8.7$, $J_{CD} = 11.2$ Hz. Reaction of the salt with concd H_2SO_4 gave a very high yield of the known alcohol $C_3F_7C(CF_3)_2OH$.[47-49]

$CF_3CF_2C(CF_3)_2OH$. $CF_3CF_2C(O)F$ (2.00 mmol) and TMS–CF_3 (4.30 mmol) were combined as above. Heating from −40 to 20 °C (9.5 h) followed by 7 h at 20 °C gave a dark brown mixture. The volatile materials were then removed by pumping to give a light brown powder in the reactor. Concentrated H_2SO_4 (5.0 mL) was then added. Crude product was collected by pumping through a trap cooled to −196 °C. Fractionation through traps cooled to −45, −85, and −196 °C gave the known compound[1,45,50] $CF_3CF_2C(CF_3)_2OH$ (1.70 mmol, 85.0%) in the −85 °C trap.

$CF_3CF_2C(CF_3)_2O^-K^+$. Using Excess TMS–CF_3. Hexafluorpropanoyl fluoride (2.08 mmol), TMS–CF_3 (4.66 mmol), KF (0.31 g, 5.3 mmol), and 4.0 mL of CH_3CN were combined as above. Upon warming with stirring in an ice bath to 20 °C over 16 h, the mixture turned first yellow then brown. The volatile materials were removed under vacuum with occasional heating with a heat gun. Extraction of the remaining light brown powder as above gave $CF_3CF_2C(CF_3)_2O^-K^+$ (0.45 g, 66.7%). The new compound was characterized by its ^{19}F NMR spectrum: $CF_3{}^ACF_2{}^BC(CF_3)_2{}^CO^-K^+$ (acetone-d_6) δ A −78.5 (3 F, sept), B −118.9 (2 F, sept), C −74.8 (6 F, br s) ppm; $J_{AC} = 5.4$, $J_{BC} = 11.0$ Hz.

Using Equimolar $CF_3CF_2C(O)F$ and TMS–CF_3 with a Catalytic Amount of KF. Potassium fluoride (0.02 g, 0.3 mmol), $CF_3CF_2C(O)F$ (2.03 mmol), TMS–CF_3 (2.02 mmol), and 4.0 mL of CH_3CN were combined as above and allowed to warm with stirring from −25 to 20 °C over 14 h. The volatiles were collected by pumping through traps at −58 and −196 °C. Further trap-to-trap distillation through −85, −124, and −196 °C traps gave unreacted $CF_3CF_2C(O)F$ (0.06 mmol) in the −196 °C trap. The −124 °C trap contained 2.90 mmol of material determined by ^{19}F NMR to consist of (mol %) $(CH_3)_3SiF$ (71.7), $CF_3CF_2C(O)CF_3$ (22.2), and $CF_3CF_2C(O)F$ (6.0). Total recovery of $CF_3CF_2C(O)F$ was 11.3%, while the amount of $CF_3CF_2C(O)CF_3$ corresponded to a 31.5% yield. The −85 °C trap contained acetonitrile and $CF_3CF_2C(CF_3)_2OC(O)CF_2CF_3$ with an estimated yield of 20% based on $CF_3CF_2C(O)F$. Workup of the residue left behind in the original reactor with Et_2O gave 0.08 g (12.1% yield) of $CF_3CF_2C(CF_3)_2O^-K^+$. $CF_3CF_2C(O)CF_3$[61] was identified by IR ν (C═O) 1798 cm^{-1}) and ^{19}F NMR: $CF_3{}^ACF_2{}^BC(O)CF_3{}^C$ ($CDCl_3$) δ A −82.3 (s), B −122.1 (q), C −75.3 (t) ppm; $J_{BC} = 8.2$ Hz. The ester $C_2F_5C(CF_3)_2OC(O)C_2F_5$ was identified in the same manner: ν (C═O) 1844 cm^{-1}; $CF_3{}^ACF_2{}^BC(CF_3)_2{}^COC(O)CF_2{}^DCF_3{}^E$ ($CDCl_3$) δ A −80.3 (3 F, m), B −117.2 (2 F, sept), C −67.5 (6 F, m), D −121.1 (2 F, m), E −83.2 (3 F, m) ppm; $J_{BC} = 10.7$ Hz. With a stoichiometric amount of KF, as above, the reaction of $CF_3CF_2C(O)F$ (2.02 mmol) gave a −196 °C fraction which on further separatio through traps at −83, −126, and −196 °C gave $CF_3CF_2C(O)F$ (0.07 mmol) in the −196 °C trap; 2.93 mmol of material in the −126 °C trap which by ^{19}F NMR consisted of (mol %) TMSF (70.2), $CF_3CF_2C(O)F$ (12.7), and $CF_3CF_2C(O)CF_3$ (17.2, 24.8% yield); and 2.27 mmol of material in the −83 °C trap which consisted of CH_3CN (92.5), $CF_3CF_2C(CF_3)_2OC(O)CF_2CF_3$ (7.5, 16.8% yield), and a trace of TMSF based on NMR. Total recovery of unreacted $CF_3CF_2C(O)F$ was 21.8%. Workup of the reactor residue with Et_2O gave $CF_3CF_2C(CF_3)_2O^-K^+$ (0.19 g, 29.2%).

