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New or improved syntheses of the polyfluoroalcohols HOC(cyclo-C_6H_{11})$_2$(CF_3), HO(cyclo-C_6H_{11})(CF_3)$_2$, and HOC(Ar)(CF_3)$_2$ (Ar = 4-C_6H_4(*t*-Bu), 2,4,6-C_6H_2(CF_3)$_3$, 4-Si(*i*-Pr)$_3$-2,6-C_6H_2(CF_3)$_2$, 3,5-C_6H_3(CH_3)$_2$), and 2-C_6H_4(C(OH)(CF_3)$_2$)☆

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Abstract

Five new polyfluoroalcohols, HOC(cyclo-C_6H_{11})$_2$(CF_3), HO(cyclo-C_6H_{11})(CF_3)$_2$, HOC(2,4,6-C_6H_2(CF_3)$_3$)(CF_3)$_2$, HOC(4-Si(*i*-Pr)$_3$-2,6-C_6H_2(CF_3)$_2$)(CF_3)$_2$, and HOC(3,5-C_6H_3(CH_3)$_2$)(CF_3)$_2$, have been synthesized, and new procedures with improved yields for two known polyfluoroalcohols (HOC(cyclo-C_6H_{11})(CF_3)$_2$, HOC(4-C_6H_4(*t*-Bu))(CF_3)$_2$) have been developed. Variable temperature ^{19}F NMR spectra and the X-ray structure of one of the new polyfluoroalcohols, HOC(2,4,6-C_6H_2(CF_3)$_3$)(CF_3)$_2$, are also reported. In hydrocarbon solution, the OH hydrogen atom of this compound interacts with one of the fluorine atoms of one of the *o*-CF_3 groups in a manner identical to that previously reported by us for HOC(4-Si(*i*-Pr)$_3$-2,6-C_6H_2(CF_3)$_2$)(CF_3)$_2$. In the solid-state, however, the OH hydrogen atom in HOC(2,4,6-C_6H_2(CF_3)$_3$)-(CF_3)$_2$ appears to interact with one fluorine atom from each of the two geminal CF_3 groups.

Keywords: Polyfluoroalcohols; Geminal; Fluoroalkoxide; Hydrogen bonding

1. Introduction

Highly fluorinated alcohols and the metal alkoxides that can be derived from them are of current interest for a number of reasons [1,2]. In general, polyfluoroalkoxides are more chemically stable and more resistant to oxidation than their hydrocarbon equivalents, enabling fluoroalkoxides to be used as ligands to stabilize metal atoms in high oxidation states. In addition, the high electronegativities of the polyfluoro substituents reduce the basicity of the oxygen atom, which inhibits the formation of extended –M–O(R)–M–O(R)– alkoxy-bridged species. This in turn leads to a higher solubility in low-dielectric solvents and a higher volatility of complexes with these types of ligands. Furthermore, the steric and electronic properties can be readily modified by substitution allowing for a wide variety of OR_F^- ligands. Tungsten and molybdenum complexes containing polyfluoroalkoxide ligands are important olefin metathesis catalysts [3–6]. It was found that varying the steric and electronic properties of the fluoroalkoxide ligands had a significant effect on catalyst activity [3–6]. Metal fluoroalkoxides have also found use as precursors for chemical vapor deposition of metal fluorides [7,8] and fluorine-doped metal oxides [9,10].

Our work with polyfluoroalkoxides involves the synthesis and use of new weakly coordinating anions [11–13] such as tetrakis- or hexakis(polyfluoroalkoxy)metallates [14–22]. Examples include Al(OCR(CF_3)$_2$)$_4$ (R = H [14–19], CH_3 [14–19], Cy [14,18,19], Ph [14,17–20], 4-$C_6H_4CH_3$ [14,18,19], 4-C_6H_4(*t*-Bu) [14,18,19], CF_3 [14,18,19,21]), Al(OCPh$_2$(CF_3))$_4^-$ [14,16,18], and Nb(OCH(CF_3)$_2$)$_6^-$ [22]. We have synthesized a number of new polyfluoroalcohols to make these anionic species, and this paper reports on our progress in this area. Many abbreviations are used in the following discussion; Table 1 lists these abbreviations, their corresponding formulas and structures, as well as the yields of the preparative reactions.

☆ This paper is dedicated to Karl Christe, a true pioneer in the field of fluorine chemistry.

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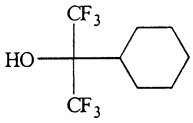
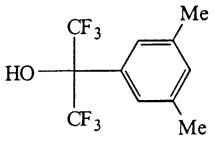
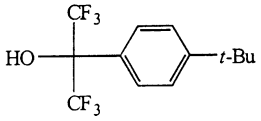
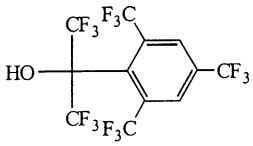
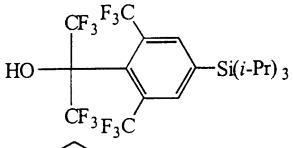
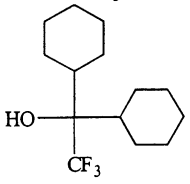
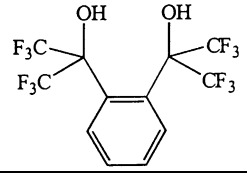
Table 1
Abbreviations, formulas, structures, and yields

