Journal of Fluorine Chemistry 139 (2012) 4–11

Contents lists available at SciVerse ScienceDirect

Journal of Fluorine Chemistry

journal homepage: www.elsevier.com/locate/fluor

Chemoselective halogenation of 2-hydroperfluoroalkyl aldehydes

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ARTICLE INFO

Article history:
Received 21 February 2012
Received in revised form 11 March 2012
Accepted 12 March 2012
Available online 21 March 2012

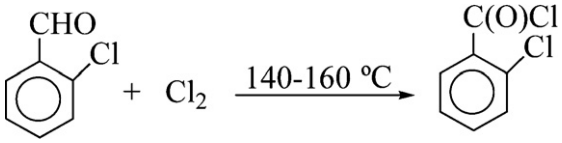
Keywords:
Fluorinated vinyl ethers
2-Hydroperfluoroalkylaldehydes
2-Hydroperfluoroacyl halides
2-Haloperfluoroaldehydes
2-Hydro-branched perfluorocarboxylic acids
Chemoselective halogenation
Perfluoroalkyl effect
Free-radical halogenation of 2-hydroaldehydes

ABSTRACT

2-Hydroaldehydes, $R_fCH(R)CHO$, where $R_f = CF_3$, C_2F_5, n-C_3F_7 and $R = CF_3$, C_2F_5, n-C_3F_7, Ph, H, were prepared *via* acid hydrolysis of the corresponding vinyl ethers, $R_fC(R) = CHOCH_3$, which can be readily prepared by reaction of $[Ph_3\overset{+}{P}\bar{C}HOCH_3]$ with the corresponding ketone. The 2-hydroaldehydes can be chemoselectively converted to the acyl halide, $R_fCH(R)C(O)X$ (X = Cl, Br), *via* free-radical halogenation. The perfluoroalkyl group deactivates the 2-position toward radical abstraction of the 2-hydrogen, and halogenation occurs exclusively at the formyl hydrogen. However, halogenations of the 2-hydroaldehydes in glacial acetic acid chemoselectively gives the 2-haloaldehydes, $R_fCX(R)CHO$, X = Cl, Br. Hydrolysis of the 2-hydroperfluoroacyl halides provides a useful route to 2-hydroperfluoroalkyl branched carboxylic acids, useful ketene precursors. This route avoids the use of toxic fluoroolefins, such as perfluoroisobutylene.

1. Introduction

Halogenation of aldehydes under free radical conditions can be a non-selective hydrogen abstraction process that results in a variety of products. However, the halogenation can be selective if the halogenation is carefully controlled, or the aldehyde has only one hydrogen capable of abstraction. For example, aromatic aldehydes have only the formyl hydrogen that can be abstracted in a free-radical process and readily yield only the acid chloride (Eq. (1)) [1]. Similarly, Ginsburg reacted a series of aromatic



(1)

aldehydes with *t*-butyl hypochlorite and isolated the products as the corresponding carboxylic acids [2]. Similarly, Arai chlorinated aromatic aldehydes to yield the corresponding acid chlorides with sulfuryl chloride in CCl_4 as solvent and benzoyl peroxide as the radical initiator [3,4]. Lee reported a study of substituent effects for the conversion of aromatic aldehydes to the corresponding acid chlorides with sulfuryl chloride and trichloromethylsulfuryl chloride as the halogenation agents [5].

The selective free-radical halogenation of the α-hydrogen of a non-aromatic aldehyde has been reported. Darzans and Meyer reported the photobromination of acetaldehyde in ether to yield α-bromoacetaldehyde, isolated as the acetal [6]. Brown and Ash chlorinated butyraldehyde in methylene chloride with sulfuryl chloride and benzylperoxide to yield α-chlorobutyraldehyde (Eq. (2)) [7].

$$CH_3CH_2CH_2CHO + SO_2Cl_2 \xrightarrow[CH_2Cl_2]{Bz_2O_2} CH_3CH_2CHClCHO \quad (2)$$

Brace reported that photochlorination of a polyfluorinated aldehyde at −20 °C yielded the acyl chloride [8] (Eq. (3)). At higher temperatures, the halogenation resulted

$$H(CF_2CF_2)_2CHO \xrightarrow[CCl_4]{Cl_2/h\nu,\ -20\ ^\circ C} H(CF_2CF_2)_2C(O)Cl \quad (3)$$

in decarbonylation and formation of polychlorofluoroalkenes [8] (Eq. (4)).

$$H(CF_2CF_2)_2CHO + Cl_2 \xrightarrow[20-40\ ^\circ C_{CCl_4}]{h\nu} H(CF_2CF_2)_2Cl \quad (4)$$

Aldehydes may decarbonylate by a free-radical mechanism. The initially formed radical may rearrange after the decarbonylation.

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doi:10.1016/j.jfluchem.2012.03.013

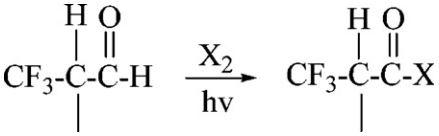
For example, treatment of 3-methyl-3-phenylbutanal with peroxide yields both 2-methyl-2-phenylpropane and 1-phenyl-2-methylpropane [9,10]. Based on some earlier work by Henne and co-workers, Tedder studied in detail the free-radical chlorination and bromination of 1,1,1-trifluoropentane [11]. Their results confirmed Henne's earlier work and showed that the trifluoromethyl group exerts a very powerful deactivating effect on halogenation at adjacent sites. The relative selectivities for these chlorination and bromination are summarized below.

Relative selectivities for the halogenation of $CF_3CH_2CH_2CH_2CH_3$ [11]:

	CF_3CH_2 -	CH_2 -	CH_2 -	CH_3
(Cl_2 at 60 °C)	0.04	1.21	4.38	1
(Br_2 at 150 °C)	<1	7	90	1

Tedder's work illustrates that a trifluoromethyl group exerts a deactivating effect on chlorination and bromination at the β-carbon. Halogenation is almost completely inhibited at the carbon atom α to the trifluoromethyl group. On the basis of the relative selectivities, it appears that a trifluoromethyl group has no effect on the rate of halogenation at the terminal δ carbon atom and very little influence at the γ position.

This work by Tedder suggested that free-radical chlorination or bromination of 1-hydroaldehydes containing a perfluoroalkyl group attached to the α-carbon of the aldehyde could potentially be chlorinated or brominated selectively at the formyl hydrogen (as outlined below) (Eq. (5)). Hydrolysis of the acyl halide would afford the



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corresponding 2-hydroperfluoroalkyl carboxylic acid – a useful precursor to perfluoroalkylketenes. To evaluate this proposed selectivity, we undertook the following approach: (a) develop a useful synthesis of a variety of 2-hydroperfluoroalkyl aldehydes; (b) free-radical chlorination and bromination of the titled aldehydes to evaluate the selectivity of attack at the formyl hydrogen; (c) evaluation of selective halogenation of the α-hydrogen of the aldehyde to give the 2-haloperfluoroalkyl aldehydes; (d) hydrolysis of the acyl halides to give the corresponding 2-hydroperfluoroalkyl carboxylic acids.

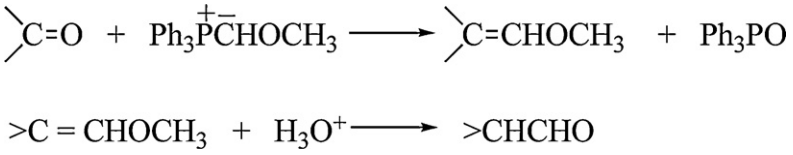
2. Results and discussion

2.1. Preparation of 2-hydroperfluoroaldehydes

Taylor and co-workers reported the preparations of polyfluorinated vinyl ethers from terminal hydro-chloroolefins and potassium hydroxide in methanol [12]. The polyfluorinated aldehydes, obtained by hydrolysis of the vinyl ethers, were oxidized with aqueous hydrogen peroxide to the corresponding polyfluorinated carboxylic acids (Eq. (6)).

$$\begin{aligned}&(CF_3)_2C{=}CHCl \xrightarrow[MeOH]{KOH} (CF_3)_2C{=}CHOCH_3\\ &(CF_3)_2C{=}CHOCH_3 \xrightarrow{H_2SO_4} (CF_3)CHCHO\\ &(CF_3)_2CHCHO \xrightarrow[H_2O]{H_2O_2} (CF_3)_2CHCO_2H\end{aligned} \tag{6}$$

The hydrolysis of octafluoroisobutylene under mild conditions also yields 2-trifluoromethyl-3,3,3-trifluoropropanoic acid in good yield [13,14]. However, the reaction is very specific for the propanoic acid analog and is not a general preparation of branched polyfluorinated acids. Other disadvantages are: the starting material is not readily available and must be handled with extreme care due to its high toxicity. An alternative route to the vinyl ethers was reported by Wittig and Schlosser [15,16], who reacted ketones with methoxymethylenetriphenylphosphorane to prepare vinyl ethers. The vinyl ethers were readily hydrolyzed in acid media to the corresponding aldehydes (Eq. (7)).