Results and Discussion

Initial Attempts Using Ethereal Solvents. Early reactions using hexafluoroacetone in diglyme or diethyl ether showed the technique to be applicable to the preparation of perfluoro-*tert*-butyl alcohol. At first, diglyme was used with $(CF_3)_2C{=}O$, TMS–CF_3, and KF. Since at that time the principal intermediate was expected to be $(CF_3)_3C$–OTMS because of the mechanism proposed by Olah et al.,[16] the diglyme was not removed but concd aqueous HCl or anhydrous HCl was added directly to the reaction solution to hydrolyze the expected intermediate to the parent alcohol. The resulting alcohol (IR, ^{19}F NMR) could not be separated from the solution apparently due to complex formation between the alcohol and diglyme.[51,52]

The use of Et_2O rather than diglyme enabled the solvent to be easily removed under vacuum. By addition of concd H_2SO_4 to the residue $(CF_3)_3COH$ was first isolated in 29% yield from a $(CF_3)_2C{=}O$/TMS–CF_3/KF reaction by using this procedure with Et_2O. NMR analysis showed unreacted TMS–CF_3 and no evidence for $(CF_3)_3COSiMe_3$. At this point it was clear that the reaction was not catalytic in KF and that a more polar solvent was needed.

Exploratory NMR Experiments. A series of reactions was conducted in NMR tubes to determine the require-

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ments and scope of the reaction. Products were not isolated but were observed by NMR in order to design subsequent preparative methodologies.

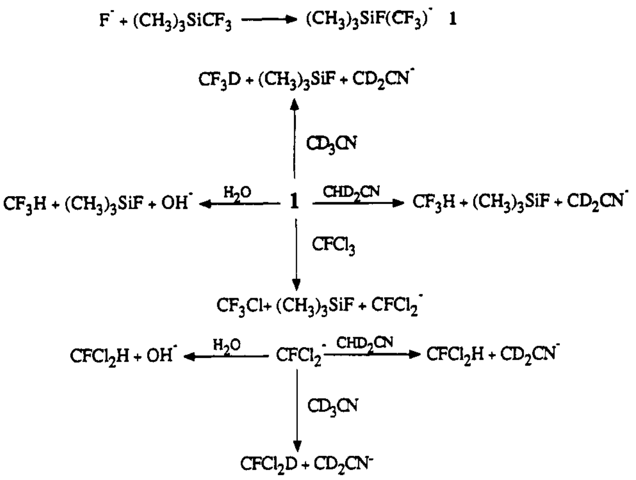
The weakly nucleophilic perfluoro-*tert*-butoxide anion was shown to be incapable of propagating a TMS–CF_3 reaction in an Olah-type mechanism[16] involving nucleophilic attack of the alkoxide on silicon, since an equimolar mixture of Na^+ $^-OC(CF_3)_3$, TMS–CF_3, and hexafluoroacetone in $Et_2O/CFCl_3$, in which all the components were soluble, failed to undergo any reaction during 29 h at 20 °C. This ruled out catalysis of reactions of TMS–CF_3 and highly fluorinated ketones by alkoxides; Olah's reactions can be catalyzed by the much more nucleophilic $(CH_3)_3CO^-$.

