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SnX_2/Al-promoted formylation of per(poly)fluoroalkyl halides with *N,N*-dimethylformamide

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Abstract

In the presence of catalytic amounts of stannous salts (20 mol%) and aluminium powder, per(poly)fluoroalkyl iodides or bromides react smoothly with DMF under mild conditions to give the corresponding per(poly)fluoroalkyl aldehydes in good to excellent yield. A tin-containing intermediate was obtained. A possible mechanism is proposed.

Introduction

Per(poly)fluoroalkyl aldehydes and their monohydrates are useful intermediates [1]. Several classical methods have been used to synthesize such compounds [2–4] but all suffer from poor yields or tedious procedures. Recently, it was reported that some initiators could effectively promote the formylation of per(poly)fluoroalkyl halides with DMF to give the corresponding per(poly)fluoroalkyl aldehydes [5].

Stannous salts have been used extensively as Barbier-type allylation reagents for carbonyl compounds [6]. In the presence of a stoichiometric amount of $SnCl_2$, Kitazume and Ishikawa reported the per(poly)fluoroalkylation of aldehydes and ketones with R_fI [7]. In our continuing studies on redox couple-promoted reactions in organofluorine chemistry, we found that a bimetal redox couple composed of a catalytic amount of an anhydrous stannous salt and aluminium powder was sufficiently active to promote the formylation of R_fI or R_fBr with DMF. A possible mechanism involving an adduct intermediate is proposed.

Results and discussion

In the presence of catalytic amounts of anhydrous stannous chloride and aluminium powder, per(poly)fluoroalkyl halides (iodides **1** or bromides **2**) react readily with DMF to give the formylation products $R_fCH(OH)_2$ **4** in good yield. These per(poly)fluoroalkylaldehyde monohydrates (**4**) were dehydrated with phosphorus pentoxide at 60 °C to give the corresponding anhydrous aldehydes **5** in nearly quantitative yield. The yields and reaction conditions are listed in Table 1.

$$R_fX + DMF \xrightarrow{a} R_fCH(OH)_2 \xrightarrow{b} R_fCHO$$

(**1**) X=I (**4**) (**5**)
(**2**) X=Br
(**3**) X=Cl

(**1a**) ClC_4F_8I; (**1b**) $ClC_6F_{12}I$; (**1c**) $ClC_8F_{16}I$; (**1d**) C_4F_9I; (**2a**) $C_6F_{13}Br$; (**2b**) $C_8F_{17}Br$; (**3**) $CH_2{=}CHC_6F_{12}Cl$

a. $SnCl_2$ (20 mol%), 1 equiv. Al, r.t., 10 h; b. 2.5 equiv. P_2O_5, 60 °C.

Scheme 1.

Under such conditions, the reaction proceeded smoothly at room temperature within 10 h. The corresponding per(poly)fluoroalkyl aldehyde monohydrates **4** were obtained in good yield. Perfluoroalkyl bromides gave similar results, except that a longer reaction time was necessary. The main by-product was R_fH which amounted to less than 10%. However, perfluoroalkyl chlorides **3** remained intact under these or even more drastic conditions (Run 8). The reactivity of per(poly)fluoroalkyl halides decreased in the order: $R_fI > R_fBr \gg R_fCl$.

Polyfluoroalkyl halides such as 2-chlorotetrafluoroethyl iodide containing vicinal dihalogens were dehalogenated to give tetrafluoroethene (Run 5). In fact, $SnCl_2$ on its own was sufficiently active to eliminate halogens from vicinal dihalogen compounds.

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TABLE 1. Tin(II)/Al-promoted formylation of R_fX with DMF[a]