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This approach was employed by Mosher and co-workers for the conversion of trifluoroacetophenone into the aldehyde *via* hydrolysis with H_2SO_4. The aldehyde was subsequently oxidized with $KMnO_4/H_2SO_4$ to Mosher's acid, α-trifluoromethylphenylacetic acid [17]. Since this methodology is a convenient general route [16] to vinyl ethers and α-hydroaldehydes, we selected this route for the preparation of fluorinated vinyl ethers. The requisite precursor, methoxymethylenetriphenylphosphorane is readily prepared *via* reaction of monochloromethyl ether with triphenylphosphine [15]. The monochloromethylenemethyl ether was prepared *via* modification of the organic synthesis procedure [18] (Eq. (8)).

$$\begin{aligned}&MeOH + 37\%\ \text{formalin soln.} \xrightarrow{HCl} \underset{71\%}{ClCH_2OCH_3}\\ &ClCH_2OCH_3 + Ph_3P \xrightarrow[70\,^\circ C]{\text{benzene}} \underset{\mathbf{1},\,90\%}{[Ph_3\overset{+}{P}CH_2OCH_3]Cl^-}\end{aligned} \tag{8}$$

Subsequent reaction of the phosphonium chloride in an ethereal solvent with base yielded a bright red solution of methoxymethylene triphenylphosphorane (Wittig reagent) (Eq. (9)). Addition of a fluorinated ketone yielded the corresponding vinyl ether (Eq. (10)).

$$1 + KO^tBu \xrightarrow[5-20\,^\circ C]{Et_2O} [Ph_3\overset{+}{P}\bar{C}HOCH_3] \tag{9}$$

Table 1 summarizes the vinyl ethers prepared *via* this methodology.

$$[Ph_3\overset{+}{P}\bar{C}HOCH_3] + >C{=}O \longrightarrow >C{=}CHOCH_3 \tag{10}$$

2.2. Hydrolysis of the vinyl ethers

The hydrolysis of 1-methoxy-2-trifluoromethyl-3,3,3-trifluoropropene, **2**, with H_2SO_4 has been previously reported [12].

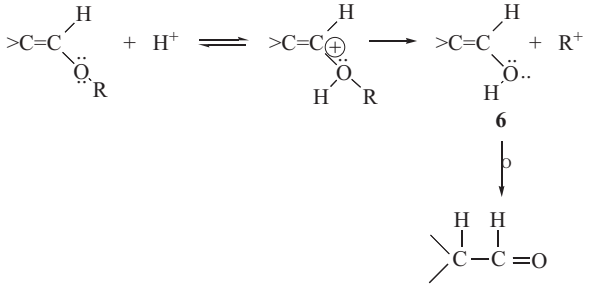
Table 1
Preparation of vinyl ethers. **1** + ketone $\xrightarrow[Et_2O]{}$ >C=CHOCH$_3$

Ketone	Vinyl ether	Yield (isolated)
$(CF_3)_2C{=}O$	$(CF_3)_2C{=}CHOCH_3$, **2**	57
$CF_3(Ph)C{=}O$	*E*/*Z* $CF_3(Ph)C{=}CHOCH_3$, **3**	89
$(CF_2Cl)_2C{=}O$	$(CF_2Cl)_2C{=}CHOCH_3$, **4**	31
$CF_3(n\text{-}Bu)C{=}O$	*E*/*Z* $CF_3(n\text{-}Bu)C{=}CHOCH_3$, **5**	48
$(CF_3CF_2)_2C{=}O$	$(CF_3CF_2)_2C{=}CHOCH_3$, **6**	64
$(CF_3CF_2CF_2)_2C{=}O$	$(CF_3CF_2CF_2)_2C{=}CHOCH_3$, **7**	60

No attempt was made to separate *E*/*Z* isomers.

Table 2
Hydrolysis of vinyl ethers with acid.

Vinyl ether	2-Hydroaldehyde	Isolated yield (%)
2	$(CF_3)_2CHCHO$, **8**	87
3	$CF_3(Ph)CHCHO$, **9**	83
5	$CF_3(n\text{-}Bu)CHCHO$, **10**	47
6	$(CF_3CF_2)_2CHCHO$, **11**	88
7	$(CF_3CF_2CF_2)_2CHCHO$, **12**	77
$CF_3CH{=}CHOCH_3$	CF_3CH_2CHO, **13**	34



Scheme 1. Acid hydrolysis of vinyl ethers.

Mechanistically, the reaction has been proposed to proceed *via* β-carbon protonation as the first step [19] (Scheme 1).

Experimentally, the hydrolysis of the vinyl ethers altered slightly from compound to compound (*cf.* Section 3). Table 2 summarizes the 2-hydroaldehydes prepared *via* hydrolysis of the vinyl ethers.

The α-hydroaldehydes were characterized *via* a combination of IR, ^{1}H NMR, ^{19}F NMR and GC–MS. The ^{19}F NMR of the aldehydes, which contained the CF_2CF_3 and $CF_3CF_2CF_2$ exhibited an AB pattern for the non-equivalent fluorines of the CF_2 group attached to the functional group (–CHO). The GC–MS generally showed a molecular ion, except for the aldehydes containing the perfluoroethyl or perfluoropropyl groups, which showed the parent ion minus fluorine.

2.3. Free radical halogenation of the 2-hydroaldehydes

The photohalogenation of the 2-hydroaldehydes were normally carried out at RT and without solvent. The halogenation was an exothermic reaction and the temperature of the reaction mixture was controlled by the addition rate of the halogen. In most cases, the only product observed was the formation of the acyl halide. No abstraction of the α-hydrogen was detected. The aldehyde of the *n*-butyl group of **10**, however, had the additional problem of abstraction of hydrogens of the butyl group, which resulted in a mixture of polyfluorochloro acid chlorides. The halogenation reaction was easily followed by removing small aliquots from the reaction mixture at different intervals and recording the ^{1}H NMR for the aliquots. The ^{1}H NMR spectra showed the loss of the formyl hydrogen, while the hydrogen changes from a doublet of heptets, in the case of **8**, to a heptet. It is not necessary to follow the reaction by ^{1}H NMR to prevent the product from reacting further with excess halogen. The product remained unchanged when reacted with excess halogen under the reaction conditions. The lack of solvent makes it convenient to follow the reaction by ^{1}H NMR. Fractional distillation of the reaction mixture afforded the acyl halide. Table 3 summarizes the halogenation of the 2-hydroaldehydes. Note that chlorination of $(CF_3)_2CClCHO$ resulted in decarbonylation and formation of the polyfluorochloroalkane [8].

The effect of the perfluoroalkyl group on the site of halogenation can be ascertained by comparison of the free-radical chlorination of 2-trifluoromethylphenyl-acetaldehyde, **9**, and diphenylacetaldehyde (Eqs. (11) and (12)).

$$\underset{\mathbf{9}}{CF_3(Ph)CHCHO} \xrightarrow[UV_{RT}]{Cl_2} \underset{\mathbf{16},\,70\%}{CF_3(Ph)CHC(O)Cl} \quad (11)$$

$$Ph_2CHCHO \xrightarrow[UV]{Cl_2} \underset{\mathbf{21},\,73\%}{Ph_2CClCHO} \quad (12)$$

2.4. Halogenation of the 2-hydroaldehydes in acetic acid

The chemoselectivity of the halogenation of the 2-hydroaldehydes can be altered *via* change of the halogenation conditions. The same series of aldehydes outlined in Table 3 could be utilized for halogenation under polar conditions, since these aldehydes have

Table 3
Free radical halogenation of 2-hydroaldehydes.

$$R_f(R')CHCHO + X_2 \xrightarrow[RT]{hv} R_f(R')CHC(=O)\text{-}X$$
no solvent

Aldehyde	Halogen	Product	Isolated yield (%)
8	Cl_2	$(CF_3)_2CHC(O)Cl$, **14**	74
8	Br_2	$(CF_3)_2CHC(O)Br$, **15**	57
9	Cl_2	$CF_3(Ph)CHC(O)Cl$, **16**	70
5	Cl_2	Mixture of acyl halides	–
11	Cl_2	$(CF_3CF_2)_2CHC(O)Cl$, **17**	79
12	Cl_2	$(CF_3CF_2CF_2)_2CHC(O)Cl$, **18**	67
13	Cl_2	$CF_3CH_2C(O)Cl$, **19**	39
$(CF_3)_2CClCHO$	Cl_2	$(CF_3)_2CCl_2$, **20**	37

Table 4
Halogenation of 2-hydropolyfluorinated aldehydes in acetic acid.

