Trifluoromethylation of Perfluorinated Diacylfluorides: Synthesis of the Diketone $CF_3C(O)CF_2C(O)CF_3$ and of New Perfluorinated Diol $(CF_3)_2C(OH)CF_2C(OH)(CF_3)_2$

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Dedicated to Prof.Dr. Boris Žemva on the occasion of receiving the Zois´ award for lifetime achievements.

Abstract

Perfluoromalonyl difluoride reacts with TMS-CF_3 (1:1) in the presence of KF to give the new diketone $CF2(C(O)CF_3)_2$. A large excess (5:1) of TMS-CF_3 results in the presumed potassium dialkoxide $[(CF_3)_2COK]_2CF_2$ which yields the 1,3-ditertiarydiol $[(CF_3)2C(OH)]_2CF_2$ on reaction with H_2SO_4.

Keywords: Perfluoromalonyl difluoride, trifluoromethylated diketone, 1,3-ditertiarydiol

1. Introduction

It has been previously reported that $(CH_3)_3SiCF_3$ (TMS-CF_3) can be employed to generate tertiary alkoxides and alcohols by nucleophilic trifluoromethylation of a variety of fluoroketones and acid fluorides in the presence of metal fluorides.[1] As an extension of this chemistry this reaction has been investigated[2] with some diacyl fluorides in an attempt to prepare fluorinated diols $(CF_3)_2C(OH)(CF_2)_nC(OH)(CF_3)_2$ of various chain lengths which would have useful solvent properties. In fact fluoroalcohols and their derivatives are attaining increasing importance in dyestuffs, plastics, pharmaceuticals and surface coatings, as well as use in fluorine-containing polymers and in organometallic chemistry. However, the reaction with $F(O)C(CF_2)_nC(O)F$ n = 2,3 resulted in novel cyclic diols via the facile cyclodimerization of the diketones with water. For n=0, the reaction led to decomposition of the starting diacylfluoride. It became of interest to investigate this trifluoromethylation reaction with the less readily available malonyl fluoride (n = 1). Herein we report the successful preparation of the diketone and the desired 1,3-tertiarydiol, but the reactions are somewhat complex.

2. Experimental Section

Caution! Working with highly acidic alcohols is potentially hazardous since perfluoropinacol has been determined to be a highly toxic material, both from the standpoint of skin contact and inhalation, while other alcohols have been tested as fumigants.[3] The compound synthesised in this work is quite similar to perfluoropinacol and should be treated as potentially highly toxic material.

General Methods. Infrared spectra were recorded on Perkin Elmer 1600 FT/IR using a 10 cm glass cell fitted with KCl windows attached with Halocarbon 1500 wax. NMR spectra were acquired at 200.13 MHz for ^1H and 188.31 MHz for ^{19}F on a Bruker AC 200. Chemical shifts are reported relative to $Si(CH_3)_4$ or $CFCl_3$ with upfield shifts 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.
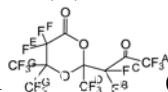
Gases and volatile compounds were handled in glass vacuum systems, equipped with glass-Teflon valves. Amounts of volatile compounds were determined by PVT measurements using a Wallace & Tiernan Series 1500 differential pressure gauge. All trap-to-trap fractionations were performed under static vacuum.

The reaction vessel for preparation of the diketone and the diol consisted of a 100 mL round bottom Pyrex flask with a glass-Teflon valve attached through an Acethread®, O-ring seal connector. The body of the flask was modified by addition of a side arm fitted with a Teflon-faced silicone septum. Liquids could be added via syringe, without compromising the ability of the system to hold vacuum after removal of the syringe needle. The reactor contained a Teflon-coated magnetic stirring bar.

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. Perfluoromalonyl difluoride[4–6] (**1**) and (trifluoromethyl)trimethylsilane[1] (TMS-CF$_3$) were prepared by literature methods. Active KF was prepared by fusion in a Pt dish followed by pulverization under very dry nitrogen in a porcelain mortar. Dry solid materials were handled inside an efficient drybox. Benzonitrile and acetonitrile were dried over P$_4$O$_{10}$.

