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A modified procedure for preparing perfluoroalkyl acetic acids from perfluoroalkyl iodides*

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Abstract

Perfluoroalkyl acetic acids, R_FCH_2COOH, can be prepared in several ways. Particular attention is here paid to the method starting from the azonitrile-initiated addition of the corresponding perfluoroalkyl iodide, R_FI, to vinyl acetate, $CH_2{=}CHOCOCH_3$, with formation of the adduct $R_FCH_2CHIOCOCH_3$. This method is reported as a four-step process that synthesizes perfluoroalkyl acetic acids through the conversion of the adduct into the corresponding ester $R_FCH_2CH_2OCOCH_3$ and alcohol $R_FCH_2CH_2OH$. A simplified procedure consisting of three steps is also suggested: starting from the same reagents, perfluoroalkyl acetic acids can be easily prepared by the oxidation of the corresponding aldehyde R_FCH_2CHO obtained directly in good yields by acid hydrolysis of the primary adduct $R_FCH_2CHIOCOCH_3$.

Introduction

Several methods, generally starting from perfluoroalkyl iodides, R_FI, have been reported for the synthesis of perfluoroalkyl acetic acids, R_FCH_2COOH. Thus, $CF_3(CF_2)_nCH_2COOH$ ($n=5$, 7 or 9) can be prepared directly from the corresponding $CF_3(CF_2)_nCH_2CF_2I$ by treatment with HNO_3 [2], or less directly from $CF_3(CF_2)_{n-1}CF_2I$ and $CH_2{=}CHOCH_2CH_3$ through the formation of the corresponding aldehyde $CF_3(CF_2)_nCH_2CHO$ [3].

Perfluoroalkyl acetic acids can be also obtained from the oxidation of the corresponding 2-perfluoroalkyl ethanols, in turn prepared in several ways. Thus, $R_FCH_2CH_2OH$ can be prepared from the corresponding 1-iodo-2-perfluoroalkyl ethane, $R_FCH_2CH_2I$, by treatment with a zinc–copper couple and subsequent oxidation [4], or from the corresponding perfluoroalkyl iodide, R_FI, by radical addition to vinyl acetate, $CH_2{=}CHOCOCH_3$, and subsequent reduction and hydrolysis [5].

This latter method was used in order to prepare perfluorohexyl acetic acid for some of our experiments in electrochemical fluorination. In practice, it consists of the following four reactions:

1. Azo-initiated radical addition of R_FI to vinyl acetate giving the corresponding adduct $R_FCH_2CHIOCOCH_3$.
2. Zinc reduction of this adduct to the corresponding ester $R_FCH_2CH_2OCOCH_3$.
3. Acidic hydrolysis of the ester to 2-perfluoroalkyl ethanol.
4. Oxidation of the alcohol to the corresponding carboxylic acid R_FCH_2COOH.

During our research, we found that steps 2 and 3 can be replaced by direct acidic hydrolysis of the adduct to the corresponding aldehyde R_FCH_2CHO, by a similar procedure reported simultaneously and independently by other authors [6]. The corresponding carboxylic acid can then be readily obtained from the aldehyde by oxidation.

This simplified method of preparing perfluoroalkyl acetic acids from the corresponding perfluoroalkyl iodides is discussed here.

Experimental

Reagents

Perfluorohexyl iodide was a commercial grade product supplied by Elf Atochem S.A. Vinyl acetate was purchased from the Aldrich Chemical Co. In order to remove the inhibitor (hydroquinone), it was treated with potassium hydroxide and distilled under nitrogen before use. AIBN was a Janssen product. The other reagents used (inorganic acids and oxidants) were usual laboratory products.

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Analysis

A Perkin-Elmer Sigma 3 instrument (1 m×2 mm stainless-steel column packed with SE30 on 100–120 mesh Chromosorb P), connected to a Sigma 1 gas chromatographic system for quantitative evaluation, was used for GLC analysis of the reaction mixtures. Operational conditions (column temperature and flow rate of gas carrier He) were varied depending upon the sample analysed. A GC–MS spectrometer Carlo Erba model MFC 500/QMD 1000 (30 m×0.5 mm capillary fused silica column packed with PS 264; various temperature programmes and flow rates of gas carrier He) was used to establish the identities of the products.

