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A new preparative route to α-fluoroacrylic acid

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Abstract

Rhodium-catalyzed hydroformylation of vinyl fluoride (VF) followed by careful oxidation of the regiospecifically produced 2-fluoropropanal afforded 2-fluoropropanoic acid (**2**) in about 70% yield. Dehydrogenation of **2** to α-fluoroacrylic acid (**1**) was accomplished by a chlorination-dehydrochlorination reaction in more than 60% yield.

Keywords: Fluoroacrylic acid; Fluoroacrylates; Fluorinated monomers

1. Introduction

Esters of α-fluoroacrylic acid (**1**) represent a class of valuable monomers to produce polymeric materials with outstanding technological properties. There are many areas of potential application of these polymers, such as optical glasses, high performance optical fibers, membranes, coatings, etc. [1–3].

Moreover, α-fluoroacrylic acid derivatives are employed as starting compounds for the synthesis of more complex organofluorine compounds [4,5]. The fact that materials based on **1** have difficulty in finding applications on a commercial scale is mainly due to the poor current accessibility to suitable precursors of α-fluoroacrylates. In the last 20 years many efforts have been made to devise synthetic schemes able to be converted into semi-industrial processes.

Among the numerous preparative methods reported in the literature, particularly interesting are those starting from monofluorinated precursors or intermediates to avoid the uneconomical loss of one or more fluorine atoms during the various steps of synthetic schemes [2].

Thus, the large-scale synthesis of 2-fluoroacrolein was accomplished by reacting chlorofluorocarbene with butyl vinyl ether followed by thermal opening of the cyclopropane adduct that, in the presence of an alcohol, leads to the acetal of α-fluoroacrolein [6]; this intermediate is transformed in three steps into α-fluoroacrylic esters [7]. The overall yields of α-fluoroacrylates were in the range of 30–32%.

More recently esters of **1** were prepared by nucleophilic addition of dialkyl fluoromalonates, easily accessible by condensation reaction between fluoroacetic acid and diethyl oxalate followed by decarbonylation of the intermediate oxoester, to formaldehyde in the presence of different bases [8–10]. The primary products of this reaction are dialkyl α-fluoro-α-hydroxymethyl malonates which undergo hydrolysis, decarboxylation and dehydration to give **1** in a yield not exceeding 50%.

In 1991, a research group of Bayer AG (Leverkusen) described a new route to **1** involving the regioselective nitrofluorination of 2,3-dichloropropene to 1-nitro-2-fluoro-2,3-dichloropropane followed by its oxidation with concentrated sulfuric acid to 2-fluoro-2,3-dichloropropanoic acid; esterification and dechlorination of this intermediate with activated zinc powder produced α-fluoroacrylates in 20–30% overall yield [2].

The synthetic schemes to **1** so far reported in the literature, however, will hardly be the basis of a semi-industrial process, because each of them involves the use of expensive, toxic or dangerous starting materials and/or reagents.

Therefore, in connection with our investigations on the preparation of acrylic monomers having one or more fluorine atoms in definite positions of their molecules [11–14] we decided to explore alternative routes to **1** capable to be scaled-up to a 10–100 kg commercial production.

In turn, these monomers, which are attracting a steadily growing interest, can be conveniently copolymerized with unfluorinated acrylic esters or vinyl ethers to give various types of new macromolecular compounds endowed with outstanding technological properties and hence, successfully employed as new protective materials for artistic and/or historical stone monuments [11,15,16].

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2. Experimental section

2.1. General

Vinyl fluoride (VF), $Rh_4(CO)_{12}$ and Aliquat® 336 were Aldrich products. SO_2Cl_2 (Aldrich) was distilled before use. α,α′-Azoisobutyronitrile (AIBN) was purchased from Fluka. Solvents were purified following well-known procedures [17]. 2-Fluoropropanal was obtained in 70% yield by hydroformylation of vinyl fluoride as described by Ojima et al. [18]. ^{1}H NMR spectra ($CDCl_3$ solutions) were recorded using a 200 MHz Brucker AC 200. IR spectra were obtained using a Bio-Rad FTS-40 interferometer. GC-MS spectra were recorded using an HP 5971 series mass spectrometer.