Preparation of CF$_3$(O)CCF$_2$C(O)CF$_3$ (2) from F(O)CCF$_2$C(O)F. Freshly fused potassium fluoride (740 mg, 12,7 mmol) was loaded into the reactor (see above), the reactor was partially evacuated and 3 mL of dry benzonitrile was added by syringe. The reactor was cooled to –196 °C and evacuated. Perfluoromalonyl difluoride (2.0 mmol) and TMS-CF$_3$ (4.0 mmol) were condensed into the reactor by vacuum transfer. The reactor was placed in a 0 °C bath and stirring was begun as soon as the reaction mixture melted. After 16 hours the volatiles were removed at room temperature by vacuum pumping through a –196 °C trap for 2 hours. The content of this trap was fractionated through traps at –33, –86, –96 and –196 °C. The –196 °C trap contained 4.2 mmol of a mixture consisting mainly of TMS-F with some CF$_3$H. Benzonitrile was retained in the –33 °C trap. The –96 °C trap gave 0.6 mmol of **2** (30 % yield). The –86 °C trap gave 0.7 mmol of compound **3** (see Discussion). Compound **2** was characterized as follows: IR (5 torr) 1806 (s), 1322 (s), 1250 (vs), 1192 (vs), 1155 (s), 1092 (m), 992 (s), 911 (s), 862 (s), 756 (m) cm^{-1}; NMR (CF$_3$^{A}(O)C)$_2$CF$_2$^{B} (CDCl$_3$, 24 °C) δ(^{19}F) A –75.2 (6 F, t), B –114.5 (2 F, sept) . Compound **3** was characterized as follows: IR (in solution CDCl$_3$): 1843 (vs), 1356 (m), 1210 (vs), 971 (s), 935 (m),

838 (s) cm–1; NMR (CDCl$_3$, 24 °C) δ(^{19}F) A –79.3 (3 F, dd), B –112.2, C –121.5 (2 F, AB pattern), D –77.2 (3 F, m), E –107.5, F –112.5 (2 F, AB pattern) G –71.0 (6 F, m); J$_{AB}$ = 17, J$_{AC}$ = 4, J$_{BC}$ = 298, J$_{EF}$ = 298 Hz.

Preparation of (CF$_3$)$_2$C(OH)CF$_2$C(OH)(CF$_3$)$_2$ (4). Activated KF (850 mg, 14.6 mmol) was loaded into the reactor (see above), the reactor was partially evacuated and 4 mL of dried acetonitrile was added by syringe. After the reactor was cooled to –196 °C and evacuated, perfluo-

romalonyl difluoride (2.0 mmol) and TMS-CF$_3$ (10.5 mmol) were condensed into the reactor by vacuum transfer. The reaction mixture was stirred for 1 hour in a –50 °C bath followed by three days additional stirring at 20 °C, giving a brown solution. Volatiles were removed under dynamic vacuum at 20 °C and the remaining brown solid was extracted with three 10 mL portions of diethyl ether [^{19}F NMR, Et$_2$O; δ –104.8 (2F, m); δ –74.0 (12F, M)]. After evaporation of the solvent, 5 mL of concentrated H$_2$SO$_4$ was added to the 492 mg of the remaining brown powder. After 5 hours the crude product was collected by vacuum pumping at 20 °C through a trap cooled at –196 °C for 4 hours. Fractionation through traps at –20 and –196 °C gave in the –20 °C trap 206 mg (30% yield) of a white solid which crystallizes by melting and slowly cooling into long white needles. The –196 °C trap contains traces of the known compound (CF$_3$)$_2$C(OH)CF$_2$C(O)CF$_3$.[7]

The new compound **4** was characterized as follows: mp 58–60 °C; IR (KBr pellet) 3448 (b), 1623 (w), 1264 (vs), 1177 (s), 1127 (m), 968 (m), 819 (m), 738 (m), 724 (m) cm^{-1}; NMR [(CF$_3$^{A})$_2$C(OH)]$_2$CF$_2$^{B} (CDCl$_3$, 24 °C) δ (^{19}F) A –72.5 (12 F, t), B –103.6 (2 F, m), J$_{AB}$ = 13 Hz; δ (^{1}H) 5.58 (br, s);