Abbreviation	Formula	Structure	Yield (%)
H(HFCP)	HO(cyclo-C_6H_{11})$(CF_3)_2$		93
H(HFDPP)	HOC(3,5-$C_6H_3(CH_3)_2$)$(CF_3)_2$		52
H(HFBuPP)	HOC(4-C_6H_4(*t*-Bu))$(CF_3)_2$		75
H(HFTFPP)	HOC-2,4,6-$C_6H_2((CF_3)_3)(CF_3)_2$		16
H(HFSiPP)	HOC(4-Si(*i*-Pr)$_3$-2,6-$C_6H_2(CF_3)_2$)$(CF_3)_2$		9
H(DCTE)	HOC(cyclo-$C_6H_{11})_2(CF_3)$		95
H_2(1,2-HFAB)	HOC(2-C_6H_4(C(OH)$(CF_3)_2$))$(CF_3)_2$		29

2. Experimental

2.1. Physical methods

Samples for NMR spectroscopy were solutions in 5 mm glass tubes. NMR spectra were recorded on a Varian Inova 300 spectrometer operating at the indicated frequencies: ^{1}H, 300.1 MHz; ^{19}F, 282.4 MHz. Chemical shifts (δ scale) are relative to $SiMe_4$ ($\delta = 0$ for ^{1}H NMR) and $CFCl_3$ ($\delta = 0$ for ^{19}F NMR) external standards. High-resolution mass spectra (HRMS) were recorded on a Fisons VG AutoSpec spectrometer by liquid secondary ion mass spectrometry (LSIMS). Gas chromatography/mass spectrometry (GC/MS) was performed using an Agilent 5973 N in electron ionization (EI) mode.

Crystals of HOC(2,4,6-$C_6H_2(CF_3)_3)(CF_3)_2$ were grown by vacuum sublimation just above room temperature. A suitable crystal was embedded in Halocarbon-25-5S grease at the end of a glass fiber and placed in the cold nitrogen stream of the low-temperature (LT) 2 u of a Siemens SMART CCD diffractometer system. The diffraction data collection and subsequent structural computations were performed using the crystallographic software supplied by Siemens [23] or by Sheldrick [24]. Lorentz and polarization corrections were applied to the data. Details of the crystallographic experiment and subsequent computations are summarized in Table 2 [25,26]. The structure was solved by direct methods and was refined using full-matrix least-squares procedures on F^2 for all data. Non-hydrogen atoms were refined anisotropically. The H1 hydrogen atom was located in the difference density map and refined. The other hydrogen atoms were placed in calculated positions. The structure has a disordered CF_3 bonded to C_7 which was modeled isotropically as 12 partial fluorine atoms, each with a site occupancy factor equal to 0.25. Crystallographic data (excluding structure factors) for this structure have been

Table 2
X-ray crystal data collection, solution and refinement details for $HOC(2,4,6\text{-}C_6H_2((CF_3)_3)(CF_3)_2$

Molecular formula	$C_{12}H_3F_{15}O$
Formula weight (g mol^{-1})	448.14
Space group	*C2/c*
Unit cell dimensions	
a (Å)	18.851(2)
b (Å)	8.4164(9)
c (Å)	17.922(2)
α (°)	90.000
β (°)	92.847(6)
γ (°)	90.000
Unit cell volume (Å^3)	2839.9(4)
Z	8
Calculated density (g cm^{-3})	2.096
Crystal dimensions (mm)	0.80 × 0.40 × 0.40
Absorption coefficient (cm^{-1})	2.66
F(0 0 0)	1744
θ range for data collection (°)	2.16–30.00
Limiting indices	$-1 \leq h \leq 26$
	$-1 \leq k \leq 11$
	$-25 \leq l \leq 25$
Reflections collected	5003
Independent corrections	4115
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	4115/1/279
Goodness-of-fit on F^2	0.871
Final *R* indices [$I > 2\sigma(I)$]	$R_1 = 0.0507$, $wR_2 = 0.1257$
R indices (all data)	$R_1 = 0.0648$, $wR_2 = 0.1416$
Extinction coefficient	0.0097(7)
Largest diffraction peak and hole (Å^3)	0.465 and −0.542

deposited with the Cambridge Crystallographic Data Center as supplementary publication numbers.[1]