General procedures

(1) First step: preparation of the adduct $C_6F_{13}CH_2CHIOCOCH_3$

For the addition of perfluorohexyl iodide to vinyl acetate, the previously reported procedure [7] was modified. Perfluorohexyl iodide (200 g, 0.448 mol) was placed in the three-necked 1 l Pyrex glass vessel together with 2 g (0.012 mol) of AIBN, whilst vinyl acetate (19.3 g, 0.224 mol) was placed in a dropping funnel. In order to remove the oxygen present, the mixture in the reactor was cooled at −36 °C and the equipment successively evacuated and filled with dry nitrogen three times. Finally, the reactor was gradually warmed up to 80 °C.

Vinyl acetate was added slowly with magnetic stirring over 20 min. When the addition was complete, the resulting solution was stirred at 80 °C for 40 min and then discharged; 219 g of reaction mixture were collected. GLC analysis showed that the conversion of vinyl acetate was almost complete with some aldehyde $C_6F_{13}CH_2CHO$ also being present. The ratio of adduct to aldehyde was determined as 3:1 by GLC methods.

Greater amounts of aldehyde were obtained under the same conditions in some experiments conducted in a stainless-steel reactor; in these cases the mean ratio of adduct to aldehyde was determined as *c.* 1.5:1 by GLC methods.

(2) Second step: hydrolysis to the aldehyde

The reaction mixture from the first step was hydrolyzed in a three-necked 1 l Pyrex glass round-bottomed flask fitted with a water-cooled condenser and mechanical stirrer, by treatment with a 15% aqueous solution of H_2SO_4 (130 ml) for 3 h at reflux temperature with vigorous stirring. After cooling, water was added and the organic phase separated and dried over $MgSO_4$. Fractional distillation *in vacuo* gave 104.8 g of unreacted perfluorohexyl iodide (28–29 °C/15 mmHg, 99.6% pure) and 74.6 g of crude aldehyde (41–42 °C/12 mmHg, 98.9% pure, 0.204 mol, 91.0% molar yield based on the initial amount of vinyl acetate). MS *m/z*: 363 ($[M+H]^+$, 2.3%); 362 (M^+, 2.7%); 361 ($[M-H)^+$, 5.5%); 342 (M^+-HF, 4.1%); 341 ($[M-H]^+-HF$, 9.2%); 314 ($C_7H_2F_{12}{}^+$, 25.2%); 295 ($C_7H_2F_{11}{}^+$, 6.9%); 245 ($C_6H_2F_9{}^+$, 3.7%); 275 ($C_7HF_{10}{}^+$, 6.0%); 231 ($C_5F_9{}^+$, 11.9%); 195 ($C_5H_2F_7{}^+$, 6.0%); 169 ($C_3F_7{}^+$, 12.4%); 145 ($C_4H_2F_5{}^+$, 10.1%); 131 ($C_3F_5{}^+$, 85.3%); 119 ($C_2F_5{}^+$, 54.1%); 100 ($C_2F_4{}^+$, 58.7%); 95 ($C_3H_2F_3{}^+$, 54.6%); 93 ($C_3H_3F_2O^+$, 52.7%); 75 ($C_3HF_2{}^+$, 45.9%); 69 ($CF_3{}^+$, 55.0%); 65 ($C_2H_3F_2{}^+$, 100.0%); 64 ($C_2H_2F_2{}^+$, 93.6%); 50 ($CF_2{}^+$, 22.5%); 45 ($C_2H_2F^+$, 75.2%); 43 ($M^+-C_6F_{13}$, 3.6%).

The corresponding phenylhydrazone was also prepared and identified. Principal MS data *m/z*: 452 (M^+, 13.8%); 432 ($[M-HF]^+$, 4.6%); 423 ($[M-CH_2NH]^+$, 2.0%); 193 ($[M-C_4H_2F_{11}]^+$, 99%); 169 ($C_3F_7{}^+$, 11.9%); 119 ($C_2F_5{}^+$, 61.5%); 93 ($C_6H_5NH_2{}^+$, 58.7%); 77 ($C_6H_5{}^+$, 100%); 69 ($CF_3{}^+$, 58.7%).

