Preliminary Note

Synthesis of per(poly)fluoroalkyl aldehydes from per(poly)fluoroalkyl chlorides

Chang-Ming Hu* and Xiao-Qing Tang

Shanghai Institute of Organic Chemistry, Academia Sinica, 345 Lingling Lu, Shanghai 200032 (China)

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

Abstract

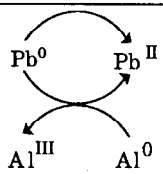
Per(poly)fluoroalkyl aldehydes can be conveniently synthesized from per(poly)fluoralkyl chlorides by their reaction with DMF promoted by a $PbBr_2$(catalyst)/Al bimetal redox system at room temperature.

Per(poly)fluoroalkyl aldehydes are important and useful intermediates in organic synthesis. They are usually prepared from the corresponding acid derivative under reduction conditions [1]. Commeyras *et al.* reported that R_fZnI reacted with *N,N*-dimethylformamide (DMF) in the presence of azobisisobutyronitrile, leading to the formation of the corresponding R_fCHO [2]. Our previous work showed that per(poly)fluoroalkyl aldehydes could be synthesized directly not only from per(poly)fluoroalkyl iodides but also from per(poly)fluoroalkyl bromides by their reaction with DMF [3]. Usually per(poly)fluoroalkyl chlorides are considered to be inert and few reactions have been attempted. Recent work in our laboratory showed that certain redox systems could activate the C–Cl bond in α-chloroper(poly)fluoroalkanes [4]. This result encouraged us to test the effectiveness of the $PbBr_2$(catalyst)/Al redox system [5] on such chloroper(poly)fluoroalkanes. We now find this redox system works well in the formyl-dechlorination of the α-chloroper(poly)fluoroalkanes with DMF. Only traces of per(poly)fluoroalkyl amide and 1-hydro-per(poly)fluoroalkane were formed as by-products in certain cases [eqn. (1)].

*Author to whom correspondence should be addressed.

0022-1139/92/$5.00

$$R_fCl + DMF \xrightarrow{PbBr_2(catalyst)/Al\text{-}DMF} R_fCHO + R_fCONMe_2 + R_fH \quad (1)$$



The reaction is considered to take place through the same mechanism as for the per(poly)fluoroalkyl iodides or bromides. Pb^0 generated *in situ* plays a significant role in such reactions [3].

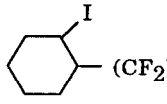
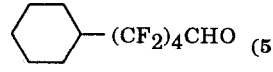
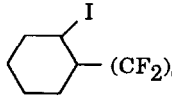
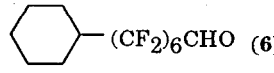
The redox system, $PbBr_2$(catalyst)/Al, can readily reduce alkyl iodide to alkanes under the above reaction conditions. Hence, the $-CHI-$ segment in substrates is reduced to $-CH_2-$ preferentially (entries 7–10 in Table 1). Functional groups such as $CH_2=CH-$ connected to $-(CF_2)_n-$ are not affected under the above conditions.

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

Reactions are conveniently carried out on a 10 mmol or 5 mmol scale with respect to per(poly)fluoroalkyl chlorides, using an equivalent amount of aluminium powder and a catalytic amount of $PbBr_2$ in an excess of DMF. Aprotic solvents such as DMSO, THF, etc. can also be used. A general

TABLE 1

Syntheses of per(poly)fluoroalkyl aldehydes from the corresponding chlorides with $PbBr_2$(catalyst)/Al in DMF

Entry No.	Substrate	Product	Isolated yield (%)
1	$H(CF_2)_4Cl$	$H(CF_2)_4CHO$ [6]	80.2
2	$H(CF_2)_6Cl$	$H(CF_2)_6CHO$ [6]	85.0
3	$H(CF_2)_8Cl$	$H(CF_2)_8CHO$ [6]	88.5
4	$Cl(CF_2)_8Cl$	$OHC(CF_2)_8CHO$ [3]	80.7
5	$CH_2=CH(CF_2)_4Cl$	$CH_2=CH(CF_2)_4CHO$ (**1**)	82.0
6	$CH_2=CH(CF_2)_6Cl$	$CH_2=CH(CF_2)_6CHO$ (**2**)	85.8
7	$n\text{-}C_4H_9CHICH_2(CF_2)_4Cl$	$n\text{-}C_6H_{13}(CF_2)_4CHO$ (**3**)	91.0
8	$n\text{-}C_4H_9CHICH_2(CF_2)_6Cl$	$n\text{-}C_6H_{13}(CF_2)_6CHO$ (**4**)	92.7
9		 (**5**)	88.7
10		 (**6**)	90.0

All reactions were carried out at room temperature under N_2. The compounds **1–6** are new and their data are given below in Table 2.