2.2. Materials

Schlenk or glovebox techniques were employed, with purified nitrogen, helium or argon used when an inert atmosphere was required [27]. All reagents and solvents were reagent grade or better. An aqueous sulfuric acid solution with a concentration of approximately 1 M was used where indicated in the experimental details. The term "brine" refers to a saturated aqueous solution of sodium chloride. The compounds LiH (Aldrich, 95%), *n*-BuLi (Aldrich, 2.5 M solution in hexane) 4-*t*-butylmagnesium bromide (Aldrich, 2.0 M solution in diethyl ether), hexafluoroacetone (Aldrich, 97%), ethanol (Fisher, 90%), hexane (mixture of isomers, Fisher, 99.9%), hydrogen (≥99.9%, Liquid Air Corp.), and Rh (Strem, 5% on carbon) were used as received. Magnesium turnings were ground using a mortar and pestle in a helium-filled glovebox. Tri-isopropylsilyl trifluoromethanesulfonate (Aldrich, 97%), 5-bromo-*m*-xylene (Alfa Aesar, 97%), *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (Aldrich, 99%), 3,5-bis(trifluoromethyl)bromobenzene (Aldrich, 99%), 1,3,5-tris(trifluoromethyl)benzene (Aldrich, 99%), and hexafluoro-2-phenyl-2-propanol (Central Glass Co. Ltd., 99%) were dried over 4 Å molecular sieves and vacuum distilled. The following solvents were purified by distillation under nitrogen or under vacuum from the indicated drying agent: diethyl ether (Na); benzene-d_6 (Cambridge, >99% D; Na); toluene-d_8 (Cambridge, >99% D; Na); methylcyclohexane-d_{14} (Cambridge, >99% D, Na); dichloromethane-d_2 (Cambridge, >99% D; P_2O_5); chloroform-*d* (Cambridge, >99% D, P_2O_5); hexafluorobenzene (P_2O_5).

2.2.1. Preparation of $HOC(3,5\text{-}C_6H_3(CH_3)_2)(CF_3)_2$ (H(HFDPP))

The compound 5-bromo-*m*-xylene (7.93 g, 42.8 mmol) was added as a solution in diethyl ether (15 ml) to a suspension of Mg (1.15 g, 47.1 mmol) in 100 ml ether. This was stirred at room temperature for 1 h, then at reflux for 18 h under Ar purge, after which time the solution turned brown and cloudy. After degassing the solution, hexafluoroacetone (7.1 g, 42.8 mmol), which had been measured out in a calibrated bulb using a high-vacuum (10^{-5} Torr) line, was added at −196°C. The mixture was warmed to room temperature and stirred for 18 h. The resulting cloudy yellow solution was cooled to 0°C and an aqueous solution of sulfuric acid was added. The organic layer was isolated, and the aqueous layer washed twice with 25 ml portions of ether. The fractions were combined, washed twice with 30 ml portions of brine, and dried over $MgSO_4$. After 18 h, the suspension was filtered, and volatiles removed to leave an orange oil. This was dissolved in hexane, and washed with 50 ml distilled water. The aqueous layer was washed twice with 25 ml portions of hexane. All hexane fractions were combined, and volatiles removed to yield a yellow oil. The alcohol was further purified by dissolving the oil in toluene, and refluxing with LiH (0.50 g, 62.5 mmol (1.5 times 5-bromo-*m*-xylene)) for 18 h. Volatiles were removed under vacuum, and the yellow solid was kept under vacuum for 18 h. The lithium salt was protonated with an aqueous solution of sulfuric acid, and extracted into 50 ml of hexane. The hexane layer was isolated, and the aqueous layer washed twice with 25 ml portions of hexane. All fractions were combined, and volatiles removed to leave a yellow oil. This was distilled at 35°C under vacuum to yield $HOC(3,5\text{-}C_6H_3(CH_3)_2)(CF_3)_2$ as a clear colorless oil (6.11 g, 52% based on 5-bromo-*m*-xylene). ^{1}H NMR (C_6D_6/C_6F_6) δ 7.35 (s, 2H), 6.69 (s, 1H), 2.59 (s, 1H), 1.96 (s, 6H); ^{19}F NMR (C_6D_6/C_6F_6) δ −75.27 (s). Based on the absence of other ^{19}F NMR resonances and the signal/noise ratio, the purity of this compound is ≥99%.

2.2.2. Preparation of $HOC(2,4,6\text{-}C_6H_2(CF_3)_3)(CF_3)_2$ (H(HFTFPP))

Over the course of 5 min, a 2.5 M hexane solution of *n*-BuLi (3.6 ml, 9.0 mmol) was added dropwise at room temperature to a stirred solution of $1,3,5\text{-}C_6H_3(CF_3)_3$ (2.59 g, 9.2 mmol) in diethyl ether (10 ml) to make a

[1] CCDC(#), copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK, fax: +44-1223-336033, e-mail: deposit@ccdc.cam.ac.uk.

yellow-orange solution. This was stirred for 2 h with no change in appearance. The solution was degassed, and hexafluoroacetone (1.43 g, 8.59 mmol), which had been measured out in a calibrated bulb using a high-vacuum (10^{-5} Torr) line, was then added at −196°C. After warming to room temperature, the reaction mixture was stirred for 18 h. After this time there was still no change in appearance, and volatiles were removed to leave a yellow solid. Concentrated sulfuric acid was added to this, and the resulting mixture distilled under vacuum through 0 and −196°C cold traps. HOC(2,4,6-$C_6H_2(CF_3)_3$)$(CF_3)_2$ was collected in the 0°C trap as clear colorless crystals (0.662 g, 16% based on 1,3,5-$C_6H_3(CF_3)_3$). ^{1}H NMR (C_6D_6) δ 7.80 (s, 1H), 7.00 (s, 1H), 3.13 (s, 1H); ^{19}F NMR (C_6D_6, 25°C) δ −53.05 (m, 3F), −54.78 (septet, J_{F-F} = 15 Hz, 3F), −63.63 (s, 3F), −69.31 (q, J_{F-F} = 15 Hz, 6F); ^{19}F NMR (CD_2Cl_2/toluene-d_8 1:1 (v:v), −98°C) δ −47.40 (t, J_{F-F} = 127 Hz, 1F), −54.17 (s, 6F), −55.59 (d, J_{F-F} = 111 Hz, 2F), −62.89 (s, 3F), −68.64 (m, 3F). Based on the absence of other ^{19}F NMR resonances and the signal/noise ratio, the purity of this compound is ≥99%.

