

Synthesis of Per(poly)fluoroalkyl Aldehydes $R_F(CH_2)_nCHO$

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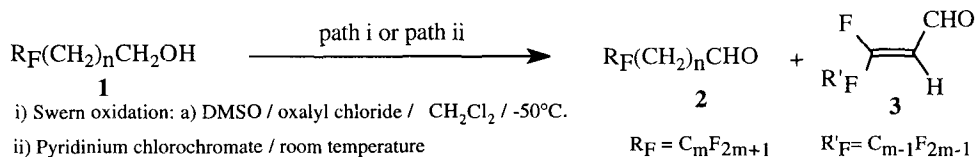
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Abstract: We report the preparation of polyfluoroalkyl aldehydes $R_F(CH_2)_nCHO$ in high yields by direct oxidation of polyfluoroalkyl alcohols; the Swern oxidation, pyridinium chlorochromate and Dess-Martin periodinane are used and compared

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Per(poly)fluorinated aldehydes R_FCH_2CHO and their hydrates may be suitable starting materials in the synthesis of polyfluorinated acids $R_FCH_2CO_2H$ or aminoacids $R_FCH_2CH(NH_2)CO_2H$, which may constitute interesting precursors of various types of surfactants bearing a linear per(poly)fluorinated chain. Among the methods describing the preparation of fluorinated aldehydes reported in the literature¹, those starting from the corresponding alcohols are rather scarce, often limited to the trifluoromethyl substituted ones and their yields are generally poor². That is why we attempted to find a method for preparing a series of polyfluoro-aldehydes $R_F(CH_2)_nCHO$ **2** of various lengths in the perfluoroalkyl end group and in the polymethylene spacer group, under mild conditions and in high yields from the corresponding primary alcohols³.

We tested first the applicability of "activated" DMSO as described by Swern et al.⁴ and of the pyridinium chlorochromate oxidation method⁵ in the oxidation of alcohols $R_F(CH_2)_nCH_2OH$ ⁶.



The results obtained by both methods were summarized and compared in table 1.

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Compound	R _F	n	Yields % i(ii)	2 %	3 %	Boiling point
2a	C ₄ F ₉	4	84(70)	100		86°C, 30 mmHg
2b	C ₆ F ₁₃	4	89(81)	100		94,5°C, 30 mmHg
2c	C ₈ F ₁₇	4	83(78)	100		101°C, 30 mmHg
2d	C ₆ F ₁₃	3	70(65)	100		45°C, 5 mmHg
2e	C ₆ F ₁₃	2	52(36)	100		40°C, 5 mmHg
2f, 3f	C ₄ F ₉	1	75(75)	8	92	37°C, 30 mmHg*
2g, 3g	C ₆ F ₁₃	1	85(75)	7	93	40°C, 30 mmHg*
2h, 3h	C ₈ F ₁₇	1	80(70)	8	92	30°C, 30 mmHg*

Table 1: Alcohol to aldehyde conversion : i) by the Swern oxidation; ii) by pyridinium chlorochromate.

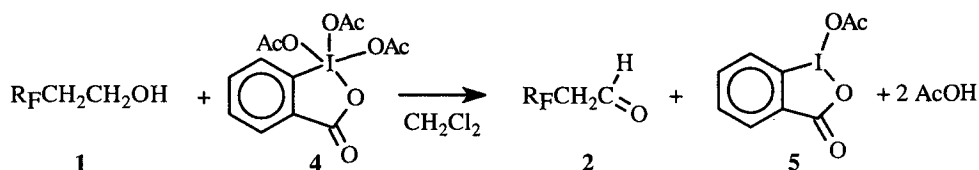
* Boiling point of the mixture

The results depend on the length of the methylene spacer. When $n = 4, 3$ and 2 both methods provided a highly efficient and useful way to obtain fluoroalkyl aldehydes especially with $n = 4$ and 3 , but although pyridinium chlorochromate was more convenient to use, it always gave slightly lower yields.

When $n = 1$, this method gave a mixture of saturated **2** and α,β unsaturated aldehyde **3**, which is the major product. Only the **Z** isomer of **3** was isolated. The **Z** configuration around the double bond was evidenced by the value of the coupling constant $^3J_{\text{H-F}} = 31\text{Hz}$, characteristic of a trans geometry between vinylic fluorine and hydrogen atoms⁷.