Aldehyde	Halogen	Product	Isolated yield (%)
8	Cl_2	$(CF_3)_2CClCHO$, **22**	79
8	BrCl	$(CF_3)_2CBrCHO$, **23**	48
9	Cl_2	$CF_3(Ph)CClCHO$, **24**	74
11	Cl_2	$(CF_3CF_2)_2CClCHO$, **25**	51
12	Cl_2	$(CF_3CF_2CF_2)_2CClCHO$, **26**	80

an α-hydrogen which allows tautomerization. The ability to tautomerize to form the enol can be regulated by the polarity of the solvent. The more polar the solvent, the greater amount of the enol formed. Acetic acid was selected as the solvent, since it has been frequently employed for addition of chlorine or bromine to aldehydes with α-hydrogens. When **8** was reacted with Cl_2 in glacial acetic acid at RT, the only product observed with 2-chloro-2-trifluoromethyl-3,3,3-trifluoropropanal, **22** (Eq. (13)). The

$$\underset{\mathbf{8}}{(CF_3)_2CHCHO} + Cl_2 \xrightarrow[RT]{CH_3COOH} \underset{\mathbf{22},\,79\%}{(CF_3)_2CClCHO} \quad (13)$$

product was readily distilled from the solvent. Table 4 summarizes the chemoselective halogenation of the 2-hydroaldehydes in acidic media. Bromination in acetic acid was accomplished with BrCl. The use of Br_2 gave a mixture of products and a more difficult isolation of the α-bromoaldehyde (*cf.* Section 3).

The ^{1}H NMR spectrum of the reaction mixture provided a useful way to monitor the reaction progress. As noted earlier, free-radical halogenation of the aldehydes was followed by disappearance of the formyl hydrogen. The polar halogenation reaction of the corresponding aldehydes was easily monitored by the disappearance of the α-hydrogen resonance. The solvent, CH_3COOH, did not interfere with the α-hydrogen or the formyl hydrogen resonance.

2.5. Hydrolysis of 2-hydroperfluoroacyl halides

As noted earlier, 2-trifluoromethyl-3,3,3-trifluoropropanoic acid can be easily converted to the corresponding ketene [14]. The free-radical halogenation reaction of the 2-hydroperfluoroaldehydes affords a convenient entry into the preparation of 2-perfluoroalkyl-2-hydro-perfluoroacyl halides (*cf.* Table 3). Hydrolysis of these acyl halides would provide the necessary precursor to the corresponding acid (ketene precursor) and avoid toxic precursors, such as perfluoroisobutylene. Consequently, we carried out the hydrolysis of the appropriate perfluoroacyl halides, and the results of this hydrolysis are summarized in Table 5. For example, reaction of **14** with THF/H_2O gave the 2-trifluromethyl-3,3,3-propanoic acid in excellent yield (Eq. (14)). The hydrolysis

$$\underset{\mathbf{14}}{(CF_3)_2CHC(O)Cl} \xrightarrow[THF]{H_2O} \underset{\mathbf{27},\,90\%}{(CF_3)_2CHCO_2H} \quad (14)$$

reaction is exothermic and the heat of the reaction can be controlled by the rate of addition of the acyl halide to the aqueous THF. The hydrolysis reaction is complete within a few minutes.

Table 5
Preparation of Branched polyfluorinated carboxylic acids. $R_fCHC(O)Cl + H_2O + H_2O \xrightarrow{THF} R_fCHCO_2H$.

Acyl halide	Product	Isolated yield (%)
14	$(CF_3)_2CHCO_2H$, **27**	90
11	$(CF_3CF_2)_2CHCO_2H$, **28**	60
12	$(CF_3CF_2CF_2)_2CHCO_2H$, **29**	**67**

3. Experimental

3.1. General experimental procedures

All glasswares were oven-dried prior to use. ^{1}H NMR was recorded utilizing either a Varian A60-A or Varian HA-100 spectrometers. Samples were studied in $CDCl_3$, unless other indicated, with TMS as an internal standard. ^{19}F NMR was recorded using a Varian HA-100 spectrometer. Samples were studied in $CDCl_3$ with CCl_3F as an internal standard. GC–MS was determined on a Hitachi Perkin Elmer RMU-6E single focusing instrument at 70 eV. The sample was normally introduced through the glass inlet system with liquids and solids. Low volatile solids were introduced *via* the direct inlet system Refractive indices were determined at 20.0 ± 0.1 °C with a Bausch and Lomb Abbe Refractometer. Infrared spectra were recorded on a Perkin-Elmer Model 21 Double Beam Spectrophotometer. Melting points were determined in ~1.2 capillary tubes placed in a Thomas Hoover "Uni-Melt" capillary melting point apparatus – all melting points are corrected. Boiling points were determined during distillation and are uncorrected. Some boiling points were determined by a micro bp method [20] and are indicated as micro bp. GLPC was carried out on an F&M Model 700 Dual Column Gas Chromatograph, with He as the carrier gas. Analytical determinations were made with a disc integrator for peak areas. Columns employed were 10% carbowax 20M, SE-30, and Fluorosilicone FS-1265.

3.2. Materials and chemicals

Acetic acid, Br_2, Cl_2, $(CF_2Cl)_2C{=}O$, diethyl ether, diphenylacetaldehyde, formalin solution, $(CF_3)_2C{=}O$, CH_2Cl_2, KO^tBu, H_2SO_4, Ph_3P were obtained from commercial sources. $CF_3C(O)Ph$ was prepared by previously described methods [21,22]. $CF_3(n\text{-}C_4H_9)C{=}O$ was prepared by the literature method [21]. $(CF_3CF_2)_2C{=}O$ and $(CF_3CF_2CF_2)_2C{=}O$ were prepared by the method of Wiley [23].

3.3. Preparation of monochloromethylmethylether

A 2-l three-necked flask was equipped with a Teflon coated magnetic stir bar, water cooled reflux condenser topped with a N_2 inlet tube and a 12 × ¼ in. section of glass tubing inserted into the lower portion of the flack. The reaction flask was charged with 350 g (428 ml, 10.9 mol) methyl alcohol and 400 g (8.4 mol) of 37% formalin solution. Anhydrous HCl was bubbled into the reaction mixture (excess HCl vented into a fume hood) for 4 h with intermittent cooling of the reaction mixture with an ice bath. The organic layer was separated from the aqueous solution, and the aqueous solution combined with ~150 g $CaCl_2$ to "salt out" additional organic material. The combined organic fractions were dried over anhydrous $CaCl_2$, filtered, and distilled to afford 480.2 g (5.97 mol) of $ClCH_2OCH_3$, bp 59–61 °C (71%). Reported for $ClCH_2OCH_3$: bp 55–60 °C [18].

3.4. Preparation of methoxymethylenetriphenylphosphonium chloride, 1

A 2-l three-necked flask was equipped with a Truebore stirrer, water cooled reflux condenser topped with a $CaCl_2$ drying tube and a 150 °C thermometer. The reaction flask was charged with 80.5 g (1.0 mol) $ClCH_2OCH_3$ and 263 g (1.0 mol) Ph_3P (dissolved in 1-l benzene). The resultant mixture was heated to 70 °C for 15 h. A white solid formed gradually as the reaction mixture was heated. The reaction mixture was cooled to ~10 °C with an ice bath and then filtered. The white solid was placed in a 2-l flask, and the benzene was evaporated with a RotoVap (aided by a hot water bath at ~70°C). The reaction yielded 307.6 g (0.90 mol, (90%) of

$[(C_6H_5)_3\overset{+}{P}CH_2OCH_3]Cl^-$, **1**, mp 189–192 °C. Reported for methoxymethylenetriphenylphosphonium chloride: mp 198–199 °C [15]. The product was not purified to remove any remaining Ph_3P because the tertiary phosphine would not interfere with the subsequent Wittig reaction.