procedure is as follows. Per(poly)fluoroalkyl chloride was added into 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 of R_fCl). The mixture was stirred under nitrogen for 16–24 h at room temperature. After the reaction was completed (monitored by ^{19}F NMR spectrum), dilute HCl (1.2 equiv.) was added and the mixture stirred for another 0.5 h and then extracted with ethyl ether (or ethyl acetate) (4×20 ml). The organic extract was combined and dried over $MgSO_4$. A pale yellow crude product, $R_fCH(OH)_2$, was obtained after the removal of solvent, which was purified by sublimation under reduced pressure or by chromatography (eluent: ethyl ether and ethyl acetate). The monohydrate, $R_fCH(OH)_2$, thus obtained was mixed with P_2O_5 and stirred at *c.* 80 °C for 1 h. Distillation under reduced pressure gave the colorless per(poly)fluoroalkyl aldehydes in approximately 70–95% yield. Aldehydes or their monohydrates synthesized in this way all gave satisfactory ^{19}F and ^1H NMR, IR, MS and elemental analyses (see Table 2).

TABLE 2

Spectroscopic and analytical data for compounds **1–6**

Compound **1**: B.p., 98.5–100.0 °C. ^{19}F NMR δ: 38.3 (m, 2F); 48.0 (s, 4F); 50.8 (s, 2F) ppm. ^1H NMR δ: 5.72 (m, 3H); 9.34 (m, 1H) ppm. MS *m/z*: 256 (M^+); 237, 209; 77; 59 (100.0). IR (cm^{-1}): 1770; 1650. Anal.: Calc. for $C_7H_6F_8O_2$ as its monohydrate: C, 30.67; H, 2.21; F, 55.45%. Found: C, 30.60; H, 2.25; F, 55.5%.

Compound **2**: B.p., 120.5–122.0 °C. ^{19}F NMR δ: 38.7 (m, 2F); 46.0 (s, 4F); 48.2 (s, 4F); 50.8 (s, 2F) ppm. ^1H NMR δ: 5.73 (m, 3H); 9.37 (m, 1H) ppm. IR (cm^{-1}): 1770; 1765. MS *m/z*: 356 (M^+); 337; 327, 309; 131; 100; 78 (100.0); 51. Anal.: Calc. for $C_9H_6F_{12}O_2$ as its monohydrate: C, 28.89; H, 1.62; F, 60.94%. Found: C, 28.82; H, 1.68: F, 60.88%.

Compound **3**: B.p., 126.0–127.8 °C. ^{19}F NMR δ: 37.3 (m, 2F); 47.7 (4F); 50.3 (2F) ppm. ^1H NMR δ: 0.80 (t, 3H); 1.2–2.5 (10H); 9.53 (m, 1H) ppm. IR (cm^{-1}): 2850; 2920; 1768. MS *m/z*: 314 (M^+); 313 (100); 293; 284; 273. Anal.: Calc. for $C_{11}H_{16}F_8O_2$ as its monohydrate: C, 39.77; H, 4.85; F, 45.75%. Found: C, 39.71; H, 4.92; F, 45.83%.

Compound **4**: B.p., 145–147.0 °C. ^{19}F NMR δ: 38.8 (m, 2F); 45.8 (s, 4F); 47.9 (s, 4F); 50.4 (s, 2F) ppm. ^1H NMR δ: 0.80 (t, 3H); 1.2–2.5 (10H); 9.49 (m, 1H) ppm. IR (cm^{-1}): 2855, 2920, 1770. MS *m/z*: 414 (M^+); 413; 395; 385; 373; 365; 85; 57; 43 (100). Anal.: Calc. for $C_{13}H_{16}F_{12}O_2$ as its monohydrate: C, 36.12; H, 3.73; F, 52.74%. Found: C, 35.84; H, 3.64; F, 52.58%.

Compound **5**: B.p., 141.5–143.5 °C. ^{19}F NMR δ: 42.3 (2F); 44.3 (2F); 48.3 (2F); 50.5 (2F) ppm. ^1H NMR δ: 1.3–2.2 (m, 11H); 9.61 (m, 1H) ppm. IR (cm^{-1}): 2855; 2920; 1768. MS *m/z*: 313 ($M^+ + 1$); 311 ($M^+ - 1$); 282; 293; 273; 83 (100). High resolution for $C_{11}H_{12}F_8O$: Calc.: 312.0814. Found: 312.0793.

Compound **6**: B.p., 164.0–167.0 °C. ^{19}F NMR δ: 42.3 (2F); 45.5 (6F); 47.5 (2F); 50.2 (2F) ppm. ^1H NMR δ: 1.2–2.5 (m, 11H); 9.66 (m, 1H) ppm. IR (cm^{-1}): 2850; 2930; 1769. MS *m/z*: 411 ($M^+ - 1$); 391; 373; 83 (100). High resolution for $C_{13}H_{12}F_{12}O$: Calc.: 412.0750. Found: 412.0761.

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