2.2.3. Preparation of 1-Si(i-Pr)$_3$-3,5-$C_6H_3(CF_3)_2$ (1)

A 2.5 M hexane solution of *n*-BuLi (4.8 ml, 12.0 mmol) was added to a solution of 1-Br-3,5-$C_6H_3(CF_3)_2$ (3.61 g, 12.3 mmol) in diethyl ether (40 ml) at −78°C. After 5 min the solution became yellow and a white precipitate formed. The solution was slowly warmed to room temperature, and after 20 min, it had become a wine red color. After an additional 60 min, it became brown. The reaction mixture was frozen at −196°C, and a solution of $CF_3SO_3Si(i\text{-}Pr)_3$ (3.70 g, 12.1 mmol) in ether (10 ml) was added. As the reaction thawed the solution became purple, then violet-black with white and black solids. The volatile material was removed under vacuum, and hexane was added to the resulting solid, making a black solution. This was filtered, and volatiles removed from the red filtrate under vacuum to leave a red liquid. Distillation at 48°C under vacuum yielded a clear colorless liquid which contained the desired product **1** and a small amount of $CF_3SO_3Si(i\text{-}Pr)_3$ starting material. This was removed by stirring an ether solution of the liquid with LiH (0.038 g, 4.8 mmol) for 15.5 h at room temperature followed by filtration, and then removal of volatiles (ether and $HSi(i\text{-}Pr)_3$) under vacuum. Hexane was added to the remaining solid to make a suspension. This was filtered, and volatiles removed from the filtrate under vacuum to yield 3,5-$(CF_3)_2C_6H_3Si(i\text{-}Pr)_3$ as a white solid (2.43 g, 53% based on 1-Br-3,5-$C_6H_3(CF_3)_2$). ^{1}H NMR ($CDCl_3$) δ 7.87 (s, 1H), 1.43 (septet, J_{H-H} = 7 Hz, 3H), 1.06 (d, J_{H-H} = 7 Hz, 18H); ^{19}F NMR ($CDCl_3$) δ −63.33 (s). Based on the absence of other ^{19}F NMR resonances and the signal/noise ratio, the purity of this compound is ≥99%.

2.2.4. Preparation of HOC(4-Si(i-Pr)$_3$-2,6-$C_6H_2(CF_3)_2$)$(CF_3)_2$ (H(HFSiPP))

The synthesis of this compound was described briefly in an earlier report [28]. A 2.5 M hexane solution of *n*-BuLi (0.63 ml, 1.58 mmol) was added to a solution of **1** (0.58 g, 1.57 mmol) in diethyl ether (40 ml) at −78°C. After 15 min of stirring the solution became pink, and was warmed to room temperature. After 5 h the solution became orange. After degassing the solution, hexafluoroacetone (0.322 g, 1.94 mmol), which had been measured out in a calibrated bulb using a high-vacuum (10^{-5} Torr) line, was added at −196°C. As the solution thawed, it became yellow. The reaction mixture was stirred for 12 h, after which time there was no change in appearance. After this time, CF_3CO_2H (1 ml) was added. Volatiles were then removed under vacuum, during which time the solution remained yellow until only a small amount was left, upon which time the color changed to purple. When almost no liquid was remaining, hexane was added and the resulting suspension filtered. Volatiles were removed from the filtrate under vacuum to yield an oily yellow solid. Several recrystallizations from 5 to 10 ml hexane at −78°C yielded HOC(4-Si(*i*-Pr)$_3$-2,6-$C_6H_2(CF_3)_2$)$(CF_3)_2$ as a slightly yellow solid (0.078 g, 9% based on **1**). ^{1}H NMR ($CDCl_3$) δ 8.01 (s, 1H), 7.87 (s, 1H), 3.70 (s, 1H), 1.37 (septet, J_{H-H} = 7 Hz, 3H), 1.01 (d, J_{H-H} = 7 Hz, 18H); ^{19}F NMR ($CDCl_3$, 25°C) δ −53.11 (m, 3F); −54.87 (septet, J_{F-F} = 15 Hz, 3F), −70.17 (q of m, J_{F-F} = 15 Hz, 6F); ^{19}F NMR (methylcyclohexane-d_{14}, −96°C) δ −48.79 (t, J_{F-F} = 126 Hz), 1F), −54.83 (s, 3F), −56.04 (d, J_{F-F} = 124 Hz, 2F), −70.36 (s, 6F)). GC/MS analysis evidenced a purity of ≥99%.

