

A novel synthesis of per(poly)fluoroalkyl aldehydes

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(Received February 1, 1992; accepted July 15, 1992)

Abstract

A novel synthesis of per(poly)fluoroalkyl aldehydes in high yield by the reaction of per(poly)fluoroalkyl iodides or bromides with dimethylformamide initiated by a PbBr_2 (catalyst)/Al bimetal redox system is described.

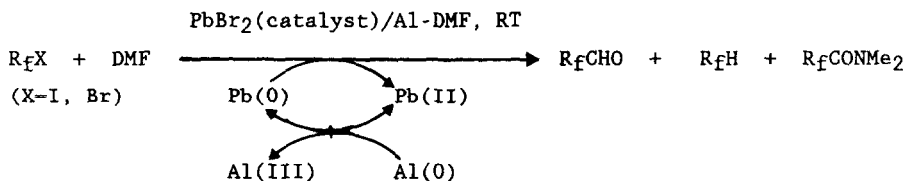
Introduction

Per(poly)fluoroalkyl aldehydes and their monohydrates are useful intermediates in the synthesis of resins, polymers, dyes, medicinals and insecticides. Several preparative methods are now available [1–4]. For example, per(poly)fluoroalkyl aldehydes may be prepared by reduction of the corresponding acids, acyl chlorides or nitriles and by oxidation of the corresponding 1,1-dihydroper(poly)fluoro alcohols. However, these methods are rather tedious, the yields were generally low and a substantial amount of by-products were also obtained. Recently, Commeyras *et al.* prepared perfluoroalkyl aldehydes by reaction of perfluoroalkylzinc iodides with *N,N*-dimethyl formamide (DMF) in the presence of azobisisobutyronitrile (AIBN) [5]. In our continuing work on the application of redox systems in organofluorine chemistry, we have found that through the use of PbBr_2 (catalyst)/Al, a redox system first introduced by Torii in the Barbier-type allylation of aldehydes [6], per(poly)fluoroalkyl aldehydes can be readily prepared not only from per(poly)fluoroalkyl iodides but also from per(poly)fluoroalkyl bromides under mild conditions and in high yield.

Results and discussion

Per(poly)fluoroalkyl halides, R_fX ($\text{X}=\text{I}, \text{Br}$), reacted with excess DMF in the presence of aluminum powder (1.2–1.5 equiv.) and a catalytic amount of PbBr_2 (0.01–0.05 equiv.) by stirring at room temperature under nitrogen to give the corresponding per(poly)fluoroalkyl aldehydes in high yield. All

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Scheme 1.

TABLE 1

Synthesis of per(poly)fluoroalkyl aldehydes from the corresponding halides with $\text{PbBr}_2(\text{catalyst})/\text{Al}$ in DMF

Substrate (mmol)	PbBr ₂ /Al (mmol)	Reaction conditions		Product	Yield (%)
		Time (h)	Temp. (°C)		
F(CF ₂) ₂ I(20)	0.6:28	4.0	5	F(CF ₂) ₂ CHO	81.2
F(CF ₂) ₄ I(10)	0.2:10	1.5	RT	F(CF ₂) ₄ CHO	89.5
F(CF ₂) ₆ I(10)	0.2:10	1.0	RT	F(CF ₂) ₆ CHO	91.2
F(CF ₂) ₈ I(5)	0.1:5	1.5	RT	F(CF ₂) ₈ CHO	95.0
F(CF ₂) ₁₀ I(5)	0.1:5	2.0	40	F(CF ₂) ₁₀ CHO	91.5
Cl(CF ₂) ₄ I(10)	0.2:10	1.0	RT	Cl(CF ₂) ₄ CHO	91.0
Cl(CF ₂) ₆ I(10)	0.2:10	1.0	RT	Cl(CF ₂) ₆ CHO	95.0
Cl(CF ₂) ₈ I(5)	0.1:5	1.0	40	Cl(CF ₂) ₈ CHO	92.1
I(CF ₂) ₄ I(10)	0.3:20	2.0	RT	OHC(CF ₂) ₄ CHO	90.0
I(CF ₂) ₆ I(5)	0.2:10	1.5	RT	OHC(CF ₂) ₆ CHO	92.0
I(CF ₂) ₈ I(5)	0.2:10	1.5	40	OHC(CF ₂) ₈ CHO	91.5
I(CF ₂) ₄ O(CF ₂) ₂ SO ₂ F (10)[7]	0.2:10	2.0	RT	OHC(CF ₂) ₄ O(CF ₂) ₂ SO ₂ F	85.0
F ₂ C=CFOCF ₂ CF(CF ₃) O(CF ₂) ₂ I(10)[8]	0.2:10	1.5	RT	F ₂ C=CFOCF ₂ CF(CF ₃) O(CF ₂) ₂ CHO	90.0
F(CF ₂) ₂ Br(20)	0.5:20	10.0	5	F(CF ₂) ₂ CH(OH) ₂	89.5
F(CF ₂) ₆ Br(2.5)	0.1:2.0	4.0	RT	F(CF ₂) ₆ CHO	91.5
F(CF ₂) ₈ Br(2.0)	0.1:2.0	4.0	RT	F(CF ₂) ₈ CHO	90.2
F(CF ₂) ₁₀ Br(2.0)	0.1:2.0	3.5	RT	F(CF ₂) ₁₀ CHO	89.0

the aldehydes synthesized in this way were characterized by their MS, IR, ¹⁹F and ¹H NMR spectra. The by-products were R_fH and R_fCONMe₂ in a total amount of less than 5.0% (Scheme 1).