Preparation of [(CF$_3$)$_2$C(ONa)]$_2$CF$_2$ 5. In a 50 mL round bottom flask 45 mg (0.11 mmol) of product **4** were dissolved in 2 mL of distilled water. 0.1 M NaOH solution was added until pH 7.0. The solution was then evaporated and the salt was dried under dynamic vacuum at 100 °C, leaving 50 mg (100% yield) of a white solid. The salt was characterized as follows: NMR [(CF$_3$^{A})$_2$C(ONa)]$_2$CF$_2$^{B} (D$_2$O, 24 °C) δ (^{19}F) A –70.4 (12 F, t), B –105.0 (2 F, m) J$_{AB}$ = 13.0 Hz.

2. 1. X-ray Crystallographic Analysis of 4

General details for the data collection and structural solution and refinement are given in Table 1.

Intensity data were measured at –70(2) °C with graphite-monochromated Mo Kα radiation (λ = 0.71073 Å) on a Nicolet R3mV serial detection system. Data were corrected for Lorentz and polarization effects and for absorption. The latter correction was based on empirical methods.

The structure was solved by direct methods and refined by using full-matrix least-squares techniques (on F^2). All non-hydrogen atoms were refined anisotropically; hydrogen atoms were refined with isotropic displacement parameters.

Structure solution, refinement and the calculation of derived results were performed with the SHELXTL[8] package of computer programs. Neutral atom scattering factors were those of Cromer and Waber,[9a] and the real and imaginary anomalous dispersion corrections were those of Cromer.[9b]

Crystallographic data have been deposited with the Crystallographic Data Center CCDC 896618. Copies may

be obtained free of charge on application to the Director, CCDC, 12 Union Road, Cambridge CB21EZ, UK. (http://www.ccdc.com.ac.uk/conts/retrieving)

Table 1. Crystal data

	Compound 1
Formula	$C_7H_2O_2F_{14}$
M_w	384.09
Crystal System	Monoclinic
Space Group	$P2_1/n$ (No. 14)
a, Å	7.0991(19)
b, Å	18.706(4)
c, Å	9.2652(18)
β, (°)	110.476(17)
V, Å^3	1152.6(4)
Z	4
$F(000)$	744
D_{calc}, g cm^{-3}	2.21
μ, mm^{-1}	0.30
Transmission coefficients	0.48–1.00
Crystal dimensions (mm)	0.14 × 0.22 × 0.29
Θ range (°)	2.6–26.6
hkl$_{range}$	0, 8; 0, 23; –11, 10
Reflections collected	2564
Reflections unique (R_{merge})	2370 (0.035)
Reflections observed ($I>2\sigma$)	1417
$R_1{}^a$	0.0362 (0.0739)
$wR_2{}^b$	0.0807 (0.0895)

$^a R_1 = \Sigma||F_o| - |F_c||/?\Sigma|F_o|$ for observed data ($I>2\sigma(I)$); number in parentheses is for all data.
$^b wR_2 = \{\Sigma[w(F_o{}^2 - F_c{}^2)^2]/\Sigma[w(F_o{}^2)^2]\}^{1/2}$ for observed data ($I>2\sigma(I)$); number in parentheses is for all data.

3. Results and Discussion

The diacylfluoride $FC(O)(CF_2)_nC(O)F$ (n = 1) is more reactive than the homologues studied previously. Depending on the ratio of TMS-CF$_3$/diacylfluoride used, different products are isolated. Using a ratio acylfluoride: TMS-CF$_3$ = 1:2 we did not observe the formation of the four-membered ring cyclic dialkoxide analogous to the 5,6-membered rings observed previously for n = 2,3. However the yield of diketone **2** is only around 30%. The starting material seems to be very reactive with formation of different compounds like the proposed lactone **3**. The reactions are summarized in Scheme 1.