3.5. Preparation of E/Z-1-methoxy-3,3,3-trifluoropropene

Trifluoropropyne was prepared from trifluoromethyltrichloroethylene *via* the method of Finnegan and Norris [24]. The propyne was reacted with absolute MeOH and KOH *via* the procedure reported by Haszeldine [25] to yield *E*/*Z* $CF_3CH{=}CHOCH_3$. Thus, 200 g (1.0 mol) $CF_3CCl{=}CCl_2$ afforded 33.2 g (0.26 mol), (26%) of $CF_3CH{=}CHOCH_3$, bp 79–82 °C, n_D^{20} = 1.3436. Reported for $CF_3CH{=}CHOCH_3$, bp 83–84 °C [25].

3.6. Preparation of 1-methoxy-2-trifluoromethyl-3,3,3-trifluoropropene, 2

A 2-l three-necked flask, equipped with a Trubore stirrer, coldfinger condenser cooled with dry ice/isopropanol, a low-temperature thermometer and a N_2 tee, was charged with 174.1 g (0.508 mol) of **1** and 1-l of anhydrous diethyl ether. The reaction flask was cooled to 5 °C in an ice bath; then 56.9 g (0.507 mol) of KO^{t}Bu was slowly added. After the addition of KO^{t}Bu was completed, the ice bath was removed and the reaction mixture allowed to warm to RT (~2 h). The resultant bright red solution was recooled to 5 °C before the addition of 64.5 g (0.389 mol) of hexafluoroacetone (the temperature of the reaction mixture was maintained below 10 °C during the addition of the ketone). Following the addition of the ketone, the reaction mixture was stirred for 8 h at RT. Approximately 300 ml of tetraglyme was then added to the reaction mixture, and most of the Et_2O was removed by distillation. Flash distillation of the remaining residue gave ~250 ml of distillate. Fractional distillation of the distillate on a 6 in. Vigreaux column yielded 42.8 g (0.221 mol) of **2**, bp 114–116 °C (57%), n_D^{20} = 1.3294. GLPC purity > 98%. ^{19}F NMR: δ −59.4 (q, $^4J_{FF}$ = 9.0 Hz), −61.8 (qd, $^4J_{FF}$ = 9.0 Hz, $^4J_{HF}$ = 1.5 Hz); ^{1}H NMR: δ 3.9 (s, 3H), 7.1 (m, 1H). IR: 1678 cm^{-1} (C=C). GC–MS, *m*/*z* (relative intensity): 194 (M^+, 100), 175 (98), 163 (70), 125 (82), 69 (72).

3.7. Preparation of E/Z-1-trifluoromethyl-2-methoxystyrene, 3

Similar to Section 3.6, 176.7 g (0.516 mol) of **1**, KO^{t}Bu, and 44.2 g (0.254 mol) of trifluoroacetophenone (added *via* a 120 ml pressure equalized addition funnel) and 1-l (1-liter) diethyl ether were stirred for 3.5 h at RT (after the addition of the ketone). Then, 400 ml of H_2O was added to the reaction mixture resulting in two layers. The ether layer was separated, dried over anhydrous $CaCl_2$, and ether removed by distillation. Flash distillation of the residue gave a mixture of ether, *t*-butanol, and **3**. Distillation of this mixture on a 6 in. Vigruex column gave 45.9 g (0.227 mol) of **3**, bp 79 °C (1 mm), (89%), n_D^{20} = 1.4807. Reported for **3**: bp 78–79 °C (3 mm) [17]. GLPC purity > 99%. ^{19}F NMR: δ −57.6 (s, 3F), −61.1 (d, $^4J_{HF}$ = 2 Hz, 3F); ^{1}H NMR: δ 3.3 (s, 3H), 3.4 (s, 3H), 6.3 (s, 1H), 7.2 (m, 5H), 6.8 (q, $^4J_{HF}$ = 2 Hz, 1H). IR: 1660 cm^{-1} (C=C). GC–MS, *m*/*z* (relative intensity): 202 (M^+, 5), 171 ($C_9H_6F_3$, 20), 106 (90), 77 (100), 69 (6), 50 (50).

3.8. Preparation of 1-methoxy-2-chlorodifluoromethyl-3,3-difluoro-3-chloropropene, 4

Similar to Section 3.7, 173.9 g (0.507 mol) of **1**, 1200 ml Et_2O, 56.3 g (0.502 mol) of KO^{t}Bu and 100 g (0.502 mol) of sym-dichlorotetrafluoroacetone were stirred at RT for 2 h before the addition of 250 ml of tetraglyme. The ether was removed by distillation, and the residual liquid was flashed distilled to give a mixture of *t*-butanol, tetraglyme and **4**. The tetraglyme was removed by extraction with 100 ml H_2O followed by extraction with 75 ml Et_2O. The ether extract was washed with 50 ml H_2O and dried over anhydrous $CaCl_2$. The dry ether extract was distilled on a 6 in. Vigreux column to afford 35.8 g (0.158 mole) of **4**: bp 52–56 °C (2 mm), (31%), n_D^{20} = 1.4089. GLPC purity > 97%. ^{19}F NMR: δ −46.8 (t, $^4J_{FF}$ = 9.0 Hz, 2F), −47.5 (t, $^4J_{FF}$ = 9.0 Hz, 2F); ^{1}H NMR: 3.97 (s, 3H), 6.95 (m, 1H). IR: 1668 cm^{-1} (C=C). GC–MS, *m*/*z* (relative intensity): 230 (M^+, 1.2), 228 (M^+, 4.5), 226 (6.2), 193 (34), 191 (100), 160 (21), 158 (59), 155 (10), 153 (28), 87 (11), 85 (38).

3.9. Preparation of E/Z-1-methoxy-2-trifluoromethylhex-1-ene, 5

Similar to Section 3.7, 171.4 g (0.50 mol) of **1**, 300 ml anhydrous Et_2O, 56.0 g (0.50 mol) KO^{t}Bu and 39.0 g (0.253 mol) of *n*-butyltrifluoromethylketone were stirred at RT for 2 h. Then 250 ml H_2O was added, which resulted in two layers. The ether layer was separated and dried over anhydrous $CaCl_2$. The ether was removed by distillation, and the residual residue flash distilled to yield a mixture of *t*-butanol, Et_2O and **5**. Distillation of this mixture through a 6 in. Vigreux column afforded 22.0 g (0.12 mol) of **5**, bp 106–108 °C (129 mm), (48%), n_D^{20} = 1.3797. GLPC purity > 95%. ^{19}F NMR: δ −60.3 (s, 3F), −64.7 (d, $^4J_{HF}$, 2 Hz, 3F); ^{1}H NMR: δ 0.8–2.3 (m, 9H), 3.60 (s, 3H), 3.65 (s, 3H), 6.10 (s, 1H), 6.62 (q, $^4J_{HF}$ = 2 Hz, 1H). IR: 1681 cm^{-1} (C=C). GC–MS, *m*/*z* (relative intensity): 182 (M^+, 11), 163 (100), 106 (22), 69 (8), 57 (9), 43 (13).

3.10. Preparation of 1-methoxy-2-pentafluoroethyl-3,3,4,4,4-pentafluoro-but-1-ene, 6

Similar to Section 3.6, 119.9 g (0.350 mol) of **1**, 500 ml anhydrous Et_2O, 38.7 g (0.345 mol) KO^{t}Bu and 63.1 g (0.24 mol) of perfluoropentan-3-one (condensed into the reaction mixture) were stirred for 10 h at RT. Then, 150 ml H_2O was added to the mixture, which resulted in two layers. The ether layer was separated and dried over anhydrous $CaCl_2$. The ether was evaporated, and the residual liquid flash distilled to yield a mixture of Et_2O, *t*-butanol and **6**. The crude distillate was distilled on a 6 in. Vigreux column to afford 45.0 g (0.152 mol) of **6**, bp 87–89 °C (133 mm), (64%), n_D^{20} = 1.3216. GLPC purity > 99%. ^{19}F NMR: δ −85.6 (m, 6F), −108.5 (m, 2F), −110.8 (m, 2F); ^{1}H NMR: δ 3.9 (s, 3H), 7.05 (m, 1H). IR: 1660 cm^{-1} (C=C). GC–MS, *m*/*z* (relative intensity): 294 (M^+, 14), 276 (27), 225 (100), 175 (28), 119 (11), 68 (36).