2.2.5. Preparation of HOC(4-C_6H_4(t-Bu))$(CF_3)_2$ (H(HFBuPP))

Hexafluoroacetone (5.58 g, 33.6 mmol), which had been measured out in a calibrated bulb using a high-vacuum (10^{-5} Torr) line, was added to a degassed solution of 4-*t*-butylphenylmagnesium bromide (16.8 ml of a 2 M diethyl ether solution, 33.6 mmol) in 40 ml diethyl ether. After stirring the resulting yellow solution for 18 h, volatiles were removed under vacuum to leave a yellow solid. Sulfuric acid was added as an aqueous solution, which turned the solid into an oil. This was isolated, and the aqueous phase was extracted three times with 20 ml portions of hexane. The organic fractions (oil and hexane) were combined and dried over $MgSO_4$ followed by 4 Å molecular sieves. After filtering this solution, volatiles were removed from the filtrate to yield a solid, which was dissolved in pentane and dried again over 4 Å molecular sieves. After filtering this solution, volatiles were removed from the filtrate under vacuum to yield HOC(4-C_6H_4(*t*-Bu))$(CF_3)_2$ as a white crystalline solid (7.55 g, 75% based on 4-*t*-butylphenylmagnesium bromide). ^{1}H NMR (C_6D_6) δ 7.95 (d, J_{H-H} = 8.1 Hz, 8H), 7.23 (d, J_{H-H} = 8.7 Hz, 8H); ^{19}F NMR (C_6D_6) δ −75.52 (s). GC/MS analysis evidenced a purity of ≥99%. HRMS: found 300.0944. $C_{13}H_{14}OF_6$ requires 300.0949.

2.2.6. Preparation of HOC(cyclo-C_6H_{11})$(CF_3)_2$ (H(HFCP))

The compound HOC(C_6H_5)$(CF_3)_2$ (19.1 g, 78.3 mmol) and rhodium on carbon (0.167 g 5% Rh/C, 0.081 mmol Rh) were combined to make a suspension. This mixture was

stirred at room temperature under 80 psi H_2 for 4 days. After this time there was no change in appearance, and the suspension was filtered through Celite to yield HOC(cyclo-C_6H_{11})$(CF_3)_2$ as a clear colorless liquid (18.2 g, 93% based on HOC(C_6H_5)$(CF_3)_2$). ^{1}H NMR (C_6D_6) δ 2.12 (s, 1H), 0.86–1.83 (1H); ^{19}F NMR (C_6D_6/C_6F_6) δ −72.72 (s). GC/MS analysis evidenced a purity of ≥99%.

2.2.7. Preparation of HOC(cyclo-C_6H_{11})$_2(CF_3)$ (H(DCTE))

The compound HOC(C_6H_5)$_2(CF_3)$ (2.00 g, 7.93 mmol) was dissolved in 25 ml of ethanol, and Rh (0.2 g 5% Rh/C, 0.097 mmol Rh) was added to make a suspension. This mixture was stirred at room temperature under 80 psi H_2 for 4 days. After this time there was no change in appearance, and the suspension was filtered through Celite and ethanol removed under vacuum to yield HOC(cyclo-C_6H_{11})$_2(CF_3)$ as a clear colorless liquid (1.98 g, 95% based on HOC(C_6H_5)$_2(CF_3)$). ^{1}H NMR (C_6D_6/C_6F_6) δ 1.55 (s, 1H), 0.99–1.86 (22H); ^{19}F NMR (C_6D_6/C_6F_6) δ −68.97 (s). GC/MS analysis evidenced a purity of ≥99%.

2.2.8. Preparation of HOC(2-C_6H_4(C(OH)$(CF_3)_2$))$(CF_3)_2$ (H_2(1,2-HFAB))

The compound Li_2(OC(C_6H_4)$(CF_3)_2$) was generated following the procedure of Barbarich et al. [28]. A 2.5 M hexane solution of *n*-BuLi (34.8 ml, 86.9 mmol) and TMEDA (1.01 g, 8.69 mmol) were dissolved in 50 ml diethyl ether and stirred for 30 min to make a cloudy white mixture. After degassing, the solution and cooling to 0°C, HOC(C_6H_5)$(CF_3)_2$ (9.634 g, 39.5 mmol) was added dropwise over 15 min as a solution in ether (15 ml). This mixture was stirred at 0°C for 30 mm, then at room temperature for 20 h. After this time, it was cloudy and yellow. The mixture was cooled to 0°C and hexafluoroacetone (6.56 g, 39.5 mmol), which had been measured out in a calibrated bulb using a high-vacuum (10^{-5} Torr) line, was added. The mixture was warmed to room temperature, and stirred for 2 days. After this time it was still cloudy and yellow, and an aqueous solution of sulfuric acid was added. The yellow organic layer was isolated, and the aqueous layer washed twice with 20 ml portions of ether. The organic fractions were combined, and washed twice with brine. Volatiles were then removed to leave a yellow oil. This was recrystallized from hexane/$CHCl_3$ (20:1 (v:v)) to yield HOC(2-C_6H_4(C(OH)$(CF_3)_2$))$(CF_3)_2$ as a slightly yellow solid (4.65 g, 29% based on HOC(C_6H_5)-$(CF_3)_2$). ^{1}H NMR (C_6D_6) δ 7.69 (m, 2H), 6.72 (m, 2H), 5.50 (s, 2H); ^{19}F NMR (C_6D_6/C_6F_6) δ −72.81 (s). GC/GS analysis evidenced a purity of ≥99%.