The reactivity of various sources of fluoride ion with TMS–CF_3 were also evaluated. In an $Et_2O/CFCl_3$ mixture, NaF was unreactive, and KF reacted slowly (over a period of days). Cesium fluoride displayed a much faster reaction, and $(n\text{-}Bu)_4N^+F^-\cdot 3H_2O$ reacted even more quickly, as would be expected from fluoride solubility considerations. The same trend was evident using a $CD_3CN/CFCl_3$ solvent system, although the tetrabutylammonium salt was not investigated. An overall increase in the reaction rate of F^- with TMS–CF_3 in CD_3CN over that in Et_2O was obvious. The very rapid reaction in the case of CsF was impressive since, although it is certainly more soluble here than in Et_2O, its solubility in acetonitrile is still quite low (3.465×10^{-4} mol/L at 29 °C[53]). As reactions between F^- and TMS–CF_3 proceeded in this solvent system without a carbonyl compound to trap the reactive intermediate, the mixture acquired a brown color and the formation of a variety of halomethanes (CF_3D, CF_3H, CF_3Cl, $CFCl_2D$, $CFCl_2H$) as well as the expected TMSF was evident by NMR. The brown color appeared in preparative-scale reactions with carbonyl compounds only when the carbonyl compound did not participate in the reaction or toward the end of successful reactions where the CF_3 transfer agent was used in excess.

Additional NMR experiments were run using TMS–CF_3 and $(CF_3)_2C{=}O$ in $CD_3CN/CFCl_3$ to further investigate whether a catalytic amount of initiator was sufficient for reactions with highly fluorinated ketones and, as an extension, whether an initiator was necessary at all. It was found that a catalytic amount of KF (3.6 mg, 0.062 mmol) underwent a small amount of immediate reaction at ambient temperature to produce TMSF, CF_3Cl, and $(CF_3)_3CO^-K^+$ as observed by NMR, followed by the slow appearance over a period of days of signals which may have been due to $(CF_3)_3COTMS$, but the amount was very small and this was not confirmed. In the absence of any initiator, no reaction was evident between hexafluoroacetone and TMS–CF_3 in $CD_3CN/CFCl_3$ during five days at 20 °C.

Olah's[16] fluoride initiator of choice was $(n\text{-}Bu)_4N^+F^-\cdot 3H_2O$, and of the fluorides tested in our work in Et_2O it proved the fastest by far in the generation of TMSF from TMS–CF_3. We viewed it as an unlikely candidate for a fluoride source in reactions of TMS–CF_3 with highly fluorinated carbonyl compounds, however, since it was a trihydrate. The recent synthesis[54] of anhydrous HF_2^--free $[N(CH_3)_4]^+F^-$ may solve this problem and enable easy extension of trifluoromethylation with TMS–CF_3 to large highly fluorinated carbonyl compounds and other fluorinated substrates which have poor solubility in acetonitrile but which are soluble in other solvents not generally suited to metal fluoride reactions. This already is being exploited[53,55] in the area of interhalogen ions and the reactions of tetramethylammonium fluoride with the solvents[56] and the resulting NMR behavior[57] have been explored.

Scheme I



Scheme I shows a proposed mechanism for the generation of TMS–F and halomethanes as observed in the $CD_3CN/CFCl_3$ solvent system. Although "CF_3^-" is useful as a shorthand formalism, the absence of any products derived from difluorocarbene argues against the presence of a free CF_3^- anion as an intermediate. While some fluoride-induced condensations of fluoroolefins with fluoroketones would seem to proceed through perfluorocarbanions such as $CF_3CF_2^-$ [45,50] or $(CF_3)_2CF^-$ [45,46] derived from addition of F^- to the olefin, $M^+(CF_3)^-$ should revert quickly to MF and $:CF_2$. A pentacoordinate silicon intermediate such as 1 as a carrier for the trifluoromethide is more likely. Quenching of 1 can occur via D^+ or H^+ abstraction. Abstraction of chlorine as Cl^+ to form $CFCl_3$ evidently takes place also, and the resulting $CFCl_2^-$ anion itself appears as $CFCl_2D$ and $CFCl_2H$.

The absence of any reaction between TMS–CF_3 and hexafluoroacetone without an initiator is significant. The reaction of trimethylsilyl halides and pseudohalides with carbonyl compounds is a valuable and widely used synthetic route.[33,58] Many such procedures rely on catalytic initiators, but some, such as the addition of TMS–CN[33] or TMS–C_6F_5[28] to benzaldehyde, proceed without a catalyst under more severe conditions. While the addition of TMS–CN to most hydrocarbon ketones without a catalyst requires even more severe conditions than for aldehydes,[33] such reactions are greatly facilitated when the substrate carbonyl or other multiple bond (e.g., a nitrile group) is rendered more electrophilic by its substituents. For instance, TMS–N_3 reacts with hexafluoroacetone under mild conditions even without a catalyst.[59,60] It is thus somewhat surprising that TMS–CF_3 displayed a lack of reactivity with $(CF_3)_2C{=}O$.

