

## A novel synthesis of per(poly)fluoroalkyl aldehydes

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### 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  $\text{PbBr}_2$ (catalyst)/Al bimetal redox system is described.

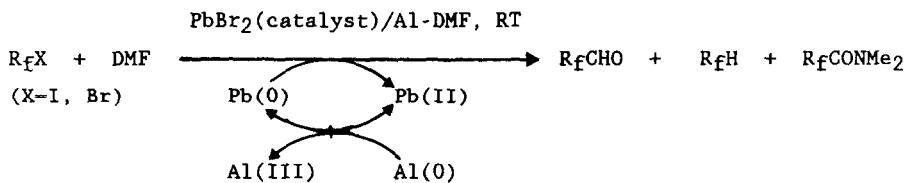
### Introduction

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  $\text{PbBr}_2$ (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,  $\text{R}_f\text{X}$  ( $\text{X}=\text{I}, \text{Br}$ ), reacted with excess DMF in the presence of aluminum powder (1.2–1.5 equiv.) and a catalytic amount of  $\text{PbBr}_2$  (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)	$\text{PbBr}_2/\text{Al}$ (mmol)	Reaction conditions		Product	Yield (%)
		Time (h)	Temp. (°C)		
$\text{F}(\text{CF}_2)_2\text{I}(20)$	0.6:28	4.0	5	$\text{F}(\text{CF}_2)_2\text{CHO}$	81.2
$\text{F}(\text{CF}_2)_4\text{I}(10)$	0.2:10	1.5	RT	$\text{F}(\text{CF}_2)_4\text{CHO}$	89.5
$\text{F}(\text{CF}_2)_6\text{I}(10)$	0.2:10	1.0	RT	$\text{F}(\text{CF}_2)_6\text{CHO}$	91.2
$\text{F}(\text{CF}_2)_8\text{I}(5)$	0.1:5	1.5	RT	$\text{F}(\text{CF}_2)_8\text{CHO}$	95.0
$\text{F}(\text{CF}_2)_{10}\text{I}(5)$	0.1:5	2.0	40	$\text{F}(\text{CF}_2)_{10}\text{CHO}$	91.5
$\text{Cl}(\text{CF}_2)_4\text{I}(10)$	0.2:10	1.0	RT	$\text{Cl}(\text{CF}_2)_4\text{CHO}$	91.0
$\text{Cl}(\text{CF}_2)_6\text{I}(10)$	0.2:10	1.0	RT	$\text{Cl}(\text{CF}_2)_6\text{CHO}$	95.0
$\text{Cl}(\text{CF}_2)_8\text{I}(5)$	0.1:5	1.0	40	$\text{Cl}(\text{CF}_2)_8\text{CHO}$	92.1
$\text{I}(\text{CF}_2)_4\text{I}(10)$	0.3:20	2.0	RT	$\text{OHC}(\text{CF}_2)_4\text{CHO}$	90.0
$\text{I}(\text{CF}_2)_6\text{I}(5)$	0.2:10	1.5	RT	$\text{OHC}(\text{CF}_2)_6\text{CHO}$	92.0
$\text{I}(\text{CF}_2)_8\text{I}(5)$	0.2:10	1.5	40	$\text{OHC}(\text{CF}_2)_8\text{CHO}$	91.5
$\text{I}(\text{CF}_2)_4\text{O}(\text{CF}_2)_2\text{SO}_2\text{F}$ (10)[7]	0.2:10	2.0	RT	$\text{OHC}(\text{CF}_2)_4\text{O}(\text{CF}_2)_2$ $\text{SO}_2\text{F}$	85.0
$\text{F}_2\text{C}=\text{CFOCF}_2\text{CF}(\text{CF}_3)$ $\text{O}(\text{CF}_2)_2\text{I}(10)$ [8]	0.2:10	1.5	RT	$\text{F}_2\text{C}=\text{CFOCF}_2\text{CF}(\text{CF}_3)$ $\text{O}(\text{CF}_2)_2\text{CHO}$	90.0
$\text{F}(\text{CF}_2)_2\text{Br}(20)$	0.5:20	10.0	5	$\text{F}(\text{CF}_2)_2\text{CH}(\text{OH})_2$	89.5
$\text{F}(\text{CF}_2)_6\text{Br}(2.5)$	0.1:2.0	4.0	RT	$\text{F}(\text{CF}_2)_6\text{CHO}$	91.5
$\text{F}(\text{CF}_2)_8\text{Br}(2.0)$	0.1:2.0	4.0	RT	$\text{F}(\text{CF}_2)_8\text{CHO}$	90.2
$\text{F}(\text{CF}_2)_{10}\text{Br}(2.0)$	0.1:2.0	3.5	RT	$\text{F}(\text{CF}_2)_{10}\text{CHO}$	89.0

the aldehydes synthesized in this way were characterized by their MS, IR,  $^{19}\text{F}$  and  $^1\text{H}$  NMR spectra. The by-products were  $\text{R}_f\text{H}$  and  $\text{R}_f\text{CONMe}_2$  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  $\text{PbBr}_2$ (catalyst)/Al in DMF

$R_f\text{I}/\text{DMF}$ (mmol/mmol)	Solvent	Time (h)	Products (%) <sup>a</sup>	
			$R_f\text{CHO}$	$R_f\text{H}$
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	$\text{CH}_3\text{CN}$	5.0	88.2	11.8
	$\text{DMF}-\text{H}_2\text{O}^b$	1.0	0	100

<sup>a</sup>Estimated by  $^{19}\text{F}$  NMR spectroscopy.