3.11. Preparation of 1-methoxy-2-heptafluoropropyl-3,3,4,4,5,5,5-heptafluoropent-1-ene, 7

Similar to Section 3.6, 119.9 g (0.35 mol) **1**, 600 ml anhydrous Et_2O, 38.8 g (0.35 mol) KO^{t}Bu, and 85.5 g (0.234 mol) of perfluoroheptan-4-one (added *via* 120 ml pressure equalized addition funnel) were stirred for 8 h at RT. Then, 150 ml H_2O was added to the reaction mixture, which resulted in two layers. The ether layer was separated and dried over anhydrous $CaCl_2$. The ether was evaporated, and the residual liquid was flash distilled to yield a mixture of *t*-butanol, Et_2O and **7**. Distillation of this mixture on a 6 in. Vigreux column afforded 55.3 g (0.140 mole) of **7**, bp 108–110 °C (125 mm), (60%), n_D^{20} = 1.3204. GLPC purity: 95%. ^{19}F NMR: δ −80.6 (m, 6F), −104.6 (m, 2F), −106.7 (m, 2F), −125.7 (m, 4F). IR: 1660 cm^{-1} (C=C). GC–MS, *m*/*z* (relative intensity): 394 (M^+, 7), 375 (51), 275 (67), 241 (38), 169 (9), 119 (25), 69 (100).

3.12. Hydrolysis of vinyl ethers

3.12.1. Preparation of 2-trifluoromethyl-3,3,3-trifluoropropanal, 8

A 50 ml flask, equipped with a 6 in. Vigerux column topped with a distillation head, thermometer, vacuum takeoff, 20 ml receiver and a

magnetic stir bar, was charged with 25 ml conc. H_2SO_4 and frozen with a liquid N_2 bath. Then, 20.7 g (0.107 mol) of **2** was added. The pressure of the system was reduced to ~150 mm, and the receiver was cooled with a liquid N_2 bath. The frozen reaction mixture was warmed to 75 °C, and the product distilled as formed, to yield 16.7 g (0.093 mol), 87% of **8**, bp 43–45 °C, $n^{20}{}_D < 1.3000$. Reported for **8**, bp 46 °C [12]. IR: 1765 cm^{-1} (CHO), reported 1750 cm^{-1} [26]. ^{19}F NMR: δ −64.2 (dd, $^3J_{HF}$ = 9.0 Hz, $^4J_{HF}$ = 2.0 Hz); ^1H NMR: δ 4.00 (heptd, $^3J_{HF}$ = 9.0 Hz, $^3J_{HH}$ = 1.5 Hz, 1H), 9.65 (m, 1H). GC–MS, *m/z* (relative intensity): 180 (M^+, 27), 161 ($C_4H_2F_5O^+$, 91), 160 ($C_4HF_5O^+$, 89), 132 ($C_3HF_5^+$, 53), 113 ($C_3HF_4^+$, 100), 112 ($C_3F_4^+$, 83), 69 (CF_3^+, 87), 29 (77).

3.12.2. Preparation of 2-trifluoromethylphenylacetaldehyde, 9

The procedure of Aaron et al. [17] was employed for the hydrolysis of **3**. A 250 ml 1-necked flask, equipped with a magnetic stir bar and a water cooled reflux condenser topped with a drying tube was charged with 160 g conc. H_2SO_4 and 65 ml of ice water. The acid solution was cooled to RT, then 45.9 g (0.227 mol) of **3** was added. The resultant mixture was heated at 65 °C for 3 h, then poured over 200 g ice, extracted with 250 ml Et_2O, and the ether extract dried over anhydrous $CaCl_2$. The ether was evaporated, and the residual liquid distilled through a 6 in. Vigreux column to give 34.0 g (0.190 mol) of **9**, bp 78–83 °C (15 mm), 83%, $n_D{}^{20}$ = 1.4637. Reported for **9**, bp 90–100 °C (20 mm) [17]. IR: 1743 cm^{-1} (CHO). ^{19}F NMR: δ −65.9 (dd, $^3J_{HF}$ = 8.3 Hz, $^4J_{HF}$ = 2.6 Hz); ^1H NMR: δ 4.3 (qd, $^3J_{HF}$ = 8.3 Hz, $^3J_{HH}$ = 1.4 Hz, 1H), 7.25 (s, 5H), 9.50 (m, 1H). IR: 1743 cm^{-1} (CHO). GC–MS, *m/z* (relative intensity): 188 (M^+, 28), 168 ($C_9H_6F_2O^+$, 27), 160 ($C_8H_7F_3^+$, 24), 140 ($C_8H_6F_2^+$, 65), 109 ($C_3HF_3O^+$, 63), 91 ($C_7H_7^+$), 100), 59 (CF_3^+, 6), 29 (14).

3.12.3. Preparation of 2-trifluoromethylhexanal, 10

Similar to Section 3.12.2, a 100 ml flask, equipped with a magnetic stir bar, water cooled reflux condenser and an ice bath was charged with 40 ml of 70% perchloric acid saturated with Et_2O. To the cooled solution was added 23.6 g (0.130 mol) of **5**. The resultant solution was stirred for 30 min and then poured into 200 ml ice water. The aqueous mixture was extracted with 200 ml Et_2O; the ether extract was washed with 2× 50 ml of ice water, and the ether layer dried over anhydrous $CaCl_2$. The ether was evaporated; distillation of the residual liquid through a 6 in. Vigreux column afforded 10.3 g (0.061 mol), 47% of **10**, bp 108–112 °C, $n_D{}^{20}$ = 1.3784. ^{19}F NMR: δ −68.9 (d, $^3J_{HF}$ = 8.3 Hz); ^1H NMR: δ 0.07–2.10 (m, 9H), 3.05 (m, 1H), 9.43 (m, 1H). IR: 1729 cm^{-1} (CHO). GC–MS, *m/z* (relative intensity): 168 (M^+, 1), 91 ($C_3H_1F_2O^+$, 16), 69 (CF_3^+, 30), 57 ($C_4H_9^+$, 69), 56 ($C_4H_8^+$, 85), 55 ($C_4H_7^+$, 35), 43 ($C_3H_7^+$, 48), 42 ($C_3H_6^+$, 66), 41 ($C_3H_5^+$, 100), 29 (77).

3.12.4. Preparation of 2-pentafluoroethyl-3,3,4,4,4-pentafluorobutanal,11

Similar to Section 3.12.1, 31.5 g (0.107 mol) of **6**, 70 ml conc. H_2SO_4, were heated to 110 °C and the pressure reduced to 20 mm. The product, **11**, distilled into the 50 ml receiver at 55–58 °C. Redistillation of the crude product through a 6 in. Vigreux column afforded 26.5 g (0.095 mol) of **11**, bp 73–74 °C, 88%, $n_D{}^{20}$ = 1.3018. ^{19}F NMR δ −84.65 (m, 6F), the nonequivalent groups appeared as an AB pattern at −112.40 and −115.85 respectively ($J_{Fa,Fb}$ = 302.6 Hz); ^1H NMR: δ 3.83 (m, 1H), 9.60 (m, 1H). IR: 1750 cm^{-1} (CHO). GC–MS, *m/z* (relative intensity): M^+ not observed, 261 (M−F, $C_6H_2F_9O^+$, 18), 260 ($C_6HF_9O^+$, 15), 191 ($C_5HF_6O^+$, 24), 144 ($C_4HF_5^+$, 35), 119 ($C_2F_5^+$, 20), 69 (CF_3^+, 60), 29 (100).

3.12.5. Preparation of 2-heptafluoropropyl-3,3,4,4,5,5,5-heptafluoropentanal, 12

Similar to Section 3.12.4, 12.0 g (0.03 mol) of **7** and 25 ml conc. H_2SO_4 were heated to 85 °C while the pressure was reduced to 65 mm (the receiver was cooled with dry ice/isopropanol bath). The product was distilled over as formed to yield 9.0 g (0.024 mol) of **12**, bp 45–48 °C (65 mm), 77%, $n_D{}^{20}$ = 1.3000. IR: 1752 cm^{-1} (CHO). ^{19}F NMR: δ −80.67 (m, CF_3, 6F), AB pattern for CF_2 groups attached to the aldehyde group at −108.77 and −111.11 respectively, $J_{Fa,Fb}$ = 293 Hz, −124.67 (m, 4F). GC–MS, *m/z* (relative intensity): M^+ not observed; 361 (M−F, $C_8H_2F_{13}O^+$, 4), 244 ($C_6HF_9^+$, 10) 242 ($C_6H_2F_8O^+$, 16), 194 ($C_5HF_7^+$, 18), 119 ($C_2F_5^+$, 10), CF_3^+, 56), 29 (100).