Preparative Reactions. The knowledge obtained from the above NMR experiments enabled the successful ap-

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Table I. Preparation of Fluorinated Tertiary Alcohols from Carbonyl Compounds, TMS–CF_3, and KF in CH_3CN[a]

carbonyl compd (mmol)	TMS–CF_3 (mmol)	KF (mmol)	initial T^b (°C)	product (% yield)[c]
$(CF_3)_2C{=}O$ (3.50)	2.19	2.8	–40	$(CF_3)_3COH$ (91.3)
$CF_3C(O)CF_2Cl$ (3.50)	2.19	2.4	–40	$CClF_2C(CF_3)_2OH$ (88.6)
$CF_3C(O)CF_2H$ (2.40)	2.30	2.6	–40	$CHF_2C(CF_3)_2OH$ (17.1) $CF_3C(O)CF_2C(CF_3)(CF_2H)(OH)$ (13.3)
$[(CF_3)_2CF]_2C{=}O$ (3.00)[d]	3.30	3.4	–10	$[(CF_3)_2CF]C(CF_3)_2OH$ (21.2)
$CF_3CF_2C(O)F$ (2.00)	4.30	4.5	–40	$CF_3CF_2C(CF_3)_2OH$ (85.0)
$F_2C{=}O$ (2.10)	6.66	7.6	–40	$(CF_3)_3COH$ (77.1)
$Cl_2C{=}O$ (2.02)	6.74	8.1	–40	$F_2C{=}O$ (77.2)

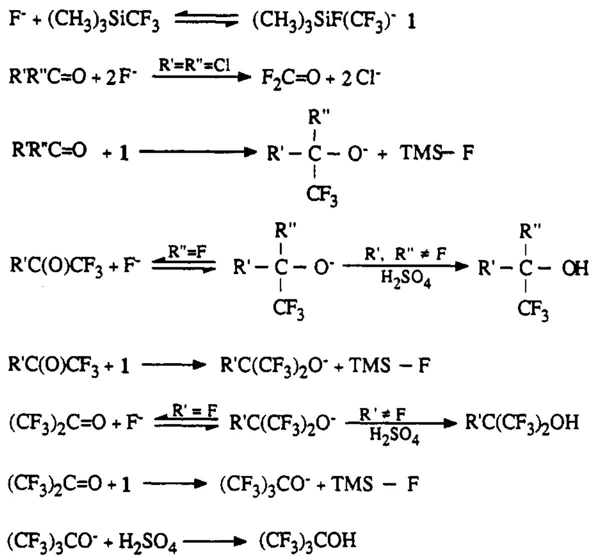
[a] Alcohol isolated after treatment of involatile residue with concd H_2SO_4. [b] Reactions were slowly warmed from this to ambient temperature; see Experimental section for times. [c] Isolated yields. [d] Et_2O was used as solvent rather than CH_3CN; 18-crow-6 was also added.

Table II. Isolation of Fluorinated Tertiary Alkoxides from Carbonyl Compounds, TMS–CF_3, and KF in CH_3CN[a]

carbonyl compd (mmol)	TMS-CF_3 (mmol)	KF (mmol)	initial T^b (°C)	product (% yield)
$(CF_3)_2C{=}O$ (3.63)	2.21	3.8	–25	$(CF_3)_3CO^-K^+$ (90.8)
$CF_3C(O)CF_2Cl$ (3.61)	2.24	3.8	–25	$CClF_2C(CF_3)_2O^-K^+$ (83.0)
$CF_3CF_2CF_2C(O)F$ (2.00)	4.69	6.0	–25	$CF_3CF_2CF_2C(CF_3)_2O^-K^+$ (73.5)
$CF_3(CF_2)_6C(O)F$ (3.17)	7.34	9.1	–25	$CF_3(CF_2)_6C(CF_3)_2O^-K^+$ (10.4)
$CF_3CF_2C(O)F$ (2.08)	4.66	5.3	0	$CF_3CF_2C(CF_3)_2O^-K^+$ (66.7)
$CF_3CF_2C(O)F$ (2.03)	2.02	0.3	–25	$CF_3CF_2C(O)F$ (11.3)[c] $CF_3CF_2C(O)CF_3$ (31.5)[c] $CF_3CF_2C(CF_3)_2O^-K^+$ (12.1) $C_2F_5C(CF_3)_2OC(O)C_2F_5$ (~20)
$CF_3CF_2C(O)F$ (2.02)	2.02	2.1	–25	$CF_3CF_2C(O)F$ (21.8)[c] $CF_3CF_2C(O)CF_3$ (24.8)[c] $CF_3CF_2C(CF_3)_2O^-K^+$ (29.2) $C_2F_5C(CF_3)_2OC(O)C_2F_5$ (16.8)[c]