<sup>b</sup>10:1 by volume.

The results of the syntheses of per(poly)fluoroalkyl aldehydes from the corresponding halides with  $\text{PbBr}_2$ (catalyst)/Al are listed in Table 1.

With  $\alpha,\omega$ -dihaloper(poly)fluoroalkanes, the corresponding  $\alpha,\omega$ -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  $\alpha,\omega$ -dihaloper(poly)fluoroalkanes with two different halogen atoms, C-formylation takes place preferentially at the more reactive site.  $\omega$ -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.  $^1\text{H}$  NMR data (with chemical shifts in ppm from external TMS) and  $^{19}\text{F}$  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  $^1\text{H}$  and 56.4 Mz for  $^{19}\text{F}$ ) 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  $\text{PbBr}_2$  (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,  $^1\text{H}$  and  $^{19}\text{F}$  NMR spectra of per(poly)fluoroalkyl aldehydes

Compounds	Boiling points (°C)	$^{19}\text{F}$ (ppm)	$^1\text{H}$ (ppm)	IR ( $\text{cm}^{-1}$ )	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 <sup>a</sup>	5.7 (3F); 46.2 (16F); 51.0 (2F)	9.85 <sup>b</sup>	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 <sup>a</sup>	–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 <sup>a</sup>	46.3 (12F); 50.0 (4F)	9.85 <sup>b</sup>	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)	<sup>19</sup> F (ppm)	<sup>1</sup> H (ppm)	IR (cm <sup>-1</sup> )	Ref.
		46.2 (2F); 49.3 (2F); 50.2 (2F); -121.2 (1F)			
F <sub>2</sub> C=OCF <sub>2</sub> CF(CF <sub>3</sub> )O(CF <sub>2</sub> ) <sub>2</sub> CHO <sup>i</sup>	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	

<sup>a</sup>Melting points.<sup>b</sup>From internal TMS.

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

<sup>c</sup>MS: 265 (M<sup>+</sup> + 1); 267; 245; 247; 235; 237; 229; 216; 131 (100); 100; 85; 87.Elemental analysis: for its monohydrate C<sub>5</sub>H<sub>3</sub>ClF<sub>8</sub>O<sub>2</sub>: Calculated: C, 21.26; H, 1.07; F, 53.80%. Found: C, 21.34; H, 1.18; F, 53.61%.<sup>d</sup>MS: 365 (M<sup>+</sup> + 1); 367; 345; 347; 325; 327; 131 (100); 100; 85; 87.Elemental analysis: for its monohydrate C<sub>7</sub>H<sub>3</sub>ClF<sub>12</sub>O<sub>2</sub>: Calculated: C, 21.98; H, 0.79; F, 59.60%. Found: C, 21.81; H, 0.92; F, 59.49%.<sup>e</sup>MS: 465 (M<sup>+</sup> + 1); 467; 445; 447; 429; 416; 131 (100); 100; 85; 87.Elemental analysis: for its monohydrate C<sub>9</sub>H<sub>3</sub>ClF<sub>16</sub>O<sub>2</sub>: Calculated: C, 22.40; H, 0.63; F, 62.99%. Found: C, 22.27; H, 0.82; F, 62.86%.<sup>f</sup>MS: 359 (M<sup>+</sup> + 1); 360; 339; 331; 319; 311; 309; 291; 132 (100); 131; 100.Elemental analysis: for its hydrates C<sub>8</sub>H<sub>6</sub>F<sub>12</sub>O<sub>4</sub>: Calculated: C, 24.38; H, 1.53; F, 57.85%. Found: C, 24.52; H, 1.62; F, 57.61%.<sup>g</sup>MS: 459 (M<sup>+</sup> + 1); 460; 439; 431; 411; 391; 369; 362; 341; 131 (100); 100.Elemental analysis: for its hydrates C<sub>10</sub>H<sub>6</sub>F<sub>16</sub>O<sub>4</sub>: Calculated: C, 24.31; H, 1.22; F, 61.52%. Found: C, 24.12; H, 1.35; F, 61.70%.<sup>h</sup>MS: 429 (M<sup>+</sup> + 1); 409; 380; 229; 183; 131; 119 (100); 100; 51.Elemental analysis: for its monohydrate C<sub>7</sub>H<sub>3</sub>F<sub>13</sub>O<sub>5</sub>S: Calculated: C, 18.85; H, 0.68; F, 55.36%. Found: C, 18.78; H, 0.72; F, 55.38%.<sup>i</sup>MS: 393 (M<sup>+</sup> + 1); 373; 364; 345; 325; 295; 247; 131; 97; 59 (100).Elemental analysis: for its monohydrate C<sub>7</sub>H<sub>3</sub>F<sub>12</sub>O<sub>4</sub>: 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 MgSO<sub>4</sub> overnight. A crude pale yellow product was obtained after the removal of solvent, which was then dehydrated with P<sub>2</sub>O<sub>5</sub> to give the corresponding per(poly)fluoroalkyl aldehydes R<sub>f</sub>CHO.

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

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