2.2. Preparation of 2-fluoropropanoic acid (2)

A solution of $NaClO_2$ (22 g, 0.24 mol) in 240 ml of water was added drop-wise to a stirred solution of 2-fluoropropanal (13 g, 0.17 mol) in 170 ml of acetonitrile, NaH_2PO_4 (5.5 g, 0.046 mol) in 68 ml of water and 17 ml of 35% H_2O_2, keeping the temperature at 10°C with ice-cooling. Oxygen evolution from the solution was monitored, by a bubbler connected to the apparatus, until the end of the reaction and Na_2SO_3 (1.7 g, 0.03 mol) was added to destroy the unreacted H_2O_2 and HOCl. The solution was acidified with 10% HCl and pure 2-fluoropropanoic acid (**2**) was obtained by distillation in vacuo (59–60°C/8 mmHg) [19] in 80% yield.

^{1}H NMR ($CDCl_3$) δ (ppm), J (Hz): 7.5 (bs, 1H), 5.09 (dq, 1 h, $J_{H-F} = 48.2$, $J_{H-H} = 6.71$), 1.66 (dd, 3H, $J_{H-F} = 23.2$, $J_{H-H} = 6.71$).

GC-MS (*m/e*): 92 $(M)^+$, 75 $(M–OH)^+$, 55 $(75\text{-}HF)^+$, 47 $(CH_3CHF)^+$, 27 $(CH_2CH)^+$. IR (KBr) ν (cm^{-1}): 3500–3000 (OH), 2990 (CH), 1740 (C=O), 1464 (δ_{ass} CH_3).

2.3. Preparation of 2-chloro-2-fluoro-propanoic acid (3) and 3-chloro-2-fluoro-propanoic acid (4)

A solution of 2-fluoropropanoic acid (**2**) (1.5 g, 16.2 mmol) in 30 ml of anhydrous benzene was heated at reflux in a nitrogen atmosphere and SO_2Cl_2 (4.37 g, 32.4 mmol) was added drop-wise. Then, AIBN (0.2 g, 1.2 mmol) was added in small portions. The mixture was maintained at reflux for 82 h, adding every 12 h SO_2Cl_2 (1 ml) and small portions of AIBN to a total amount of 0.1 g. The solution was then cooled to room temperature and excess SO_2Cl_2 and benzene were distilled off. ^{1}H NMR analysis of the reaction mixture showed an 80% conversion with the formation of 2-chloro-2-fluoro-propanoic acid (**3**) (62%) and 3-chloro-2-fluoro-propanoic acid (**4**) (18%). ^{1}H NMR spectrum of the reaction mixture showed, besides the signals due to the unreacted 2-fluoropropanoic acid, the following pattern:

^{1}H NMR ($CDCl_3$) δ (ppm): 5.78 (bs, 1H, –OH), 5.36–5.12 (tt, 2H, C**H$_2$**Cl–CHF–), 4.04–3.90 (dd, 1H, CH_2Cl–C**H**F–), 2.20–2.10 (d, 3H, C**H$_3$**–CFCl–).

2.4. Preparation of α-fluoroacrylic acid (1)

A mixture of *t*-BuOK (5.67 g, 0.05 mol) in 20 ml of anhydrous toluene and Aliquat® 336 (0.22 g, 10% by weight) was heated at reflux in a nitrogen atmosphere, and a solution of 13 mmol of the two fluoro-chloro-propanoic acids **3** and **4** previously obtained dissolved in 15 ml of anhydrous toluene, was added drop-wise. The mixture was maintained at reflux for 5 h and then cooled to room temperature. The solid product formed was filtered, washed several times with diethyl ether, suspended in ether and acidified with anhydrous HCl. Pure α-fluoroacrylic acid (**1**) was obtained by sublimation in vacuo in 60% yield with respect to 2-fluoropropanoic acid (**2**).

^{1}H NMR ($CDCl_3$) δ (ppm), J (Hz): 6.75 (bs, 1H), 5.85 (dd, 1H, $J_{H-F} = 42.7$, $J_{H-H} = 3.4$), 5.5 (dd, 1H, $J_{H-F} = 12.8$, $J_{H-H} = 3.4$).

IR (KBr) ν (cm^{-1}): 3150 (OH), 2925 (C–H), 1734 (C=O), 1654 (C=C), 1200 (C–F); pf 51°C.

3. Results and discussion

It is known that vinyl fluoride (VF), an easily available important monomer used in the polymer industry to produce high-performance homo- and co-polymers [20], can be hydroformylated under standard conditions in the presence of rhodium carbonyl complexes to 2-fluoropropanal in good yields (up to 81%) [18]. This aldehyde is regiospecifically formed regardless of the metal catalyst species, but only rhodium based catalytic systems ensure satisfactory yields (50–80%) [18].