In the reaction of $FC(O)(CF_2)_nC(O)F$ (n=2,3) with excess of TMS-CF$_3$ the corresponding dialkoxides are not observed due to the facile intramolecular cyclization of the intermediate diketone with fluoride. In this case the free diketone was obtained by thermal decomposition of the monoalkoxide under vacuum, but no available route to the diols $(CF_3)_2C(OH)(CF_2)_nC(OH)(CF_3)_2$ was possible. In the case of $CF_2[C(O)F]_2$, excess TMS-CF$_3$ gives the tetra(trifluoromethylated) dialkoxide along with an unidentified cyclic compound and probably some $(CF_3)_2C(OK)CF_2C(O)CF_3$ and other unidentified products.

$$4TMS\text{-}CF_3 + CF_2(C(O)F)_2 \xrightarrow{KF} [(CF_3)_2COK]_2CF_2 \quad (1)$$

While the potassium dialkoxide was not unequivocally identified, its reaction with H$_2$SO$_4$ to give **4** and the ^{19}F NMR makes the identity fairly certain. Also the reac-
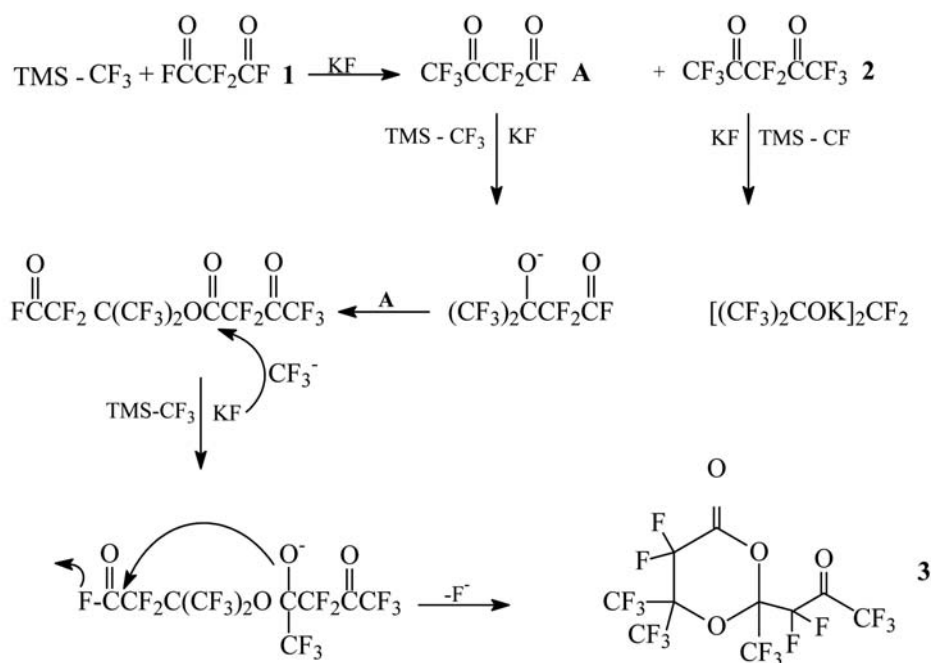
Scheme 1. Reaction of **1** with TMS-CF$_3$/KF and suggested route to **3**.

tion of **4** with NaOH gives the pure disodium alkoxide **5** with nearly identical ^{19}F NMR.

The new compound $(CF_3)_2C(OH)CF_2C(OH)(CF_3)_2$ **4** crystallizes in long white needles in the monoclinic space group, *P2$_1$/n* (No. 14). The molecule occupies a general position within the unit cell, and is shown as a thermal ellipsoid plot in Figure 1. The intramolecular bonding parameters are given in Table 2, and are all within normal ran-

Table 2. Geometric parameters

Bond Distances (Å)

O1 C1 1.394(3)	F10 C6 1.338(3)
O2 C3 1.391(3)	F11 C6 1.317(3)
F1 C2 1.346(3)	F12 C7 1.325(3)
F2 C2 1.341(3)	F13 C7 1.315(3)
F3 C4 1.321(3)	F14 C7 1.329(3)
F4 C4 1.323(3)	C1 C5 1.541(3)
F5 C4 1.331(3)	C1 C4 1.547(3)
F6 C5 1.315(3)	C1 C2 1.581(3)
F7 C5 1.336(3)	C2 C3 1.572(3)
F8 C5 1.317(3)	C3 C6 1.544(3)
F9 C6 1.312(3)	C3 C7 1.564(4)