It was observed that lead metal generated *in situ* plays a significant role in such reactions since aluminum powder or lead powder (>99.9% pure) alone were incapable of initiating the reaction.

Such a synthesis is applicable to a wide range of iodo- and bromo-per(poly)fluoroalkanes. Functional groups such as trifluorovinyl ether and sulfonyl fluorides are not affected by the reaction. Perfluoroalkyl bromides usually react under the same conditions as the iodides, except that a longer reaction time is required.

TABLE 2

Effect of solvent on the synthesis of perfluoroalkyl aldehyde from the corresponding iodide with PbBr_2 (catalyst)/Al in DMF

$R_f\text{I}/\text{DMF}$ (mmol/mmol)	Solvent	Time (h)	Products (%) ^a	
			$R_f\text{CHO}$	$R_f\text{H}$
1:5	EtOH	8.0	15.0	85.0
1:5	MeOH	8.0	10.0	90.0
1:4	THF	8.0	85.9	14.1
1:3	DMSO	6.0	88.0	12.0
1:3	CH_3CN	5.0	88.2	11.8
	$\text{DMF}-\text{H}_2\text{O}^b$	1.0	0	100

^aEstimated by ^{19}F NMR spectroscopy.

^b10:1 by volume.

The results of the syntheses of per(poly)fluoroalkyl aldehydes from the corresponding halides with PbBr_2 (catalyst)/Al are listed in Table 1.

With α,ω -dihaloper(poly)fluoroalkanes, the corresponding α,ω -per(poly)fluorodialdehydes are formed. The reactivity of per(poly)fluoroalkyl halides decreases in the order: $R_f\text{I} > R_f\text{Br} \gg R_f\text{Cl}$ [9]. Thus for α,ω -dihaloper(poly)fluoroalkanes with two different halogen atoms, C-formylation takes place preferentially at the more reactive site. ω -Haloper(poly)fluoroalkyl aldehydes can thus be synthesized.

DMF acts both as a reactant and a solvent in such reactions. Other aprotic solvents such as DMSO, THF, etc. can also be used. However, in protic solvents like alcohols, $R_f\text{H}$ becomes the main product. If the reaction system contains 1 equiv. of water, then $R_f\text{H}$ becomes the sole product (as shown in Table 2).

Experimental

All reactions were carried out in DMF under nitrogen. ^1H NMR data (with chemical shifts in ppm from external TMS) and ^{19}F NMR data (with chemical shifts in ppm from external TFA and positive for upfield shifts) were recorded on a Varian EM-360 spectrometer (60 Mz for ^1H and 56.4 Mz for ^{19}F) neat or in $(\text{CD}_3)_2\text{CO}$ for solid products. Infrared spectra were recorded on a Shimadzu IR-400 spectrometer and mass spectra on a Finnigan GC-MS 4021 mass spectrometer. All temperatures were uncorrected and the yields of products are reported as those isolated.

A typical procedure was as follows: $R_f\text{X}$ ($X = \text{I}, \text{Br}$) was added to a stirred suspension of aluminum powder (1.0–1.2 equiv.) and PbBr_2 (0.01–0.05 equiv.) in dry DMF (c. 2 ml solvent/mmol $R_f\text{X}$). The mixture was stirred under nitrogen for 1–4 h. Dilute aqueous HCl was then added and the mixture

TABLE 3

Boiling points, melting points, IR spectra, ^1H and ^{19}F NMR spectra of per(poly)fluoroalkyl aldehydes