3.12.6. Preparation of 3,3,3-trifluoropropanal, 13

Similar to Section 3.12.1, 45.0 g of 57% HI, 33.2 g (0.263 mol) of *E*/*Z*-1-methoxy-3,3,3-trifluoropropene were heated to 90 °C. The 50 ml receiver was cooled with a dry ice/isopropanol bath to collect the CH_3I and **13** as they formed. Distillation of the crude material through a 6 in. Vigreux column afforded 10.0 g (0.090 mole) of **13**, bp 56 °C, 34%. The product was ~75% pure by GLPC. The product was further purified by preparative GLPC, bp 56 °C, $n_D{}^{20}$ = 1.3187. Reported for **13**, bp 57 °C, $n_D{}^{20}$ = 1.3168 [27] and bp 56.2, $n_D{}^{25}$ = 1.3190 [28]. IR: 1739 cm^{-1} (CHO). ^{19}F NMR: δ −62.89 (td, $^3J_{HF}$ = 10.5 Hz, $^4J_{HF}$ = 2 Hz); ^1H NMR: δ 3.33 (qd, $^3J_{HF}$ = 10.5 Hz, $^3J_{HH}$ = 1.5 Hz, 2H), 9.70 (m, 1H). GC–MS, *m/z* (relative intensity): 112 (M^+, 56), 93 ($C_3H_3F_2O^+$, 17), 83 ($C_2H_2F_3^+$, 15), 69 (CF_3^+, 40), 64 ($C_2H_2F_2^+$, 92) 45 ($C_2H_2F^+$, 19), 29 (100).

3.13. Free-radical halogenation of 2-perfluoroalkylaldehydes

3.13.1. Free-radical chlorination of 8

A 20 ml flask was equipped with a Teflon coated stir bar and a dry ice/isopropanol cooled cold finger condenser attached to a trap cooled with a dry ice/isopropanol bath. The reaction flask was charged with 11.8 g (0.066 mole) of **8**. Chlorine was slowly condensed into the reaction vessel as the mixture was irradiated with an ultraviolet lamp. The addition of chlorine was continued until the uptake of chlorine ceased. The reaction mixture was irradiated an additional 1 h after the uptake of chlorine ceased to insue complete reaction. Distillation of the reaction mixture through a 6 in. Vigreux column afforded 10.5 g (0.049 mol), 74%, of 2-trifluoromethyl-3,3,3-trifluouropropanoylchloride, **14**, bp 54–56 °C, $n_D{}^{20}$ = 1.3075; reported for **14**. bp 54 °C [26]. IR: 1800 cm^{-1} (C(O)Cl). ^{19}F NMR: δ −64.5 (d, $^3J_{HF}$ = 7.5 Hz); ^1H NMR: δ 4.40 (heptet, $^3J_{HF}$ = 7.0 Hz). GC–MS, *m/z* (relative intensity): M^+ not observed, 179 (M^+−Cl, 28), 160 ($C_4HF_5O^+$, 62), 69, (CF_3^+, 100).

3.13.2. Free-radical bromination of 8

Similar to Section 3.13.1, 8.5 g (0.047 mol) of **8** and 8.0 g (0.05 mol) of bromine were irradiated with an ultraviolet lamp for 3 h. Hydrogen bromide was collected in the cold trap as it was formed during the irradiation. Distillation of the reaction mixture through a 6 in. Vigreux column afforded 7.0 g (0.027 mol), 57% of 2-trifluoromethyl-3,3,3-trifluouropropanoyl bromide, **15**, bp 64–66 °C, $n_D{}^{20}$ = 1.3299. Reported for **15**. bp 67 °C [26]. IR: 1820 cm^{-1} (C(O)Br). ^{19}F NMR: δ −64.5 (d, $^3J_{HF}$ = 7.0 Hz); ^1H NMR: δ 4.6 (heptet, $^3J_{HF}$ = 7.0 Hz). GC–MS, *m/z* (relative intensity): M^+ not observed, 179 (M−Br, 26), 160 ($C_4HF_5O^+$, 55), 69 (CF_3^+, 100).

3.13.3. Free-radical chlorination of 9

Similar to Section 3.13.2, 12.1 g (0.064 mol) of **9**, and chlorine were irradiated with an ultraviolet lamp. The chlorination was an exothermic reaction and HCl was evolved from the reaction as formed. The addition of chlorine was discontinued after chlorine was no longer reacting and its yellow-green color persisted. The mixture was then irradiated an additional 1 h to insue complete reaction. A more definitive test was to analyze an aliquot of the mixture by ^1H NMR. The ^1H NMR spectrum should be absent a resonance due to the formyl hydrogen, and the α-hydrogen should be a quartet rather than a doublet of quartets. Distillation of the

reaction mixture through a 6 in. Vigreux column afforded 10.0 g (0.045 mole), 70%, of 2-trifluoromethylphenylacetyl chloride, **16**, bp 74–76 °C (7 mm), n_D^{20} = 1.4665. IR: 1792 cm^{-1} (C(O)Cl). ^{19}F NMR: δ −55.2 (d, $^3J_{HF}$ = 8.0 Hz); ^1H NMR: δ 4.70 (q, $^3J_{HF}$ = 8.0 Hz, 1H), 7.3 (s, 5H). GC–MS, *m*/*z* (relative intensity): 224 (M^+, 6), 222 (M^+, 19), 195 ($C_8H_5{}^{37}ClF_3{}^+$, 7.3), 193 ($C_8H_5{}^{35}ClF_3{}^+$, 100), 159 ($C_8H_6F_3{}^+$, 24), 110 ($C_3HF_3O^+$, 72), 69 ($CF_3{}^+$, 7).

3.13.4. Free-radical chlorination of 10

Similar to Section 3.13.1, chlorination of **10**, gave a mixture of products. ^1H NMR analysis of the reaction mixture showed complete loss of the resonance for the formyl hydrogen. The α-hydrogen changed from a doublet of quartets to a simple doublet. However, the butyl group changed and it was assumed that the chlorine radicals were also attacking the methylene hydrogens of the *n*-butyl groups.

3.13.5. Free-radical chlorination of 11

Similar to Section 3.13.1, 8.3 g (0.030 mol) of **11**, and chlorine 3.5 g (0.05 mol) were irradiated with an ultraviolet lamp for 3 h. Distillation of the reaction mixture through a 6 in. Vigreux column afforded 7.4 g (0.024 mol), 79% of 2-pentafluoroethyl-3,3,4,4,4-pentafluorobutanoyl chloride, **17**, bp 82–83 °C, n_D^{20} = 1.3026. IR: 1800 cm^{-1} (C(O)Cl). ^{19}F NMR: δ −83.5 (m, 6F), non-equivalent CF_2 groups (AB pattern) at δ −113.6 and −115.3 respectively, J_{FaFb} = 286.8 Hz. ^1H NMR: δ 4.38 (m, 1H). GC–MS, *m*/*z* (relative intensity): M^+ not observed, 279 (M^+−Cl, 4), 260 ($C_6HF_9O^+$, 39), 210 ($C_5HF_7O^+$, 100), 159 ($C_4F_5O^+$, 64), 119 ($C_2F_5{}^+$, 34), 69 ($CF_3{}^+$, 88).

3.13.6. Free-radical chlorination of 12

Similar to Section 3.13.1, 3.5 g (0.009 mol) of **12** and chlorine were irradiated with an ultraviolet lamp for 4 h. Distillation of the reaction mixture through a 6 in. Vigreux column afforded 2.6 g (0.006 mol), 67% of 2-heptafluoropropyl-3,3,4,4,5,5,5-heptafluoropentanoyl chloride, **18**, bp 70–72 °C (85 mm), n_D^{20} = 1.3081. IR: 1820 cm^{-1} (C(O)Cl). ^{19}F NMR: δ −80.7 (m, 6F), non-equivalent CF_2 groups (AB pattern) at −108 and −111 respectively, $J_{Fa,Fb}$ = 290 Hz, −124.0 (m, 4F); ^1H NMR: 4.60 (m, 1H). GC–MS, *m*/*z* (relative intensity): M^+ not observed, 379 (M^+−Cl, 0.7), 360 ($C_8HF_{13}O^+$, 44), 260 ($C_6HF_9O^+$, 100), 169 ($C_3F_7{}^+$, 62), 119 ($C_2F_5{}^+$, 50), 69 ($CF_3{}^+$, 54).