C-F$_{avg}$ 1.326(11)
C-C$_{avg}$ 1.558(17)

Bond Angles (°)

O1 C1 C5 109.03(19)	F3 C4 C1 110.8(2)
O1 C1 C4 109.23(19)	F4 C4 C1 112.8(2)
C5 C1 C4 109.91(19)	F5 C4 C1 109.1(2)
O1 C1 C2 107.11(17)	F6 C5 F8 108.5(2)
C5 C1 C2 110.77(19)	F6 C5 F7 107.1(2)
C4 C1 C2 110.72(18)	F8 C5 F7 108.3(2)
F2 C2 F1 105.22(18)	F6 C5 C1 110.8(2)
F2 C2 C3 107.25(18)	F8 C5 C1 112.9(2)
F1 C2 C3 109.28(18)	F7 C5 C1 109.1(2)
F2 C2 C1 109.65(18)	F9 C6 F11 108.8(2)
F1 C2 C1 106.98(18)	F9 C6 F10 106.9(2)
C3 C2 C1 117.77(17)	F11 C6 F10 107.4(2)
O2 C3 C6 104.52(19)	F9 C6 C3 111.1(2)
O2 C3 C7 109.3(2)	F11 C6 C3 112.5(2)
C6 C3 C7 108.48(19)	F10 C6 C3 109.9(2)
O2 C3 C2 113.09(18)	F13 C7 F12 107.8(2)
C6 C3 C2 109.81(18)	F13 C7 F14 107.4(2)
C7 C3 C2 111.29(19)	F12 C7 F14 108.2(2)
F3 C4 F4 108.8(2)	F13 C7 C3 110.3(2)
F3 C4 F5 107.4(2)	F12 C7 C3 112.5(2)
F4 C4 F5 107.7(2)	F14 C7 C3 110.4(2)

C-C-C$_{avg}$ 111(3)
C-C-O$_{avg}$ 109(3)
C-C-F$_{avg}$ 110(2)
F-C-F$_{avg}$ 108(1)

Hydrogen Bonds (Å,°)

O1-H1 0.77(3)	H1···O2^a 2.01(3)	O1···O2^a 2.740(2)	O1-H1···O2^a 158(3)
O2-H2 0.74(3)	H2···O1 1.91(3)	O2···O1 2.561(3)	O2-H2···O21 147(3)

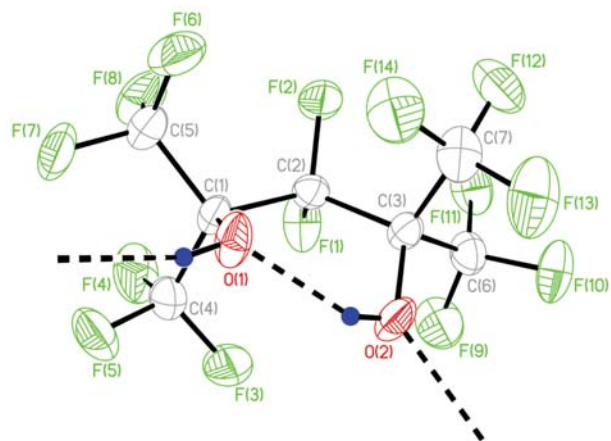a) Atom generated by symmetry operation: ½+*x*, ½-*y*, ½+*z*