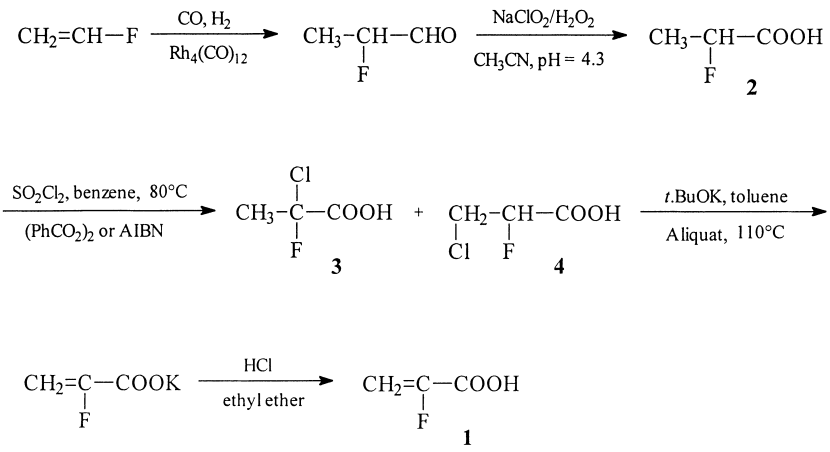
In the synthetic scheme used by us, this aldehyde, obtained in 70% yield by subjecting VF to the *oxo*-reaction at 100°C and 100 atm ($CO/H_2 = 1$) using $Rh_4(CO)_{12}$ as the catalyst precursor in toluene, was converted in high yield to 2-fluoropropanoic acid (**2**) by oxidation with $NaClO_2/H_2O_2$ system in acetonitrile (Scheme 1) [21].

This two-step transformation of vinyl fluoride to 2-fluoropropanoic acid represents the first example of a particularly attractive straightforward route to 2-fluoroalkanoic acids, a class of compounds which have currently aroused great interest of the researchers in the biochemistry area [22–24].

To our knowledge, only few methods for the preparation of these fluorinated acids are described in the literature [25–27].

Our alternative method, that might turn out to be more convenient, involves the hydroformylation of alkenyl fluorides, R–CH=CH–F or RR′C=CH–F, a class of substrates easily accessible from the corresponding aldehydes or ketones by Wittig reactions [28].

Acid **2** underwent free-radical chlorination with SO_2Cl_2 in benzene at 80°C, using α,α′-azoisobutyronitrile (AIBN) or dibenzoyl peroxide as radical initiator [29]. Beside the expected α-chlorination of **2**, β-chlorination also took place under the adopted reaction conditions; the total chlorination



Scheme 1.

yield reached about 80%. The value of **3**-to-**4** molar ratio (3.4/1) was determined by ^{1}H NMR analysis, from the signals at 2.20–2.10 (d, C**H**$_3$–CFCl–), at 4.04–3.90 (dd, CH$_2$Cl–C**H**F–) and at 5.36–5.12 (tt, C**H**$_2$Cl–CHF–).

The first dehydrochlorination experiments of the mixture of the haloacids **3** and **4** were accomplished using potassium hydroxide in methanol at reflux [30]: whereas the β-chlorinated acid was transformed into **1** (potassium salt), compound **3** did not react. In order to transform both **3** and **4** into the acid **1**, we carried out this reaction with *t*-butoxide (3.1 mol excess) in toluene at reflux [31]. In this case, the halo acid **4** was rapidly converted into **1** but the acid **3** required a much longer reaction time (8 h) and underwent no more than 30% dehydrochlorination. This elimination reaction, however, was carried out in a non homogeneous medium: this might be responsible for the low reaction rate observed, even though we used very efficient stirring. The use of a phase-transfer agent such as Aliquat® 336 brought about a remarkable enhancement of the dehydrochlorination rate: after 5 h both compounds **3** and **4** were converted to **1** (potassium salt) in about 80% yield. The free acid **1** was then easily obtained by treatment of an etheral suspension of the potassium salt with anhydrous HCl.

The synthetic scheme to **1** proposed by us needs further studies for optimization; however, it allows preparation of the valuable monomer **1** from an easily available starting compound (VF) in four steps using relatively simple reactions and cheap chemicals.

References

[1] L.S. Boguslavskaya, I. Yu Panteleeva, T.V. Morozova, A.V. Chuvatkin, N.N. Kartashov, Russian Chem. Rev. 59 (1990) 906, and references therein.

[2] K-R. Gassen, D. Bielefeldt, A. Marhold, P. Andres, J. Fluor. Chem. 55 (1991) 149, and references therein.