[a] Alkoxide isolated after extraction of involatile residue into diethyl ether. [b] Reactions were slowly warmed from this to ambient temperature; see Experimental Section for times. [c] NMR yield; all others are isolated yields.

Scheme II



$$F^- + (CH_3)_3SiCF_3 \rightleftharpoons (CH_3)_3SiF(CF_3)^-\ \mathbf{1}$$

$$R'R''C{=}O + 2F^- \xrightarrow{R'=R''=Cl} F_2C{=}O + 2Cl^-$$

$$R'R''C{=}O + \mathbf{1} \longrightarrow R'-C(R'')(CF_3)-O^- + TMS-F$$

$$R'C(O)CF_3 + F^- \underset{}{\overset{R''=F}{\rightleftharpoons}} R'-C(R'')(CF_3)-O^- \xrightarrow[H_2SO_4]{R',\ R''\neq F} R'-C(R'')(CF_3)-OH$$

$$R'C(O)CF_3 + \mathbf{1} \longrightarrow R'C(CF_3)_2O^- + TMS-F$$

$$(CF_3)_2C{=}O + F^- \overset{R'=F}{\rightleftharpoons} R'C(CF_3)_2O^- \xrightarrow[H_2SO_4]{R'\neq F} R'C(CF_3)_2OH$$

$$(CF_3)_2C{=}O + \mathbf{1} \longrightarrow (CF_3)_3CO^- + TMS-F$$

$$(CF_3)_3CO^- + H_2SO_4 \longrightarrow (CF_3)_3COH$$

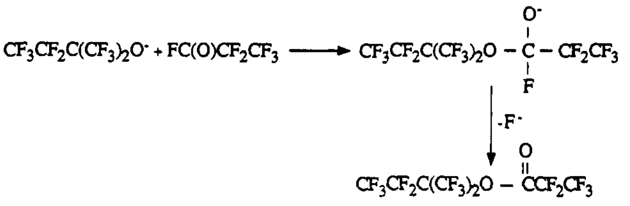
plication of the trifluoromethylation technique to highly fluorinated carbonyl compounds. This extension proved remarkably easy once the proper solvent (CH_3CN) was combined with an excess of a suitable fluoride (KF). It was not even necessary to take extraordinary precautions with regard to solvent purity; commercial anhydrous-grade CH_3CN gave excellent results without further purification. High-quality "activated" KF was used in all of the reactions, however (see Experimental section). Potassium fluoride was chosen over CsF to minimize complexation with carbonyl reactants and products.

In one preparative method, intermediates from reactions of KF and TMS–CF_3 with carbonyl compounds were not isolated; rather, the residue remaining after removal of the reaction solvent under vacuum was acidified with concd H_2SO_4 and the resulting alcohol was distilled out of the acid. A summary of reactions conducted in this fashion appears in Table I. In another set of experiments, summarized in Table II, the solid remaining behind after removal of volatiles and solvent was directly extracted with diethyl ether. This gave the potassium salt free of KF. When the alcohol end product is desired on a larger scale, isolation of the alkoxide is still preferable since its separation from the unreacted KF before addition of sulfuric acid eliminates problems due to HF formation.

A particularly exciting development was that readily available acid fluorides could react via loss of the carbonyl fluorine from an intermediate alkoxide, followed by addition of a second trifluoromethyl group to give a tertiary alkoxide. The substitution of CF_3 for F on the carbonyl group should thus be catalytic in fluoride, while additional fluoride is required to achieve in situ conversion of the resulting trifluoromethyl ketone to a tertiary alkoxide in high yield through the addition of another CF_3 group from TMS-CF_3. The ketone formed by the initial CF_3-for-F substitution was observed in several cases.