3.13.7. Free-radical chlorination of 13

Similar to Section 3.13.1, 3.5 g (0.031 mol) of **13** and chlorine were irradiated with an ultraviolet lamp for 4 h. Distillation of the reaction mixture through a 6 in. Vigreux column afforded 1.8 g (0.012 mol) of 3,3,3-trifluoropropanoyl chloride, **19**, 39%, bp 68–69 °C, n_D^{20} = 1.3392. Reported for **19**, bp 70 °C, n_D^{29} = 1.3382 [29]. ^{19}FNMR: δ −64.91 (t, $^3J_{HF}$ = 9.0 Hz); ^1H NMR: δ 3.78 (q, $^3J_{HF}$ = 9.0 Hz). IR: 1820 cm^{-1} (C(O)Cl). GC–MS, *m*/*z* (relative intensity): 148 ($C_3H_2{}^{37}ClF_3O^+$, 1.7), 147 ($C_3H^{37}ClF_3O^+$, 2.2) 146 ($C_3H_2{}^{35}ClF_3O^+$, 5.6), 145 ($C_3H^{35}ClF_3O^+$, 6.1), 111 ($C_3H_2F_3O^+$, 100), 92 ($C_3H_2F_2O^+$, 88) 83 ($C_2H_2F_3{}^+$, 29), 69 ($CF_3{}^+$, 78), 63 ($C_2HF_2{}^+$, 58).

3.13.8. Free-radical chlorination of 22

Similar to Section 3.13.1, 8.1 g (0.038 mol) of **22** and chlorine were irradiated with an ultraviolet lamp for 8 h. Distillation of the reaction mixture through a 6 in. Vigreux column afforded 3.1 g (0.014 mol) of 2,2-dichlorohexafluoropropane, **20**, 37%, bp 32–34 °C [30]. A pure sample of **20** and an authentic sample supplied by Naae were identical.

3.13.9. Free-radical chlorination of diphenylacetalkehyde

Similar to Section 3.13.1, 24.6 g (0.125 mol) of diphenylacetaldehyde and chlorine were irradiated with an ultraviolet lamp until the chlorine color persisted. Distillation of the reaction mixture through a 6 in. Vigreux column afforded 21.3 g (0.092 mol) of **21**, bp 145–150 °C (1 mm), 73%, n_D^{20} = 1.5960. Reported for **21**, bp 98 °C (0.1 mm), n_D^{20} = 1.5969 [31]. IR: 1739 cm^{-1} (CHO). Reported for **21**, 1737 cm^{-1} [31]. ^1H NMR: δ 7.106 (m, 10H), 9.47 (s, 1H).

3.14. Halogenation of 2-perfluoroalkylaldehydes in acetic acid

3.14.1. Preparation of 2-chloro-2-trifluoromethyl-3,3,3-trifluoropropanal, 22

A 100 ml flask was equipped with a Teflon coated stir bar and a dry ice/isopropanol cooled cold finger condenser attached to a trap coated with a dry ice/propanol bath was charged with 11.0 g (0.061 mol) of **8** and 40 ml of glacial acetic acid. An excess amount of chlorine was slowly condensed into the reaction mixture. The resultant mixture was stirred for 5 h at RT. Distillation of the reaction mixture through a 6 in. Vigreux column afforded 10.4 g (0.048 mol) of **22**, 79%, bp 50–52 °C, n_D^{20} = 1.3119. Reported for **22**, bp 52–54 °C, n_D^{20} = 1.3115 [26]. IR: 1780 cm^{-1} (CHO). Reported: 1760 cm^{-1} [26]. ^{19}F NMR: δ −69.5 (d, $^4J_{HF}$ = 2 Hz); ^1H NMR: δ 9.40 (hept, $^4J_{HF}$ = 2 Hz). GC–MS, *m*/*z* (relative intensity): 216 (M^+, 0.15), 214 (M^+, 0.5), 168 ($C_3{}^{37}ClF_5{}^+$, 33), 166 ($C_3{}^{35}ClF_5{}^+$, 100), 159 ($C_4F_5O^+$, 17), 149 ($C_3{}^{37}ClF_4{}^+$). 30). 147 ($C_3{}^{35}ClF_4{}^+$, 90), 131 ($C_3F_5{}^+$, 36), 118 ($C_2{}^{37}ClF_3{}^+$, 10), 116 ($C_2{}^{35}ClF_3{}^+$, 33), 69 ($CF_3{}^+$, 41), 29 (36).

3.14.2. Preparation of 2-bromo-2-trifluoromethyl-3,3,3-trifluoropropanal, 23

Similar to Section 3.14.1, 11.9 g (0.066 mol) of **8** and a freshly prepared solution of 0.1 mol of BrCl in 40 ml glacial acetic acid was stirred for 1.5 h at RT. Flash distillation of the reaction mixture removed the excess BrCl and the product from the glacial acetic acid. Distillation of the crude product through a 6 in. Vigreux column afforded 8.3 g (0.032 mol) of **23**, 48%, bp 70–71 °C, n_D^{20} = 1.3319. Reported for **23**, bp 73–74 °C [26]. IR: 1780 cm^{-1} (CHO). ^{19}F NMR: δ −67.1 (d, $^4J_{HF}$ = 2 Hz), ^1H NMR: δ 9.35 (hept, $^4J_{HF}$ = 2 Hz). GC–MS, *m*/*z* (relative intensity): 260 (M^+, 1.5), 258 (M^+, 1.5), 231 ($C_3{}^{81}BrF_6{}^+$. 31.3), 229 ($C_3{}^{79}BrF_6{}^+$, 31.8), 212 ($C_3{}^{81}BrF_5{}^+$, 99.5), 210 ($C_3{}^{79}BrF_5{}^+$, 100), 193 ($C_3{}^{81}BrF_4{}^+$, 71.3), 191 ($C_3{}^{79}BrF_4{}^+$, 72.3), 179 ($C_4HF_6O^+$, 34), 160 ($C_4HF_5O^+$, 41), 159 ($C_4F_5O^+$, 68), 132 ($C_3HF_5{}^+$, 64), 113 ($C_3HF_4{}^+$, 43), 112 ($C_3F_4{}^+$, 48), 69 ($CF_3{}^+$, 74), 29 (59).

3.14.3. Preparation of 2-chloro-2-trifluoromethylphenylacetaldehyde, 24

Similar to Section 3.14.1, 12.5 g (0.066 mol) of **9**, 20 ml glacial acetic acid and 8.5 g (0.12 mol) chlorine were stirred for 2 h at RT. The reaction mixture was combined with 150 ml H_2O, and the aqueous solution was extracted with 200 ml H_2O and dried over anhydrous $CaCl_2$). The ether extract was washed with 2× 50 ml H_2O and dried over anhydrous $CaCl_2$. The ether was evaporated, and the residual liquid distilled through a 6 in. Vigreux column to afford 11.0 g (0.049 mol) of **24**, 74%, bp 82–85 °C (11 mm), n_D^{20} = 1.4715. IR: 1748 cm^{-1} (CHO). ^{19}F NMR: δ −71.2 (d, $^4J_{HF}$ = 2 Hz); ^1H NMR δ −7.30 (s, 5H), 9.15 (q, $^4J_{HF}$ = 2 Hz, 1H). GC–MS, *m*/*z* (relative intensity): 224 (M^+, 2.6), 222 (M^+, 8.4), 196 ($C_8H_6{}^{37}ClF_3{}^+$, 23.5), 195 ($C_8H_5{}^{37}ClF_3{}^+$, 16.3), 194 ($C_8H_6{}^{35}ClF_3{}^+$, 7.2), 193 ($C_8H_5{}^{35}ClF_3{}^+$, 36.6), 176 ($C_8H_5{}^{37}ClF_2{}^+$, 17.0), 174 ($C_8H_5{}^{35}ClF_2{}^+$, 52.3), 158 ($C_8H_5F_3{}^+$, 100), 139 ($C_8H_5F_2{}^+$, 49.0), 109 ($C_3F_3O^+$, 62), 89 ($C_7H_5{}^+$, 58), 77 ($C_6H_5{}^+$, 16), 69 ($CF_3{}^+$, 10), 29 (32).