[3] C. Botteghi, U. Matteoli, S. Paganelli, V. Fassina, V. Castelvetro, M. Aglietto, in: Proceedings of the 5th International Symposium on the Conservation of Monuments in the Mediterranean Basin, Seville, Spain, 5–8 April 2000, p. 222.

[4] C. Wakselmann, Macromol. Symp. 82 (1994) 77, and references therein.

[5] K.W. Laue, G. Haufe, Synthesis (1998) 1453.

[6] H. Molines, T. Nuygen, C. Wakselmann, J. Chem. Soc., Chem. Commun. (1985) 754.

[7] H. Molines, T. Nuygen, C. Wakselmann, Synthesis (1985) 755.

[8] R. Heumüller, G. Siegemund, G. Wieners, P. Herbrechtsmeier (Hoechst AG), European Patent 0 203 462 (1986/85); C.A. 106 (1987) 156993u.

[9] A. Thenappan, D.J. Burton, J. Org. Chem. 55 (1990) 4639.

[10] A. Thenappan, D.J. Burton, J. Fluor. Chem. 48 (1990) 153.

[11] M. Aglietto, E. Passaglia, L. Montagnini di Mirabello, C. Botteghi, S. Paganelli, U. Matteoli, Macromol. Chem. Phys. 196 (1995) 2843.

[12] C. Botteghi, C. Lando, U. Matteoli, S. Paganelli, G. Menchi, J. Fluor. Chem. 83 (1997) 67.

[13] U. Matteoli, C. Botteghi, F. Sbrogiò, V. Beghetto, S. Paganelli, A. Scrivanti, J. Mol. Catal. A: Chem. 143 (1999) 287.

[14] C. Botteghi, S. Paganelli, F. Sbrogiò, C. Zarantonello, Tetrahedron Lett. 40 (1999) 8435.

[15] C. Botteghi, U. Matteoli, S. Paganelli, R. Arbizzani, F. Ciardelli, M. Aglietto, E. Taburoni, V. Fassina, Sci. Technol. Cult. Herit. 1 (1992) 111.

[16] U. Matteoli, M. Aglietto, V. Fassina, C. Botteghi, E. Passaglia, F. Ciardelli, in: Proceedings of the International Colloquium on Methods of Evaluation of Products for the Conservation of Porous Building Materials in Monuments, Rome, 19–21 Giugno 1999, p. 373.

[17] D. Perrin, L.F. Armarego, Purification of Laboratory Chemicals, 3rd Edition, Pergamon Press, Oxford, 1988.

[18] I. Ojima, K. Kato, M. Okabe, T. Fuchikami, J. Am. Chem. Soc. 109 (1987) 7714.

[19] G.A. Olah, J.T. Welch, Y.D. Vankar, M. Nojima, I. Kerekes, J.A. Olah, J. Org. Chem. 44 (1979) 3872.

[20] D.E. Brasure, in: Kirk-Othmer (Ed.), Encyclopedia of Chemical Technology, 3rd Edition, Vol. 11, Wiley, New York, 1980, p. 57.

[21] E. Dalcanale, F. Montanari, J. Org. Chem. 51 (1986) 567.

[22] M. Schlosser, Tetrahedron 34 (1978) 3.

[23] R. Filler, Y. Kobayashi (Eds.), Biomedical Aspects of Fluorine Chemistry, Kodansha and Elsevier Biomedical, Tokio, 1983, and references therein.

[24] R.E. Banks, B.E. Smart, J.C. Tatlow (Eds.), Organo Fluorine Chemistry: Principles and Commercial Applications, Plenum, New York, 1994, and references therein.

[25] F.L.M. Pattison, R.L. Buchanan, F.H. Dean, Can. J. Chem. 43 (1965) 1700.
[26] T. Fuchigami, Y. Nakagawa, T. Nonaka, Tetrahedron Lett. 33 (1986) 3869.
[27] S. Nakamura, H. Nohira, Mol. Cryst. Liq. Cryst. 185 (1990) 199.
[28] D.J. Burton, P.E. Greenlimb, J. Org. Chem. 40 (1975) 2796.
[29] G.M. Lampman, J.C. Aumiller, Org. Syn. 51 (1971) 73.
[30] L.S. Boguslovskaya, K.V. Yarovykh, A.B. Bulovyatova, J. Org. Chem. (USSR) (1969) 1879.
[31] D.H.R. Barton, J. Call, J.F. Mc Garrity, D.A. Widdowson, J. Chem. Soc., Perkin Trans. 1 (1973) 1565.