Compounds	Boiling points (°C)	^{19}F (ppm)	^1H (ppm)	IR (cm^{-1})	Ref.
$\text{F}(\text{CF}_2)_2\text{CHO}$	6.0	6.1 (3F); 56.0 (2F)	9.32	1775	1a
$\text{F}(\text{CF}_2)_4\text{CHO}$	47.0–49.0	6.7 (3F); 49.7 (2F); 51.3 (4F)	9.31	1772	10
$\text{F}(\text{CF}_2)_6\text{CHO}$	90.0–92.0	6.5 (3F); 46.7 (2F); 48.0 (4F); 48.5 (2F); 51.3 (2F)	9.40	1775	11
$\text{F}(\text{CF}_2)_8\text{CHO}$	125.0–126.5	6.4 (3F); 46.4 (8F); 48.3 (2F); 51.2 (4F)	9.44	1770	11,12
$\text{F}(\text{CF}_2)_{10}\text{CHO}$	70.0–72.0 ^a	5.7 (3F); 46.2 (16F); 51.0 (2F)	9.85 ^b	1770	11
$\text{Cl}(\text{CF}_2)_4\text{CHO}^c$	84.0–85.5	–7.1 (2F); 44.6 (2F); 47.7 (2F); 50.8 (2F)	9.42	1775	
$\text{Cl}(\text{CF}_2)_6\text{CHO}^d$	131.0–132.0	–7.3 (2F); 45.0 (2F); 45.9 (4F); 48.2 (2F); 50.8 (2F)	9.45	1778	
$\text{Cl}(\text{CF}_2)_8\text{CHO}^e$	36.0–38.0 ^a	–7.3 (2F); 44.9 (2F); 45.8 (8F); 48.0 (2F); 50.7 (2F)	9.45	1773	
$\text{OHC}(\text{CF}_2)_4\text{CHO}$	121.5–123.5	48.0 (4F); 50.7 (4F)	9.48	1768	2
$\text{OHC}(\text{CF}_2)_6\text{CHO}^f$	144.0–146.0	46.1 (4F); 48.3 (4F); 50.7 (4F)	9.50	1768	
$\text{OHC}(\text{CF}_2)_8\text{CHO}^g$	68.0–70.5 ^a	46.3 (12F); 50.0 (4F)	9.85 ^b	1769	
$\text{OHC}(\text{CF}_2)_4\text{O}(\text{CF}_2)_2\text{SO}_2\text{F}^h$	156.0–159.0	6.2 (2F); 6.7 (2F); 36.7 (2F);	9.47	1770	

(continued)

TABLE 3 (continued)

Compounds	Boiling points (°C)	¹⁹ F (ppm)	¹ H (ppm)	IR (cm ⁻¹)	Ref.
		46.2 (2F); 49.3 (2F); 50.2 (2F); -121.2 (1F)			
F ₂ C=OCF ₂ CF(CF ₃)O(CF ₂) ₂ CHO ⁱ	130.0-132.0	5.5 (3F); 7.4 (2F); 9.4 (2F); 40.8 (1F); 48.5 (1F); 54.0 (2F); 62.2 (1F); 70.0 (1F)	9.34	1772	

^aMelting points.^bFrom internal TMS.

Products c-i are new compounds and other data are given below:

^cMS: 265 (M⁺ + 1); 267; 245; 247; 235; 237; 229; 216; 131 (100); 100; 85; 87.Elemental analysis: for its monohydrate C₅H₃ClF₈O₂: Calculated: C, 21.26; H, 1.07; F, 53.80%. Found: C, 21.34; H, 1.18; F, 53.61%.^dMS: 365 (M⁺ + 1); 367; 345; 347; 325; 327; 131 (100); 100; 85; 87.Elemental analysis: for its monohydrate C₇H₃ClF₁₂O₂: Calculated: C, 21.98; H, 0.79; F, 59.60%. Found: C, 21.81; H, 0.92; F, 59.49%.^eMS: 465 (M⁺ + 1); 467; 445; 447; 429; 416; 131 (100); 100; 85; 87.Elemental analysis: for its monohydrate C₉H₃ClF₁₆O₂: Calculated: C, 22.40; H, 0.63; F, 62.99%. Found: C, 22.27; H, 0.82; F, 62.86%.^fMS: 359 (M⁺ + 1); 360; 339; 331; 319; 311; 309; 291; 132 (100); 131; 100.Elemental analysis: for its hydrates C₈H₆F₁₂O₄: Calculated: C, 24.38; H, 1.53; F, 57.85%. Found: C, 24.52; H, 1.62; F, 57.61%.^gMS: 459 (M⁺ + 1); 460; 439; 431; 411; 391; 369; 362; 341; 131 (100); 100.Elemental analysis: for its hydrates C₁₀H₆F₁₆O₄: Calculated: C, 24.31; H, 1.22; F, 61.52%. Found: C, 24.12; H, 1.35; F, 61.70%.^hMS: 429 (M⁺ + 1); 409; 380; 229; 183; 131; 119 (100); 100; 51.Elemental analysis: for its monohydrate C₇H₃F₁₃O₅S: Calculated: C, 18.85; H, 0.68; F, 55.36%. Found: C, 18.78; H, 0.72; F, 55.38%.ⁱMS: 393 (M⁺ + 1); 373; 364; 345; 325; 295; 247; 131; 97; 59 (100).Elemental analysis: for its monohydrate C₇H₃F₁₂O₄: Calculated: C, 23.43; H, 0.74; F, 60.23%. Found: C, 23.34; H, 0.82; F, 60.14%.

was extracted four times diethyl ether. The organic layer was combined and dried over MgSO₄ overnight. A crude pale yellow product was obtained after the removal of solvent, which was then dehydrated with P₂O₅ to give the corresponding per(poly)fluoroalkyl aldehydes R_fCHO.

All boiling points, melting points, IR spectra, ¹H and ¹⁹F NMR spectra of the per(poly)fluoroalkyl aldehydes synthesized in this way are described in Table 3.

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