(3) Third step: aldehyde oxidation

In a four-necked 1 l Pyrex glass round-bottomed flask fitted with a water-cooled condenser, dropping funnel, thermometer and mechanical stirrer, the aldehyde was added to a 20% aqueous solution of H_2SO_4 (300 ml). Then a 7% aqueous solution of $KMnO_4$ (380 ml) was added over 1 h with vigorous stirring. A dark precipitate began to form and the temperature rose to a maximum value of 41 °C. When addition was complete, the slurry was heated at reflux and vigorously stirred for 1 h. After cooling, the precipitate was removed by filtration, washed with water and then three times with acetone (100 ml each time). The acetone solutions were combined and most of the solvent distilled off; the residue was extracted three times with ether (50 ml) and the extracts combined and dried over magnesium sulfate. Ether was distilled off to give 69.9 g of crude perfluorohexyl acetic acid (98.0% pure, 0.18 mol, 80.9% molar yield based on the initial amount of vinyl acetate). The corresponding methyl and ethyl esters were prepared and identified. MS *m/z*: ethyl ester: 407 ($[M+H]^+$, 1.4%); 406 (M^+, 3.2%); 379 ($C_8H_4F_{13}O_2{}^+$, 51.6%); 361 ($M^+-C_2H_5O$, 71.2%); 359 ($C_8H_3F_{12}O_2{}^+$, 26.0%); 339 ($C_8H_2F_{11}O_2{}^+$, 15.5%); 311 ($C_7H_2F_{11}O^+$, 2.7%); 291 ($C_7HF_{10}O^+$, 3.2); 269 ($C_5F_{11}{}^+$, 3.2%); 195 ($C_5H_2F_7{}^+$, 2.7%); 169 ($C_3F_7{}^+$, 17.8%); 137 ($C_5H_7F_2O_2{}^+$, 27.9%); 131 ($C_3F_5{}^+$, 79.4%); 119 ($C_2F_5{}^+$, 65.3%); 109 ($C_3H_3F_2O_2{}^+$, 48.4%); 100 ($C_2F_4{}^+$, 49.3%); 95 ($C_3H_2F_3{}^+$, 100.0%); 89 ($C_3H_2FO_2{}^+$, 54.8%); 69 ($CF_3{}^+$, 71.2%); 50 ($CF_2{}^+$, 8.2%); 45 ($C_2H_5O^+$, 65.7%); 42 ($C_2H_2O^+$, 4.9%).

Results and discussion

Figure 1 summarizes the reaction steps to be discussed. The first step is the well-known azonitrile-initiated radical addition of 1-iodoperfluoroalkanes to

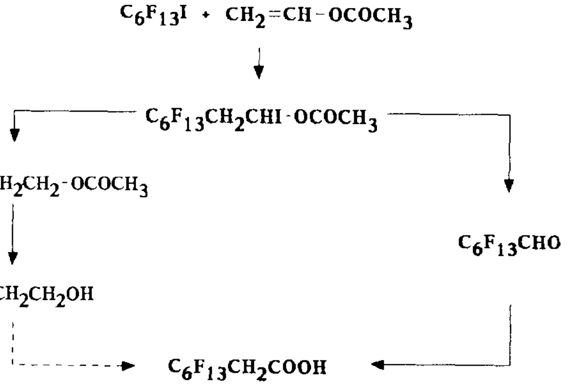

Fig. 1. Outline of the perfluorohexyl acetic acid synthesis using (a) the modified method and (b) the previous method. The dashed line refers to the oxidation step (not reported in ref. 5) of the alcohol to the corresponding carboxylic acid.

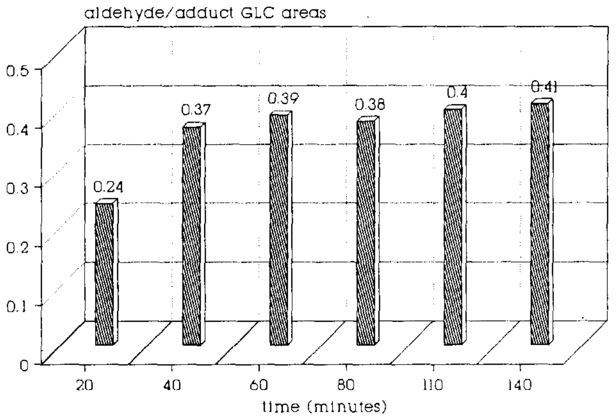

Fig. 2. Aldehyde/adduct GLC areas ratio versus time in the radical addition step.