3.14.4. Preparation of 2-chloro-2-pentafluoroethyl-3,3,4,4,4-pentafluorobutanal, 25

Similar to Section 3.14.1, 4.7 g (0.017 mol) **11**, 20 ml glacial acetic acid and excess chlorine were stirred for 10 h at RT. The reaction mixture was combined with 20 ml H_2O, and the aqueous solution extracted with 40 ml Et_2O. The ether extract was washed with 20 ml H_2O and dried over anhydrous $CaCl_2$. The ether was

removed by distillation, and the residual liquid was distilled through a 6 in. Vigreux column from 20 ml conc. H_2SO_4 to yield 2.7 g (0.009 mol) of **25**, 51%, bp 92–95 °C, n_D^{20} = 1.3144. IR: 1768 cm^{-1} (CHO). ^{19}F NMR: δ −78.6 (m, 6F), non-equivalent CF_2 groups (AB pattern) at −110.6 and −112.8 respectively, ($J_{Fa,Fb}$ = 284.7 Hz); ^1H NMR: δ 9.57 (m, 1H). GC–MS, *m/z* (relative intensity): M^+ not observed, 268 ($C_5{}^{37}ClF_9{}^+$, 3.8), 266, ($C_5{}^{35}ClF_9{}^+$, 13.5), 199 ($C_4{}^{37}ClF_6{}^+$, 12.2), 197 ($C_4{}^{35}ClF_6{}^+$, 37.8), 149 ($C_3{}^{37}ClF_4{}^+$, 10.9), 147 ($C_3{}^{35}ClF_4{}^+$, 37.2), 119 ($C_2F_5{}^+$, 40), 69 ($CF_3{}^+$, 71), 29 (100).

3.14.5. Preparation of 2-chloro-2-heptafluoropropyl-3,3,4,4,5,5,5-heptafluoropentanal, 26

Similar to Section 3.14.1, 4.1 g (0.011 mol) of **12**, 15 ml glacial acetic acid, and excess chlorine were stirred for 10 h at RT. The reaction mixture was combined with 25 ml conc. H_2SO_4 and flash distilled. The flash distillate was combined with 5 ml conc. H_2SO_4 and distilled through a 6 in. Vigreux column to afford 3.6 g (0.009 mol), 80%, bp 75–78 °C (85 mm), n_D^{20} = 1.3118. IR 1770 cm^{-1} (CHO). ^{19}F NMR: δ −81.1 (m, 6F), −107.0 (m, 4F), and the non-equivalent CF_2 groups (AB pattern) at −118.81 and −122.00 respectively ($J_{Fa,Fb}$ = 287.6 Hz). GC–MS, *m/z* (relative intensity): M^+ not observed, 368 ($C_7{}^{37}ClF_{13}{}^+$, 0.3), 366 ($C_7{}^{35}ClF_{13}{}^+$, 1.1), 249 ($C_5{}^{37}ClF_8{}^+$, 4.3), 247 ($C_5{}^{35}ClF_8{}^+$, 12.9), 169 ($C_3F_7{}^+$, 60), 119 ($C_2F_5{}^+$, 21), 69 ($CF_3{}^+$, 100), 29 (50).

3.15. Preparation of polyfluorinated carboxylic acids

3.15.1. Preparation of 2-trifluoromethyl-3,3,3-trifluoropropanioc acid, 27

A 100 ml flask equipped with a Teflon coated stir bar, water cooled reflex condenser and a septum covered opening was charged with 40.9 g (0.189 mol) of **14** and 50 ml tetrahydrofuran. The reaction mixture was cooled to 10 °C with an ice bath before the addition of 3 ml H_2O was syringed into the mixture to ensure complete reaction. The resultant mixture was stirred 4 h at RT. The reaction mixture was combined with an equal volume of conc. H_2SO_4. Distillation of the mixture through a 6 in. Vigreux column afforded 33.4 g (0.170 mol) of **27**, 90%, mp 50 °C. Reported for **27**, mp 49–50 °C [14]. IR: 1753 cm^{-1}. ^{19}F NMR: δ −65.2 (d, $^3J_{HF}$ = 7.5 Hz), ^1H NMR: δ 3.95 (heptet, $^3J_{HF}$ = 7.5 Hz, 1H), 10.55 (s, 1H). GC–MS, *m/z* (relative intensity): M^+, not observed, 132 ($C_3HF_5{}^+$, 65), 113 ($C_3HF_4{}^+$, 72), 94 ($C_3HF_3{}^+$, 23.0), 82 ($C_2HF_3{}^+$, 38), 69 ($CF_3{}^+$, 62), 63 ($C_2HF_2{}^+$, 17), 44 (100). **27** was also prepared in 40% isolated yield by oxidation of **8** *via* the procedure of Aaron [17].

3.15.2. Preparation of 2-pentafluoroethyl-3,3,3-pentafluorobutanoic acid, 28

Similar to Section 3.15.1, 2.9 g (0.013 mol) of **17**, 15 ml THF, and 5 ml H_2O gave an exothermic reaction. The resultant mixture was stirred 1 h at RT, before the addition of 35 ml conc. H_2SO_4. Distillation of the reaction mixture afforded 1.6 g (0.008 mol) of **28**, 60%, bp 133 °C (micro), n_D^{20} = 1.3034, IR: 1760 cm^{-1}. ^{19}F NMR: δ −84.01 (m, 6F) and the non-equivalent CF_2 groups (AB pattern) at −113.72 and −115.76, respectively, $J_{Fa,Fb}$ = 287.9 Hz; ^1H NMR: δ 4.00 (m, 1H), 10.37 (s, 1H). GC–MS, *m/z* (relative intensity): M^+, not observed, 232 ($C_5HF_9{}^+$, 0.3), 213 ($C_5HF_8{}^+$, 22), 163 ($C_4HF_6{}^+$, 96), 119 ($C_2F_5{}^+$, 94), 113 ($C_3HF_4{}^+$, 8), 69 ($CF_3{}^+$, 55), 44 (100).

3.15.3. Preparation of 2-heptafluoropropyl-3,3,4,4,5,5,5-heptafluoropentanoic acid, 29

Similar to Section 3.15.1, a 20 ml flask equipped with a Teflon coated stir bar, distillation head, 150 °C immersion thermometer, vacuum take off, and a 10 ml receiving flask was charged with 2.6 g (0.006 mol) of **18**, 5 ml THF and 1 ml H_2O, which resulted in an exothermic reaction. The resultant mixture was stirred for 1 h before the addition of 10 ml conc. H_2SO_4. Distillation of the acid mixture afforded 1.7 g (0.0004 mol), 67% of **29**, mp 60–61 °C. The product crystallized throughout the distillation apparatus and required the use of a 150 W sunlamp to melt the product for collection. IR: (Nujol) 1735 cm^{-1}. ^{19}F NMR: δ −80.6 (m, 6F), the non-equivalent CF_2 groups at −109.29 and −111.10, respectively, $J_{Fa,Fb}$ = 282.6 Hz, −124.6 (m, 4F); ^1H NMR: δ 4.53 (m, 1H), 8.67 (m, 1H). GC–MS, *m/z* (relative intensity): M^+, not observed, 313 ($C_7HF_{12}{}^+$, 4.2), 213 ($C_5HF_8{}^+$, 39), 169 ($C_3F_7{}^+$, 74), 163 ($C_4HF_6{}^+$, 27), 119 ($C_2F_5{}^+$, 22), 113 ($C_3HF_4{}^+$, 35), 69 ($CF_3{}^+$, 100), 44 (54).

4. Conclusions

2-Hydroaldehydes, containing one or more α-perfluoroalkyl groups are readily prepared *via* conversion of perfluoroalkyl ketones to the corresponding vinyl ethers, which, on acid hydrolysis, give the titled 2-hydroaldehydes. The 2-hydroaldehydes can be chemoselectively converted to the corresponding α-hydroacyl halides *via* free-radical halogenation. The perfluoroalkyl group deactivates halogenation at the 2-hydro site, and halogenation occurs exclusively at the formyl hydrogen site. Halogenation of the 2-hydroaldehyes with halogen in glacial acetic acid chemoselectively occurs at the 2-hydro site to give exclusively the corresponding 2-haloaldehydes. Hydrolysis of the 2-hydroperfluoroacyl halides gives the corresponding 2-hydro-branched perfluorocarboxylic acids, potential perfluoro ketene precursors.

Acknowledgments

The authors thank Dr. D. Naae for the authentic sample of $CF_3CCl_2CF_3$, and DAW thanks the University of Iowa for financial support.

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