3. Results and discussion

3.1. Synthesis of new polyfluoroa!cohols

Table 1 lists the compounds discussed below with their abbreviations, structures, and yields of the preparative reactions. Alcohols of the type HOCR$(CF_3)_2$ (R = H, non-fluorinated alkyl, aryl) may be prepared by addition of hexafluoroacetone (HFA) to the appropriate Grignard or organolithium reagent [1] followed by protonation:

$$MR + (CF_3)_2CO \rightarrow MOCR(CF_3)_2 \xrightarrow{H^+} HOCR(CF_3)_2$$

where, M = Li, MgX (X = Cl, Br, I)

Using the appropriate Grignard reagents, this method was used to synthesize the new alcohol H(HFDPP), and to improve the yield of the previously reported compound H(HFBuPP). The reported synthesis for the latter compound, for which the purified yield was only 43%, consisted of electrophilic aromatic substitution of HFA on *t*-butylbenzene catalyzed by $AlCl_3$ [30]. Using the Grignard reagent 4-*t*-butylphenylmagnesium bromide, our yield of purified alcohol was increased to 75%.

The yield of the new compound H(HFDPP) was not as high as for H(HFBuPP), which was most likely due to the longer purification process. The crude product (orange oil) was first dissolved in hexane and washed with water to remove any hexafluoroacetone trihydrate. Deprotonation by LiH was then performed to facilitate the removal of diethyl ether and other volatile impurities under vacuum. These impurities proved to be difficult to separate from the alcohol by distillation or column chromatography. Reprotonation with sulfuric acid followed by vacuum distillation resulted in a 52% yield of purified H(HFDPP).

The new alcohols H(HFSiPP) and H(HFTFPP) were prepared in a similar manner to H(HFBuPP) and H(HFDPP), but the appropriate organolithium reagents were used instead of the corresponding Grignard reagents. For H(HFSiPP), the silyl arene (1) was lithiated with *n*-BuLi and then treated with HFA. Purification by successive recrystallizations from hexane at −78°C resulted in a yield of 9%. To make H(HFTFPP), 1,3,5-tris(trifluoromethyl)benzene was lithiated with *n*-BuLi and then treated with HFA. Distillation of the crude product resulted in purified H(HFTFPP) in a yield of 16%.

The known compound H(HFCP) and the new fluoroalcohol H(DCTE) were synthesized by catalytic hydrogenation of HOC(C_6H_5)$(CF_3)_2$ and HOC(C_6H_5)$_2(CF_3)$, respectively, over Rh/C. Alcohol/Rh ratios of 966:1 and 326:1 were used to prepare H(HFCP) and H(DCTE), respectively. Higher ratios were found to work as well, but reaction times were longer. Overall, this method was very efficient: the only purification necessary was filtration to remove Rh/C and removal of ethanol in the case of H(DCTE). Isolated yields were very high, 95% for H(DCTE) and 93% for H(HFCP). The previously reported method for synthesizing H(HFCP) consisted of a free radical-initiated reaction between cyclohexane and HFA [31], resulting in an isolated yield of only 69%.

The synthesis of H_2(1,2-HFAB) completes the series of bis(2-hydroxyhexafluoro-2-propyl)benzene derivatives. The 1,3- and 1,4- varieties have been reported, and were made by

$AlCl_3$-catalyzed electrophilic aromatic substitution of benzene with HFA [32]. The 1,2-isomer was not formed in this reaction, presumably due to steric hindrance considerations. The first attempt to synthesize a 1,2-diol consisted of the reaction of H(HFBuPP) with HFA in the presence of $AlCl_3$. It was hoped that the *t*-butyl group would favor substitution of HFA in the *ortho*-position by (a) blocking the *para*-site, and (b) effectively blocking the *meta*-site by steric hindrance. However, no reaction was observed. This could be due to excessive steric hindrance at both the *ortho*- and *meta*-sites. The successful synthesis of H_2(1,2-HFAB) resulted from the reaction of the dilithiated LiOC(2-$C_6H_4Li)(CF_3)_2$ with HFA in diethyl ether. Adding two equivalents of *n*-BuLi to $HOC(C_6H_5)(CF_3)_2$ in the presence of TMEDA leads to an *ortho*-lithiated dianion (after deprotonation of the alcohol) [29]. The carbanion then reacts with HFA, overcoming the steric hindrance barrier to form Li_2(1,2-HFAB). Protonation with H_2SO_4 followed by recrystallization yielded H_2(1,2-HFAB) in 29% yield. This diol may be useful as a bidentate ligand: both oxygen atoms are weak donors, but can form stable complexes with a central atom by virtue of its chelating nature.

3.2. Structure and ^{19}F NMR spectra of H(HFTFPP)

The structure of this compound, shown in Fig. 1, consists of discrete HOC-2,4,6-$C_6H_2((CF_3)_3)(CF_3)_2$ molecules. Selected interatomic bond distances and angles are listed in Table 3. The hydrogen atoms were placed in calculated positions except for the hydroxyl group proton (H1), which was located in the Fourier maps and refined. The O–H1 distance of 0.76(4) Å is considerably shorter than the value of 0.967 Å typically found for alcohols by neutron diffraction [33,34]. For this reason, inter- and intramolecular contacts involving H1 were normalized by fixing the O–H1 distance at 0.967 Å along the refined H1 vector, a procedure commonly used when evaluating X-ray-derived results involving hydrogen atoms [33–37]. The *p*-CF_3 is disordered and was modeled isotropically as 12 partial fluorine atoms, each with a site occupancy factor equal to