Run No.	R_fX	SnY_2	Temp./time (°C/h)	Product	Yield[b] (%)
1	$Cl(CF_2)_4I$	$SnCl_2$	16/6	$Cl(CF_2)_4CHO$	80
2	$Cl(CF_2)_6I$	$SnCl_2$	15/8	$Cl(CF_2)_6CHO$	97
3	$Cl(CF_2)_8I$	$SnCl_2$	15/10	$Cl(CF_2)_8CHO$	88
4	$F(CF_2)_4I$	$SnCl_2$	15/8	$F(CF_2)_4CHO$	90
5	$Cl(CF_2)_2I$	$SnCl_2$	15	no product	c
6	$F(CF_2)_8Br$	$SnCl_2$	15/12	$F(CF_2)_8CHO$	89
7	$F(CF_2)_6Br$	$SnCl_2$	15/12	$F(CF_2)_6CHO$	84
8	$CH_2=CH(CF_2)_6Cl$	$SnCl_2$	60/10	no reaction	d
9	$Cl(CF_2)_4I$	$SnBr_2$	15/6	$Cl(CF_2)_4CHO$	83
10	$Cl(CF_2)_6I$	$SnBr_2$	15/9	$Cl(CF_2)_6CHO$	75
11	$Cl(CF_2)_8I$	$SnBr_2$	15/10	$Cl(CF_2)_8CHO$	79
12	$F(CF_2)_8Br$	$SnBr_2$	15/15	$F(CF_2)_8CHO$	74
13	$Cl(CF_2)_6I$	SnF_2	15/5	$Cl(CF_2)_6CHO$	85
14	$F(CF_2)_8Br$	SnF_2	15/6	$F(CF_2)_8CHO$	90
15	$Cl(CF_2)_6I$	SnI_2	15/10	no reaction	d

[a] All compounds had similar boiling or melting points, and ^1H NMR, ^{19}F NMR, MS and IR spectra identical to those described in the literature [5].

[b] Isolated yields based on R_fX.

[c] $CF_2=CF_2$ was obtained.

[d] Starting material was completely recovered.

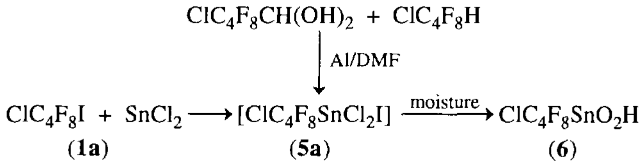
$$ClCF_2CF_2I \xrightarrow[SnCl_2]{SnCl_2/Al\ or} CF_2=CF_2$$

The solvent seemed to play quite an important role. DMF could be used both as a reactant and a solvent. DMSO could also be used as a solvent without significant difference. However, in acetonitrile, THF or protic solvents, only R_fH was obtained.

It was shown that catalytic amounts of both stannous chloride and aluminium powder were necessary because stoichiometric amounts of $SnCl_2$ or of aluminium on their own were unable to promote the reaction. On the other hand, stannous chloride could be replaced by other stannous salts. For example, SnF_2 was more and $SnBr_2$ less effective than $SnCl_2$, but SnI_2 would not promote the reaction at all. The catalytic activity of these stannous salts decreased in the order: $SnF_2 > SnCl_2 > SnBr_2 \gg SnI_2$. Aluminium could not be replaced by other metals such as zinc, magnesium or iron.

$$ClC_6F_{12}I + DMF \xrightarrow{SnCl_2/Mg,\ Zn\ or\ Fe} no\ reaction$$

Although stoichiometric amounts of $SnCl_2$ were incapable of promoting the formylation reaction, $SnCl_2$ did react with a per(poly)fluoroalkyl iodide to form an adduct. Thus, in dimethyl sulfoxide (DMSO), ClC_4F_8I **1a** reacted with $SnCl_2$ to give an adduct **5a** in *c*. 50% conversion. Although compound **5a** could not be isolated pure, its presence in DMSO was evident [7] since the ^{19}F NMR signal of CF_2I was shifted upfield by *c*. 40 ppm and became a broad singlet. DMF was then added to this solution. It was found that in the absence of aluminium powder the 4-chloroperfluorobutyltin(IV) halide **5a** remained intact. In contrast, when aluminium powder was added, the desired product and ClC_4F_8H were obtained.



$$\begin{tikzcd} & ClC_4F_8CH(OH)_2 + ClC_4F_8H & \\ ClC_4F_8I + SnCl_2 \; \textbf{(1a)} \arrow[r] & {[ClC_4F_8SnCl_2I]} \; \textbf{(5a)} \arrow[u, "Al/DMF"'] \arrow[r, "moisture"] & ClC_4F_8SnO_2H \; \textbf{(6)} \end{tikzcd}$$