Figure 1. Thermal ellipsoid plot (50% probability) of compound **4**. Hydrogen bonds are shown as dashed lines.
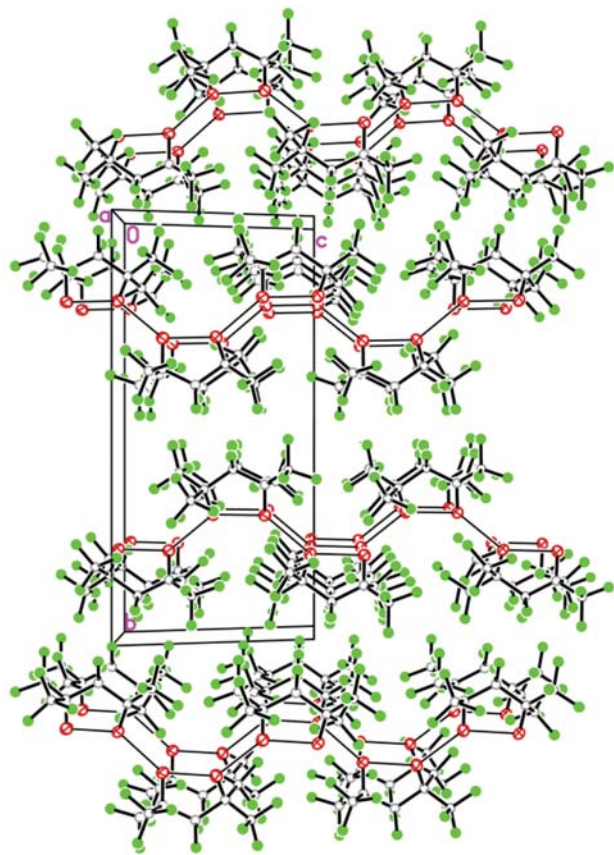

Figure 2. Crystal packing viewed down the a-axis for compound **4**. Oxygen atoms are represented as red boundary ellipses, fluorine atoms as solid green spheres, and carbon atoms as black hollow spheres. Hydrogen atoms are not shown.

ges. The hydroxyl groups participate in both intramolecular and intermolecular hydrogen bonding (shown as dashed lines in Figure 1). The latter intermolecular hydrogen bonds link the molecules into infinite chains running perpendicular to {1 0 1}. The crystal packing is shown in Figure 2.

The melting point of **4** at atmospheric pressure is 58–60 °C; it has a low vapor pressure but it can be readily sublimed under dynamic vacuum. The compound is soluble in $CHCl_3$, slightly soluble in ethyl ether and has low solubility in H_2O (pH of water solution is acidic). Because of its low solubility in H_2O, attempts to measure the p-K_a were unsuccessful. The corresponding potassium and sodium salt are very hygroscopic and they are very soluble in ether and water.

This new product could have the same importance in the preparation of six-membered rings as the corresponding $(CF_3)_2C(OH)C(OH)(CF_3)_2$ has for a variety of five-membered rings. The perfluoropinacol molecule is known to form the basis of a number of five-membered heterocycles of type $-OC(CF_3)_2C(CF_3)_2OM$ where the element M is Si, Ge, Sn, B, S or P.

4. Conclusions

The reaction of $FC(O)(CF_2)_nC(O)F$ (n = 1) with TMS-CF_3/KF is more complex than previous results with n = 2,3. Very facile cyclization of the latter diketones is probably the reason for the clean reactions. In contrast for n = 1, the unfavorable cyclization to a four-membered ring allows the open chain intermediates/products to undergo further reactions. However the 1,3 trifluoromethylated diketone **2** could be isolated in modest yield and in contrast to n = 2,3, the 1,3 tetra(trifluoromethylated) diol **4** was isolated.

6. Reference

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9. *International Tables for X-ray Crystallography*, Vol. C (1992), Ed. A. J. C. Wilson, Kluwer Academic Publishers, Dordrecht: a) Table 6.1.1.4, pp. 500–502; b) Table 4.2.6.8, pp. 219–222.

Povzetek

Perfluoromalonil difluorid reagira s TMS-CF_3 (1:1) v prisotnosti KF v nov diketon $CF_2(C(O)CF_3)_2$. Večji presežek (5:1) TMS-CF_3 predvidoma vodi do nastanka kalijevega dialkoksida $[(CF_3)_2COK]_2CF_2$, ki da po reakciji s H_2SO_4 1,3-diterciarni diol $[(CF_3)_2C(OH)]_2CF_2$.