Table 3
Selected interatomic distances (Å) and angles (°) for HOC(2,4,6-$C_6H_2((CF_3)_3)(CF_3)_2$

O–H1	0.76(4)	C1–C4–C5	118.5(2)
O–C1	1.407(2)	C1–C4–C9	125.4(2)
C1–C2	1.566(3)	C5–C4–C9	115.7(2)
C1–C3	1.575(3)	C4–C5–C6	120.9(2)
C1–C4	1.553(2)	C5–C6–C7	120.7(2)
C4–C5	1.442(2)	C6–C7–C8	119.2(2)
C5–C6	1.391(2)	C7–C8–C9	122.8(1)
C6–C7	1.383(3)	C8–C9–C4	121.2(2)
C7–C8	1.375(3)	C4–C5–C10	126.3(2)
C8–C9	1.393(2)	C6–C5–C10	112.5(2)
C9–C4	1.413(2)	C4–C9–C11	126.4(2)
C5–C10	1.528(3)	C8–C9–C11	112.1(2)
C9–C11	1.522(2)		
H1–O–C1	109.3(2)		
O–C1–C4	104.54(14)		
O–C1–C2	101.5(2)		
O–C1–C3	110.3(2)		
C2–C1–C3	111.7(2)		
C2–C1–C4	113.1(2)		
C3–C1–C4	114.6(2)		

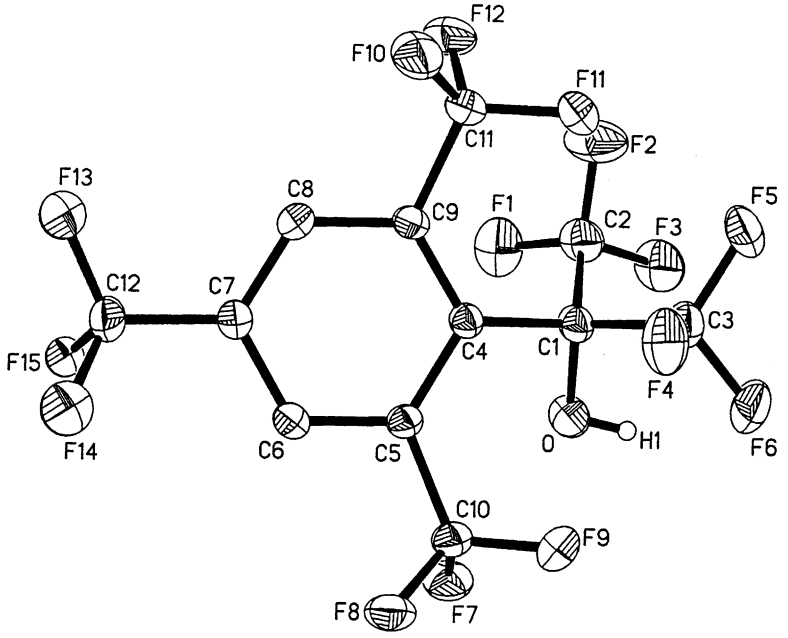


Fig. 1. Drawing of HOC(2,4,6-$C_6H_2(CF_3)_3)(CF_3)_2$ with 50% probability thermal ellipsoids. The disordered CF_3 group bonded to C7 was modeled isotropically as 12 partial fluorine atoms, each with a site occupancy factor equal to 0.25 (only three of the partial fluorine atoms are shown). The two hydrogen atoms bonded to C6 (H2) and C8 (H3) have been omitted for clarity.

Table 4
Interatomic distances (Å) and angles (°) involving the hydroxyl group in HOC(2,4,6 $C_6H_2((CF_3)_3)(CF_3)_2$[a]

O–H1	0.76(4)	[0.967]
H1···F3	2.37(4)	[2.35]
H1···H4	2.17(4)	[2.11]
O–H1···F3	96.6 (3.0)	[91.7]
O–H1···F4	110.3(3.3)	[104.8]
O···F3	2.570(2)	
O···F4	2.535(2)	

[a] The values in square brackets were calculated after the O–H bond was extended to 0.967 Å along the X-ray derived bond vector.

0.25. The aromatic ring is distorted from planarity, a feature commonly observed in the 2,4,6-tris(trifluoromethyl)phenyl substituent [38].

There are two relatively short intramolecular OH···FC contacts involving one fluorine atom from each of the two geminal CF_3 groups. Relevant bond distances and angles are listed in Table 4. The H1···F3 and H1···F4 distances are 2.35 and 2.11 Å, respectively, and the O–H1···F3 and O–H1···F3 angles are 91.7 and 104.8°, respectively. The distances are certainly short enough for the OH···F interactions to be considered as weak hydrogen bonds. In a previous paper [28], we reported a pair of intermolecular OH···FC contacts in the structure of HOC(4-Si(*i*-Pr)$_3$-2,6-$C_6H_2(CF_3)_2)(CF_3)_2$), which exists in the solid state as a centrosymmetric dimer apparently held together by the pair of symmetry related OH···FC contacts. In that structure, the distance H···F and O–H···F angle were found to be 2.01 Å and 171°.