Scheme II shows how the observed trifluoromethylations might proceed when **1**, the proposed pentacoordinate silicon CF_3-transfer agent, is generated in the presence of a carbonyl substrate. With simple fluorinated ketones such as $(CF_3)_2C{=}O$ and $CF_3C(O)CF_2Cl$, formal addition of CF_3^- to the carbonyl carbon occurs to give the tertiary alkoxides in high yields. When one of the groups on the original carbonyl substrate is F, the $R'(CF_3)FCO^-$ anion resulting from CF_3^- transfer to the acid fluoride can easily lose F^- to generate an intermediate ketone, $R'C(O)CF_3$. The $R'C(O)CF_3$ may then add a CF_3 group as in the case of $(CF_3)_2C{=}O$, for example, resulting in a net conversion of $R'C(O)F$ to $R'C(CF_3)_2O^-$ with 2 equiv of TMS–CF_3. When $F_2C{=}O$ is used as the starting material $(CF_3)_3CO^-$ is the final product when sufficient TMS–CF_3 is used. This reaction proceeds progressively through $CF_3C(O)F$ and $(CF_3)_2C{=}O$ as intermediates formed in situ in this one-pot conversion of $F_2C{=}O$ to $(CF_3)_3CO^-$. Clearly, $(CF_3)_3CO^-$ can be prepared starting from COF_2, $CF_3C(O)F$, or $(CF_3)_2C{=}O$.

Scheme III



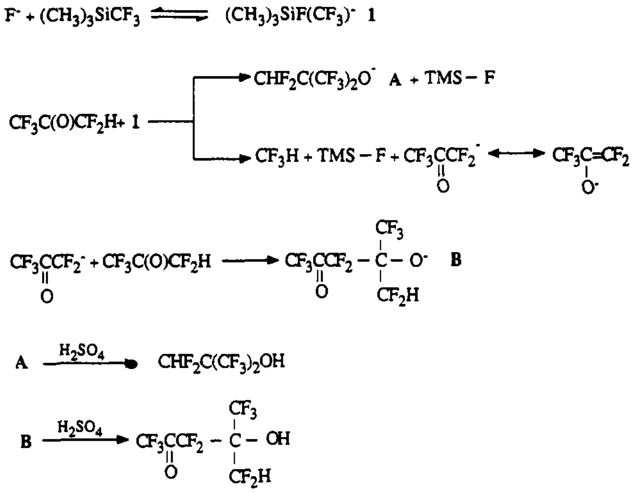
The attempt to use $COCl_2$ as the cheapest possible starting material for the preparation of $(CF_3)_3CO^-$ failed, because nucleophilic exchange of fluorine for chlorine with the KF is fast and leads to $F_2C{=}O$ as the initial product; no evidence was found for a reaction sequence proceeding through $CF_3CCl_2O^-$ followed by loss of Cl^- to give $CF_3C(O)Cl$. Of the phosgene, 18.3% was found unreacted while 77.2% was converted to $F_2C{=}O$. Most (95.0%) of the TMS–CF_3 was recovered unchanged.

The failure of the phosgene reaction under these conditions is puzzling since Prakash et al.[16b] have successfully prepared $PhC(O)CF_3$ from $PhC(O)Cl$, TMS–CF_3, and $(n\text{-}Bu)_4N^+F^-\cdot 3H_2O$. Aryl perfluoroalkyl ketones have also been made[39] by reacting $ArC(O)Cl$ directly with a mixture of a perfluoroalkyl halide and $P(NR_2)_3$ without trapping the "CF_3^-" as TMS–CF_3. Since our $Cl_2C{=}O$/KF reaction was much more heterogeneous than the above two examples for solubility reasons, it is possible that the KCl generated during the observed fluorination of $Cl_2C{=}O$ to $F_2C{=}O$ "poisons" the remaining KF surface and does not allow it to enter into a reaction with TMS–CF_3. The use of the more soluble $(CH_3)_4N^+F^-$ might be advantageous from this point of view.