It should be noted that the reaction mixture experienced basic conditions either during the decomposition of the alkoxysulfonium chloride by means of triethylamine in the Swern procedure or in the pyridinium chlorochromate method, if an excess of pyridine was present. These results prompted us to assess the Dess-Martin method using a periodinane, the 1,1,1-triacetoxy-1,1-dihydro-1,2-benziodoxol-3(1H) **4**, which is one of the mildest and most convenient reagents available for oxidation of alcohols⁸. This reagent was prepared according to Ireland procedure⁹. The ease of its implementation and the mildness of the working-up conditions are especially suitable for substrates containing sensitive functional groups.

Typically a solution of C₈F₁₇CH₂CH₂OH **1h** in methylene chloride was added with stirring to a solution of **4** in methylene chloride. After twenty minutes, the conversion of the starting materials was completed. Then, two alternative procedures were tested for the discarding of the resulting acetyliodinane **5** and the neutralisation of the acidic medium¹⁰.



In the first one, the reaction was quenched by adding aqueous sodium hydroxyde. This procedure led exclusively to the α,β unsaturated aldehyde **3**.

The second one, realized under weakly alkaline conditions by means of a sodium thiosulfate solution in an aqueous sodium bicarbonate buffer, led to the *F*-alkylethanal **2** as the sole reaction product.

This result showed that the dehydrofluorination did not occur during the oxidation step, but when the reaction medium became alkaline^{1e,11}.

The instability of the *F*-alkylethanals **2** in an alkaline medium was confirmed by treating the aldehyde **2h** with triethylamine. After stirring at room temperature during thirty minutes, its conversion into the α,β unsaturated aldehyde **3h** was complete.

In conclusion, the preparation of a series of fluoroalkylaldehydes $R_F(CH_2)_nCHO$ in good yields ($n > 2$) was achieved in good yields by oxidation of primary alcohols $R_F(CH_2)_{n+1}OH$ by three different methods. The easy dehydrofluorination of the *F*-alkylethanals ($n = 1$) can be avoided when using the Dess-Martin periodinane method.

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- 1 - a) Cantacuzene D., Dorme R., *Tetrahedron Letters*, **1975**, 25, 2031-2034. b) Pazenok S.V., Chaika E.A., Gerus I.I., Yagupolskii L.M., *Zh. Org. Khim.*, **1989**, 25, 1376-1380. c) Huang W.Y., Lu L., Zhang Y.F., *Chin. J. Chem.*, **1990**, 281-288. d) Uneyama K., Kitagawa K., *Tetrahedron Letters*, **1991**, 32, 3385-3386. e) Laurent P., Blancou H., Commeyras A., *Tetrahedron Letters*, **1992**, 33, 2489-2492. f) Tang X.Q., Hu C.M., *J. Chem. Soc. Perkin Trans. I*, **1994**, 2161-2163. g) Napoli M., Scipioni A., Conte L., Legnaro E., Krotz L.N., *J. Fluorine Chem.*, **1994**, 66, 249-252. h) Guan H.P., Hu Q.S., Hu C.M., *Synthesis*, **1996**, 997-1001.
 - 2 - a) Golding B.T., Sellars P.J., Watson W.P., *J. Fluorine Chem.*, **1985**, 30, 153-158. b) Ratier M., Pereyre M., Davies A. G., Sutcliffe R., *J. Chem. Soc. Perkin Trans.*, **1984**, 1907-1915.
 - 3- Greiner J., Milius A., Riess J.G., *J. Fluorine Chem.*, **1992**, 56, 285-293.
 - 4 - a) Mancuso A.J., Swern D., *Synthesis*, **1981**, 165-185. b) Omura K., Swern D., *Tetrahedron*, **1978**, 34, 1651-1660. c) Tidwell T.T., *Synthesis*, **1990**, 857-870.
 - 5- a) Corey E.J., Suggs J.W., *Tetrahedron Letters*, **1975**, 31, 2647-2650. b) Piancatelli G., Scettri A., D'auria M., *Synthesis*, **1982**, 245-258.
 - 6- Swern procedure: Under nitrogen, at -50°C, to a mixture of 25 ml dichloromethane and 11 mmol (1 ml) oxalyl chloride was added 22 mmol (1.5 ml) of dimethyl sulfoxide in 5 ml of dichloromethane and 10 mmol of alcohol **1** in 10 ml of dichloromethane. Stirring is continued for an additional 15 min. Triethylamine (7 ml) is added and the reaction mixture further stirred for 5 min and then allowed to warm to room temperature. Fifty ml of water was added and the aqueous layer was extracted with 30 ml of dichloromethane. The organic layers were combined, washed with a saturated sodium chloride solution and dried over anhydrous magnesium sulfate. The residual liquid was concentrated under reduced pressure. Pure aldehydes **2a-e** were isolated after distillation under reduced pressure.
 - Pyridinium chlorochromate method: At room temperature and under nitrogen, to a stirred solution of 4 ml of pyridinium chlorochromate in 10 ml of dichloromethane, a solution of 2.65 mmol of alcohol **1** in 6 ml of dichloromethane was added dropwise. The reaction mixture was further stirred and monitored by gas chromatography until completion (4 h at room temperature). It was then filtered on Florisil® and the organic solvent was removed under vacuo. Pure aldehydes **2a-e** were isolated after distillation under reduced pressure.
- C₈F₁₇(CH₂)₄CHO 2c**: IR (cm⁻¹, KBr film) 1150-1240 ν_{C-F} ; 1730, 2730 $\nu_{CH=O}$. RMN ¹H: 1.65 (m, 4H), 2.1 (m, 2H), 2.6 (t, ³J_{H-H}=7Hz, 2H), 9.8 (s, 1H). ¹³C: 19.8, 21.4, 30.6 (t, ²J_{C-F} = 22.4Hz), 43.3, 201.2. ¹⁹F: -126.6 (2F), -124 (2F), -123.3 (2F), -122.4 (6F), -114.9 (2F), -81.3 (3CF).