Many chemists and biochemists believe that the formation of intermolecular H···FC and N–H···FC hydrogen bonds may be important in the binding of fluorinated substrates to enzyme active sites [39–44]. Nevertheless, bonafide examples of O–H···FC and N–H···FC hydrogen bonding *in the absence of stronger* O–H···X and N–H···X *hydrogen bonds* (X = O, N) are rare. In a 1997 study, Dunitz and Taylor concluded that "organic fluorine hardly ever accepts hydrogen bonds" [45]. In a 1996 study, Howard et al. found only 12 compounds in the CSD containing OH···FC interactions of 2.35 Å or less (compounds containing CF_2 or CF_3 groups were excluded from their study) [46]. In a 1994 study, Shimoni and Glusker found that the mean XH···FC distance (X = N, O) for all relevant compounds in the CSD was 2.5 Å whether the acceptor fluorine atom was part of a CF_3 group or not (the median distance was also 2.5 Å) [47].

In dilute hydrocarbon solution at −96°C, the ^{19}F NMR spectrum of HOC(4-Si(*i*-Pr)$_3$-2,6-$C_6H_2(CF_3)_2)(CF_3)_2$) revealed that one of the *o*-CF_3 groups experienced slow rotation [28]. The single resonance for this group at 25°C decoalesced into a doublet (intensity = 2) and a triplet (intensity = 1) at −96°C, and this was attributed to intramolecular OH···FC hydrogen bonding involving one of the fluorine atoms of this CF_3 group. It was also found that the average J_{C-F} value for the doublet and triplet was equal to the J_{C-F} value for this CF_3 group at 25°C and that J_{C-F} (doublet) > J_{C-F} (triplet).

We now report that HOC(2,4,6-$C_6H_2((CF_3)_3)(CF_3)_2$ behaves similarly in dilute hydrocarbon solution. The low-temperature (−98°C) ^{19}F NMR spectrum of this compound dissolved in a 1:1 (v:v) mixture of toluene-d_8 and

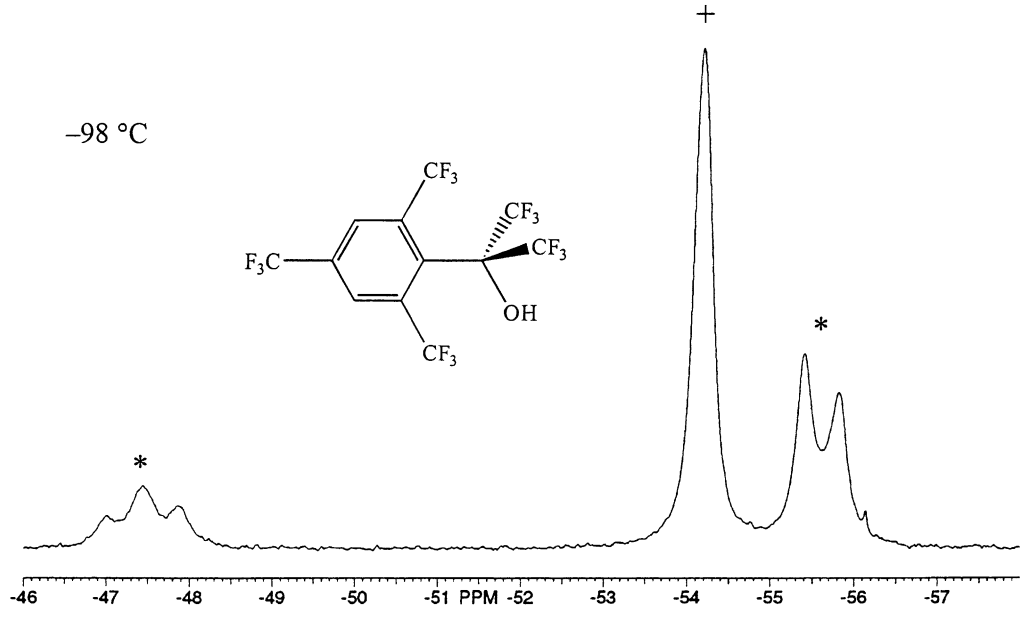


Fig. 2. A portion of the ^{19}F NMR spectrum of HOC(2,4,6-$C_6H_2(CF_3)_3)(CF_3)_2$ at −98°C (1:1 toluene-d_8/CD_2Cl_2). The singlet (+) corresponds to the *o*-CF_3 group distal to the hydroxyl group, and the doublet (∗) and triplet (∗) correspond to the *o*-CF_3 group proximal to the hydroxyl group (involved in (O)H···F(C) hydrogen bonding). The single resonance for the geminal CF_3 groups is not shown (δ −54.17).

dichloromethane-d_2 is shown in Fig. 2. The relative δ values of the doublet and the triplet, and the J_{F-F} value, are nearly the same as those reported for HOC(4-Si(*i*-Pr)$_3$-2,6-$C_6H_2(CF_3)_2)(CF_3)_2$). Therefore, we conclude that HOC(2,4,6-$C_6H_2((CF_3)_3)(CF_3)_2$, like HOC(4-Si(*i*-Pr)$_3$-2,6-$C_6H_2(CF_3)_2)(CF_3)_2$), exhibits intramolecular OH$\cdots$FC hydrogen bonding involving one of the fluorine atoms of one of the *o*-CF_3 groups.

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