Extension of this reaction to $CF_3CF_2C(O)F$ for the preparation of $CF_3CF_2C(CF_3)_2OH$ is easier and safer than the oxetane ring-opening reaction with HF/SbF_5 used previously.[1] It is noteworthy that this $CF_3CF_2C(O)F$/TMS–CF_3/KF reaction is mechanistically very similar to the other reported route[45,50] to $CF_3CF_2C(CF_3)_2OH$ involving hexafluoroacetone, $CF_2{=}CF_2$, and CsF, a reaction which is postulated to proceed via addition of the carbanion $C_2F_5^-$ to the carbonyl carbon of $(CF_3)_2C{=}O$. The reaction of $CF_3CF_2C(O)F$ with both 1 equiv and a catalytic amount of TMS–CF_3 was also investigated to see if the known[61] ketone $CF_3CF_2C(O)CF_3$ could be observed as an intermediate resulting from CF_3-for-F substitution. As noted in the last two entries of Table II, in both cases a significant amount of the acyl fluoride remained unreacted. With a catalytic amount of KF, the predominant product was in fact the ketone $CF_3CF_2C(O)CF_3$; some $CF_3CF_2C(CF_3)_2O^-K^+$ was also found. In the presence of an equimolar amount of KF the alkoxide predominated, although there was nearly as much $CF_3CF_2C(O)CF_3$ formed. These reactions imply that the ketone reacts more rapidly with "CF_3^-" than the acid fluoride. The reaction of TMS–CF_3 with an excess of $R_FC(O)F$ and a catalytic amount of KF might increase the yield of $R_FC(O)CF_3$ but this was not explored.

Both reactions using $CF_3CF_2C(O)F$ and TMS–CF_3 in a 1:1 ratio also produced the ester $CF_3CF_2C(CF_3)_2OC(O)CF_2CF_3$ in yields of about 20%, based on $CF_3CF_2C(O)F$. This is due to attack of $CF_3CF_2C(CF_3)_2O^-$ on the acyl fluoride starting material, as shown in Scheme III. This reaction is much more likely to be observed with acid fluorides than with fluoro ketones, since loss of F^- from the intermediate alkoxide with an acid fluoride is much more favorable than loss of a perfluoroalkyl anion from the analogous intermediate from the ketone. Other examples of the synthesis of esters by reaction of perfluoro tertiary alkoxide salts with acyl fluorides[62] and chlorides[63] have been reported. Similar esters can also be produced from the parent alcohols and an acid chloride if an amine base is present.[64]

Scheme IV



With sufficient TMS–CF_3/KF, $CF_3(CF_2)_2C(O)F$ reacts to give $CF_3(CF_2)_2C(CF_3)_2O^-K^+$ in good yield, but upon increasing the length of the perfluoroalkyl chain in the acyl fluoride to $CF_3(CF_2)_6C(O)F$ the yield of the corresponding tertiary alkoxide drops to 10.4%, probably because of reduced solubility. The major product is apparently the ester $CF_3(CF_2)_6C(CF_3)_2OC(O)(CF_2)_6CF_3$, formed by attack of the $CF_3(CF_2)_6C(CF_3)_2O^-K^+$ as formed on the only slightly soluble starting acid fluoride.

Complications arise, as shown in Scheme IV, upon nucleophilic trifluoromethylation of pentafluoroacetone. Some of the expected alcohol, $CHF_2C(CF_3)_2OH$, was isolated via the alkoxide $CHF_2C(CF_3)_2O^-$ (A). However, abstraction of the acidic α-hydrogen from the ketone is a significant side reaction. The $CF_3C(O)CF_2^-$ can attack $CF_3C(O)CF_2H$ leading to the alkoxide $CF_3C(O)CF_2C(CF_3)(CF_2H)O^-$ (B) which was isolated as the parent alcohol upon acidification with H_2SO_4.

Two particularly interesting features arose in characterization and identification of the dimer from $CF_3C(O)CF_2H$/TMS–CF_3/KF. The ^{19}F NMR spectrum shows the fluorines of the CF_2 next to the carbonyl group as a very complicated AB system due to the neighboring chiral center, yet the fluorines of the CF_2H group, which is also bonded directly to the chiral center, appear to be completely first order. Also, the gas-phase infrared spectrum (3 Torr) shows two –OH absorbances: a sharp one at 3611 cm^{-1} and a broader peak at 3551 cm^{-1}. Since the formation of a hydrogen bond between the hydroxyl hydrogen and the carbonyl oxygen in $CF_3C(O)CF_2C(CF_3)(CF_2H)(OH)$ would lead to a six-membered ring, it seems reasonable to interpret this spectrum in terms of a sharp free O–H stretch accompanied by a broader bound O–H stretch at the lower wavenumber.