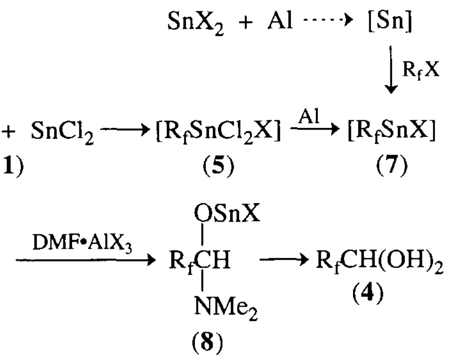
Compound **5a** was sensitive to moisture giving a colourless solid on exposure in air, whose experimental formula corresponded to the stannonic acid $ClC_4F_8SnO_2H$ (**6**) (formula weight, 387) as determined by ^{19}F NMR, ^1H NMR and IR spectroscopy, and by microanalysis (see data listed in Table 2). Mass spectrometry showed isotope peaks of tin, but there were also peaks beyond $m/z = 400$, even up to $m/z = 900$. This indicates that stannonic acid **6** is trimerized under these conditions. In fact, once converted into stannonic acids stannic alkyl trihalides polymerized readily [8]. Solid **6** remained intact both in the presence and absence of aluminium powder.

All these results seem to imply that the reaction may proceed through the following pathway. Compound **1** reacts with $SnCl_2$ to form adduct **5**, which is further reduced by aluminium into **7**. Compound **7** reacts with DMF to form adduct **8** which gives product **4** on hydrolysis.

TABLE 2. IR, ^{1}H NMR, ^{19}F NMR and MS spectra of some per(poly)fluoroalkyl aldehyde monohydrates

Compounds	^{19}F (ppm)	^{1}H (ppm)	IR (cm^{-1})	MS (*m/e* %)
$Cl(CF_2)_4CH(OH)_2$	−8.5(s, 2F) 43(s, 2F) 45(s, 2F) 54(s, 2F)	5.9(m, 1H) 6.1(s, 2H)	3300(s) 1180(s) 1160(s)	265(0.84) 131(100) 100(36.6) 85(31.6)
$Cl(CF_2)_6CH(OH)_2$[a]	−8(s, 2F) 44(s, 2F) 46(m, 6F) 52(s, 2F) 52(s, 2F)	5.8(m, 1H) 6.4(s, 2H)	3300(s) 1180(s) 1130(s)	365(4.0) 131(100)
$Cl(CF_2)_4SnO_2H$[b]	−9(s, 2F) 39(m, 4F) 43(s, 2F)	3.8(m)	3400(vs) 1610(s) 1290(m) 1250(vs)	389(M^+ +1) 121, 120, 118, 116(Sn^+)

[a] Elemental analysis: Calc. for $C_7H_3ClF_{12}O_2$: C, 23.05; H, 0.30; F, 62.55%. Found: C, 23.23; H, 0.33; F, 62.46%.
[b] Elemental analysis: Calc. for $C_4HClF_8O_2Sn$: C, 12.38; H, 0.26; Cl, 9.16%. Found: C, 12.02; H, 0.26; Cl, 8.69%.



The present work thus furnishes a readily available redox couple useful in the formylation of R_fI or R_fBr with DMF under mild conditions forming products in good to excellent yield. These aldehydes are useful starting materials in the synthesis of acids, alcohols or halides or relevant compounds containing an R_f group.

Experimental

All melting or boiling points are uncorrected. IR spectra were recorded on a Shimadzu IR-440 spectrometer. ^{19}F NMR spectra were recorded on a Varian EM-360L spectrometer in CCl_4 or $CDCl_3$ at 56.4 MHz using CF_3CO_2H as external standard. Chemical shifts in ppm were positive for upfield shifts. ^{1}H NMR spectra were recorded on a Varian EM-360A spectrometer at 60 MHz in CCl_4 or $CDCl_3$ using $SiMe_4$ as external standard. MS spectra were measured on a Finnigan MS-4021 spectrometer.

A typical procedure was as follows. To a vigorously stirred suspension consisting of 10–12 mmol of aluminium powder and 1 mmol (0.2 g) of $SnCl_2$ in 10 ml of dry *N*,*N*-dimethylformamide (DMF) was added dropwise a solution consisting of 10 mmol of R_fX (X = I, Br) in 1 ml of DMF. The mixture was stirred for several hours at room temperature. Then dilute aq. HCl was added and the residue filtered off. The filtrate was extracted three times with ethyl acetate. The combined organic extract was washed with water, brine and dried over Na_2SO_4. Removal of the solvent gave a pale yellow solid which was identified as per(poly)fluoroalkylaldehyde monohydrate. Dehydration with P_2O_5 at 60–70 °C gave the corresponding aldehyde.

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