- 7- a) Begue J.P., Bonnet-Delpon D., Mesureur D., Nee G., Wu S.W., *J. Org. Chem.*, **1992**, 57, 3807-3814. b) Shen Y., Wang T., *J. Chem. Res. (S)*, **1993**, 12, 490-491.
- 8- a) Dess D.B., Martin J.C., *J. Org. Chem.*, **1983**, 48, 4155-4156. b) Dess D.B., Martin J.C., *J. Am. Chem. Soc.*, **1991**, 113, 7277-7287.
- 9- Ireland R.E., Liu L., *J. Org. Chem.*, **1993**, 58, 2899.
- 10- Dess-Martin procedure: In a Schlenk vessel, under nitrogen, 3.7 mmol of alcohol **1h** in 25 ml of dichloromethane were added to 1.2 eq. (4.4 mmol, 1.8 g) of Dess-Martin periodinane **4** (prepared according to the Ireland's procedure⁹) in 10 ml of dichloromethane. The mixture was stirred at room temperature. After 20 min, two different isolation procedures were applied to the homogenous solution:
- Method 1*: After dilution with 25 ml of diethylether and quenching with aqueous 1N NaOH, the aqueous layer was extracted three times with diethylether. The combined ethereal layers were washed with H₂O and dried over anhydrous magnesium sulfate. Removal of ether and distillation under reduced pressure gave pure aldehyde **3h**.
- C₇F₁₅CF=CHCHO 3h**: IR (cm⁻¹, KBr film): 1150-1240 ν_{C-F}; 1700 ν_{C=C}; 1730, 2730 ν_{CH=O}. RMN ¹H: 6.1 (dd, ³J_{H-H} = 7Hz, ³J_{H-F} = 7Hz, 1H), 10.9 (d, ³J_{H-H} = 7Hz, 1H). ¹³C: 113.9 (d, ³J_{C-F} = 3.5 Hz), 159.1 (dt, ¹J_{C-F} = 289Hz, ²J_{C-F} = 29Hz), 185.3 (d, ³J_{C-F} = 8Hz). ¹⁹F: -127.1 (2F), -123.6 (4F), -120.1 (2F), -117.0 (1F), -81.8 (3F).
- Method 2*: After quenching with a saturated aqueous solution of NaHCO₃ containing Na₂S₂O₃, the homogeneous organic solution was dried over anhydrous magnesium sulfate. The distillation was effected under atmospheric pressure to give the pure aldehyde **2h** (bp = 176°C).
- C₈F₁₇CH₂CHO 2h**: IR (cm⁻¹, KBr film): 1100-1300 ν_{C-F}; 1735, 2740 ν_{CH=O}. RMN ¹H: 3.5 (t, ³J_{F-H} = 20Hz, 2H), 9.8 (s, 1H). ¹³C: 44.3 (t, ³J_{C-F} = 20.6Hz), 206.7. ¹⁹F: -125.9 (2F), -123.4 (2F), -122.6 (2F), -121.8 (6F), -110.2 (2F), -80.7 (3F).
- 11- a) M. Le Blanc, G. Santini, J. G. Riess, *Tetrahedron Lett.* **1975**, 4151-4152. b) M. Le Blanc, G. Santini, J. Gallucci, J. G. Riess, *Tetrahedron*, **1977**, 33, 1453-1456. c) S. Thiebaut, C. Gerardin-Charbonnier, C. Selve, *J. Fluorine Chem.*, **1997**, 82, 131-138.