The example of bis(perfluoroisopropyl) ketone provides another departure from the expected CF_3-addition mechanism. A trial in acetonitrile failed due to insolubility of the ketone and the observed products were the reaction

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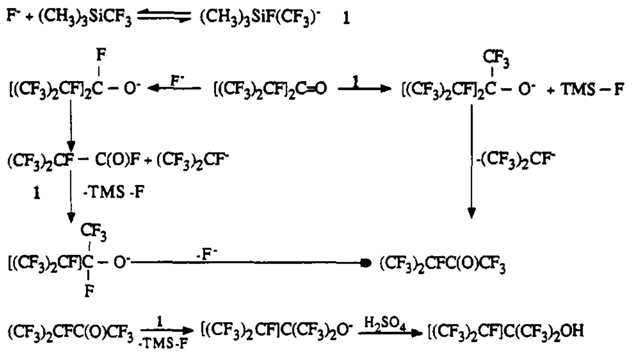
(61) Holub, F. F.; Bigelow, L. *J. Am. Chem. Soc.* **1950**, *72*, 4879–4884.

(62) Walker, N. S.; DesMarteau, D. D. *J. Fluorine Chem.* **1975**, *5*, 135–139.

(63) Moore, G. J.; Smith, C. F.; Tamborski, C. *J. Fluorine Chem.* **1975**, *5*, 77–81.

(64) De Pasquale, R. J. *J. Org. Chem.* **1973**, *38*, 3025–3030.

Scheme V



the "CF_3^-" with the solvent.

When the reaction was repeated in Et_2O to dissolved the ketone at the expense of the KF solubility (18-crown-6 was added to compensate) the ketone did undergo some reaction, but the product was that resulting from replacement of one of the $(CF_3)_2CF$ groups by CF_3 followed by addition of a second CF_3 to the carbonyl carbon. As shown in Scheme V this is envisioned to occur via trifluoromethylation of an intermediate ketone, $(CF_3)_2CFC(O)CF_3$. As noted previously in the case of $CF_3CF_2C(CF_3)_2OH$, the product, $[(CF_3)_2CF]C(CF_3)_2OH$, has also been obtained by nucleophilic attack of $(CF_3)_2CF^-$ on $(CF_3)_2C{=}O$.[45,46]

Although the use of 18-crown-6 was effective in promoting a reaction in Et_2O through increased solubilization of KF, in this situation replacement of KF by the more soluble anhydrous $(CH_3)_4N^+F^-$ would be most useful for extending the applicability of trifluoromethylation with TMS–CF_3 to solvents more effective at dissolving large highly fluorinated molecules than is CH_3CN. This should be appropriate for bis(perfluoroisopropyl) ketone as well as the long-chain $R_FC(O)F$ substrates which gave poor yields.

Further studies are underway to determine the applicability of TMS–CF_3 in the trifluoromethylation of difunctional carbonyl compounds and other electrophilic nonmetal centers.

Conclusion

Highly fluorinated ketones can be trifluoromethylated to give tertiary alkoxides in high yield using TMS–CF_3 in the presence of an excess of an anhydrous metal fluoride of high activity in CH_3CN. Acid fluorides also give tertiary alkoxides through substitution on and addition to the carbonyl carbon with an excess of TMS–CF_3. Intermediate trifluoromethyl ketones can be obtained from acid fluorides if smaller TMS–CF_3 stoichiometries are used. Very acidic hydrogens in carbonyl substrates cause condensation reactions. Branched perfluoroalkyl substituents on the carbonyl comprise relatively stable carbanion leaving groups and can be replaced by CF_3. Solubility limitations encountered with large highly fluorinated starting materials can be lessened by using a better solvent for these materials, such as Et_2O, and adding a crown ether to compensate for the reduced metal fluoride solubility. More soluble anhydrous fluorides such as $(CH_3)_4N^+F^-$ will probably proved to be a helpful extension of scope in this regard. The tertiary alkoxides produced using the method reported here may be either isolated as such or converted directly to the parent alcohols via acidification. Sulfuric acid is particularly suited for this for separation reasons. Reactions of highly fluorinated ketones with TMS–CF_3 require stoichiometric amounts of initiator for good yields, and the reactions do not propagate through attack of perfluoroalkoxides on TMS–CF_3.

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Supplementary Material Available: ^1H and ^{19}F NMR spectra of new compounds $CHF_2C(CF_3)OH$, $CClF_2C(Cf_3)_2OK$, $Cf_3(CF_2)_6C(CF_3)_2OK$, $CF_3(CF_2)_6C(CF_3)_2OH$, $CF_3CF_2CF_2C(CF_3)_2OK$, $CF_3CF_2C(CF_3)_2OK$, and $CF_3CF_2C(CF_3)_2OC(O)CF_2CF_3$ (11 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.