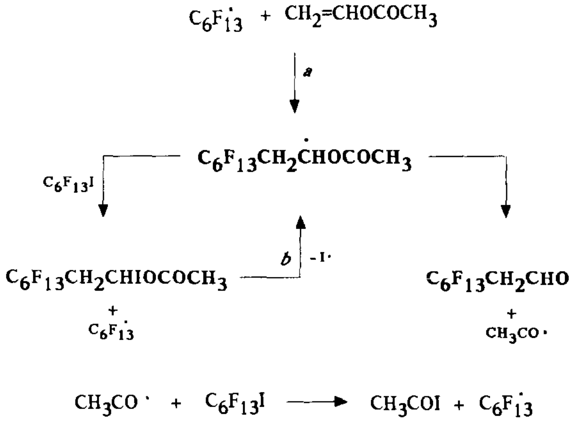

Fig. 3. Possible mechanisms for aldehyde formation during the radical addition step.

unsaturated systems [5, 7–10]. In particular, it has been found that some by-products, derived from radical addition of the adduct to the unsaturated system, formed when equimolar amounts of reactants or an excess of vinyl acetate were used [5, 10]. In our experiments, where a molar ratio 2:1 of iodide to acetate was used, no such by-products could be detected by GLC analysis, but significant amounts of aldehyde $C_6F_{13}CH_2CHO$ were found in the reaction mixture.

The presence of aldehyde in the reaction mixture obtained from the addition of perfluoroalkyl iodides to an unsaturated system has been noted by other authors independently [6]. These authors have also verified the formation of aldehyde from the adduct via spontaneous or thermal decomposition. The experimental data reported show a 30% conversion of adduct to aldehyde after 48 h at 80 °C or 30 d at 25 °C.

In an attempt to verify the thermal decomposition of the adduct to aldehyde under our experimental conditions, we conducted some experiments in which the reaction time after vinyl acetate had first reacted was prolonged. As can be seen from Fig. 2, only slight increases in aldehyde concentration were found, thus confirming the slowness of this transformation observed experimentally. On the other hand, quite considerable amounts of aldehyde were present even at early stages in the reaction. This could be due to the presence of the initiator, which should be capable of affecting the radical decomposition of the adduct to the aldehyde. If this is the case, the slight increase observed in the aldehyde concentration when the reaction time was prolonged (Fig. 2) could be explained in terms of a half-life of *c.* 1 h for AIBN [11], with the slow thermal decomposition of the adduct being now the main reaction.

To explain aldehyde formation during radical addition step, the hypothesis outlined in Fig. 3 may be advanced: aldehyde could arise from the radical $C_6F_{13}CH_2C{\cdot}H{=}OCOCH_3$ which, in turn, could either be formed from interaction of the perfluorohexyl radical with a molecule of vinyl acetate (a) or from decomposition of the adduct (b).

Due to the great sensitivity of 1-iodo-2-perfluoroalkyl ethyl acetates [5] and to the chemical inertness of iodoperfluoroalkanes under the conditions of the following step, unreacted perfluorohexyl iodide was not recovered at the end of the first step. Instead, the reaction mixture obtained from the radical addition directly underwent acid hydrolysis. The most appropriate length of time for hydrolysis was determined by recurrent GLC analysis of the reaction mixture; a period of 2 h was generally sufficient.

Finally, in an attempt to avoid the formation of a precipitate during the oxidation step, some experiments were undertaken using 7% aqueous K_2CrO_4 solution as an oxidizing agent, but an appreciable decrease in the yield of product was observed in this instance.

Comparison between the method described here and the procedure in which perfluoroalkyl acetic acids are prepared from the corresponding alcohols (Fig. 1) could be made by considering the yield of the final product obtained before the oxidation step. In ref. 5, a 67% yield was reported for $C_3F_7CH_2CH_2OH$ and a 74% yield could be calculated for $C_7F_{15}CH_2CH_2OH$. The higher yield (91.0%) for aldehyde obtained in our experiments, together with the simpler procedure, favour the modified method proposed here.

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