Pergamon

Tetrahedron Letters 39 (1998) 8857–8860

TETRAHEDRON
LETTERS

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

Laurence Lévêque, Maurice Le Blanc* and Raphaël Pastor.

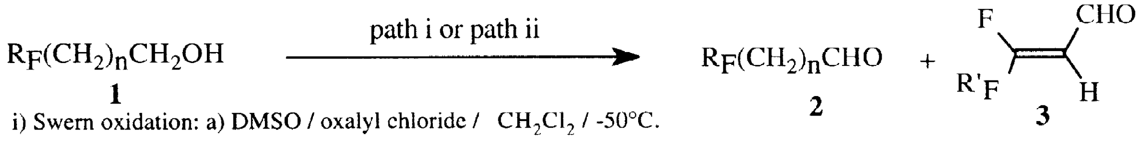
Laboratoire de Chimie Moléculaire, CNRS URA 426. Université de Nice-Sophia Antipolis.
Faculté des Sciences. Parc Valrose. F- 06108 Nice Cedex 2, France.

Received 27 July 1998; accepted 25 September 1998

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*

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 literature[1], those starting from the corresponding alcohols are rather scarce, often limited to the trifluoromethyl substituted ones and their yields are generally poor[2]. 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 alcohols[3].

We tested first the applicability of "activated" DMSO as described by Swern et al.[4] and of the pyridinium chlorochromate oxidation method[5] in the oxidation of alchols $R_F(CH_2)_nCH_2OH$[6].



i) Swern oxidation: a) DMSO / oxalyl chloride / CH_2Cl_2 / -50°C.
ii) Pyridinium chlorochromate / room temperature

$R_F = C_mF_{2m+1}$ $R'_F = C_{m-1}F_{2m-1}$

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

---

* E-mail leblanc@unice.fr ; fax (33) 04 92 07 61 44

PII: S0040-4039(98)02029-2

Compound	R_F	n	Yields % i(ii)	**2** %	**3** %	Boiling point
2a	C_4F_9	4	84(70)	100		86°C, 30 mmHg
2b	C_6F_{13}	4	89(81)	100		94,5°C, 30 mmHg
2c	C_8F_{17}	4	83(78)	100		101°C, 30 mmHg
2d	C_6F_{13}	3	70(65)	100		45°C, 5 mmHg
2e	C_6F_{13}	2	52(36)	100		40°C, 5 mmHg
2f, 3f	C_4F_9	1	75(75)	8	92	37°C, 30 mmHg*
2g, 3g	C_6F_{13}	1	85(75)	7	93	40°C, 30 mmHg*
2h, 3h	C_8F_{17}	1	80(70)	8	92	30°C, 30 mmHg*

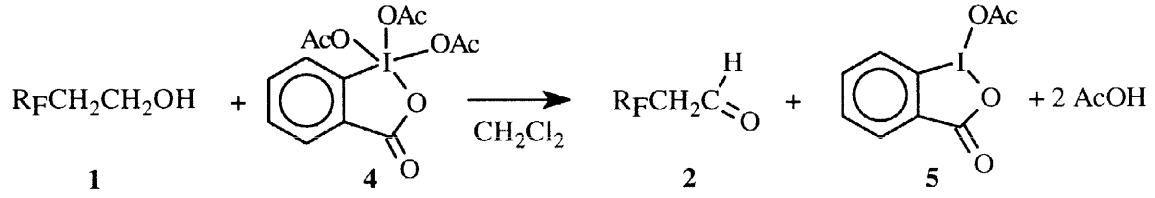
Table 1: Alcohol to aldehyde conversion : i) by the Swern oxidation; ii) by pyridinium chlorochromate.
* Boiling point of the mixture

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 unsatured 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 $^3J_{H-F}$ = 31Hz, characteristic of a trans geometry beetween vinylic fluorine and hydrogen atoms[7].

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 alcohols[8]. This reagent was prepared according to Ireland procedure[9]. 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 $C_8F_{17}CH_2CH_2OH$ **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 acetxyiodinane **5** and the neutralisation of the acidic medium[10].



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

Acknowledgements: We wish to thank ATOCHEM for the gift of the starting R_FI.

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.

$C_8F_{17}(CH_2)_4CHO$ 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). ^{13}C: 19.8, 21.4, 30.6 (t, $^2J_{C-F}$ = 22.4Hz), 43.3, 201.2. ^{19}F: -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 procedure^9) 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:

Method1: After dilution with 25 ml of diethylether and quenching with aqueous 1N NaOH, the aqueous layer was extracted three times with diethylether. Thecombined ethereal layers were washed with H_2O and dried over anhydrous magnesium sulfate. Removal of ether and distillation under reduced pressure gave pure aldehyde **3h**.

$C_7F_{15}CF{=}CHCHO$ 3h: IR (cm^{-1}, KBr film): 1150-1240 $\nu_{C\text{-}F}$; 1700 $\nu_{C=C}$; 1730, 2730 $\nu_{CH=O}$. RMN ^{1}H: 6.1 (dd,$^3J_{H\text{-}H}$ = 7Hz, $^3J_{H\text{-}F}$ = 7Hz, 1H), 10.9 (d,$^3J_{H\text{-}H}$ = 7Hz, 1H). ^{13}C: 113.9 (d, $^3J_{C\text{-}F}$ = 3.5 Hz), 159.1 (dt,$^1J_{C\text{-}F}$ = 289Hz, $^2J_{C\text{-}F}$ = 29Hz), 185.3 (d, $^3J_{C\text{-}F}$ =8Hz). ^{19}F: -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 $NaHCO_3$ containing $Na_2S_2O_3$, 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).

$C_8F_{17}CH_2CHO$ 2h: IR (cm^{-1}, KBr film): 1100-1300 $\nu_{C\text{-}F}$; 1735, 2740 $\nu_{CH=O}$. RMN ^{1}H: 3.5 (t,$^3J_{F\text{-}H}$ = 20Hz, 2H), 9.8 (s,1H). ^{13}C: 44.3 (t,$^3J_{C\text{-}F}$ = 20.6Hz), 206.7. ^{19}F: -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.