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FLUOROHALOGENO COMPOUNDS. II. SONOCHEMICAL APPROACH TO 3,3,3-TRIFLUOROPROPIONIC ACIDS

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SUMMARY

Fluoropropionic acids of the general formula CF_3CXYCO_2H (X = F,Cl,Br ; Y = F,Cl,Br,H) were obtained by the sonochemically promoted reaction of fluorohalogenoethanes CF_3CXYZ (Z = Cl,Br) with zinc and carbon dioxide. Penta- and tetrafluoroethanes (X = Y = F and X = F , respectively) gave good yields (35 - 47 %) of the acids; with trifluoro derivatives the yields were substantially lower. Hydrogenolysis of the C-Cl and C-Br bonds in $CF_3CFClCO_2H$ and $CF_3CFBrCO_2H$ afforded 2,3,3,3-tetrafluoropropionic acid.

INTRODUCTION

Polyfluorinated carboxylic acids are versatile intermediates in organofluorine chemistry. Their preparation, however, often requires special methods or rather drastic conditions [1]. Perfluoroalkyl iodides have been used for preparation of perfluorocarboxylic acids by carboxylation of Grignard reagents [2,3], or via organometallic compounds prepared by the action of a zinc-copper couple on the iodides [4]. More recently, an efficient ultrasound-promoted direct carboxylation of perfluoroalkyl iodides was reported [5].

The readily available fluorohalogenoethanes CF_3CXYZ (X = F,Cl,Br ; Y = F,Cl,Br,H ; Z = Cl,Br) may be used for introducing a fluorinated unit into organic molecules.

We have shown their synthetic utility by the low temperature preparation of Grignard reagents $CF_3CXYMgHal$ and their reactions with aldehydes and ketones giving fluorinated alcohols [6]. In our experiments, however, carboxylation of the Grignard reagents $CF_3CXYMgHal$ by carbon dioxide afforded only low yields of corresponding carboxylic acids [7].

The formation and reactivity of various organometallic reagents are significantly improved by the use of ultrasonic irradiation [8,9,10]. Ultrasound was found to be necessary for the trifluoromethylation of carbonyl compounds using zinc and trifluoromethyl iodide at room temperature [9]. Attempted sonochemical reactions of the fluorohalogenoethanes CF_3CXYZ with zinc and aldehydes or ketones in dimethylformamide gave only low yields of alcohols [7].

In the effort to convert the fluorohalogenoethanes CF_3CXYZ into carboxylic acids, we applied the recently published Ishikawa s method of direct carboxylation using zinc and carbon dioxide under ultrasonic irradiation [5]. Reactivity of various combinations of halogens in the -CXYZ moiety was compared, and in the case of CF_3CFBr_2 (III), comparison between mechanically stirred and ultrasound-promoted reaction was made. Carboxylation of the low-boiling bromopentafluoroethane (I) at atmospheric pressure seemed to be a useful alternative for the synthesis of pentafluoropropionic acid (VII). Conversions of the chlorine- and bromine-containing acids $CF_3CFClCO_2H$ (VIII) and $CF_3CFBrCO_2H$ (IX) were expected to provide a route to 2,3,3,3-tetrafluoropropionic acid (XI).

RESULTS AND DISCUSSION

Fluorohalogenoethanes CF_3CXYZ (I-VI) reacted with zinc and carbon dioxide in dimethylformamide under ultrasonic irradiation in a flask immersed in a laboratory cleaning bath to give 3,3,3-trifluoropropionic acids (VII-XIV) according to Table 1. Yields of the reactions depended strongly on the structure of the ethanes. The best results were obtained with the tetrafluoro (II and III) and pentafluoro (I) derivatives. The other ethanes, including hydrogeno compound VI, gave only low yields of the corresponding acids.

TABLE 1

Sonochemical reactions of fluorohalogenoethanes with zinc and carbon dioxide

$$\underset{\text{I - VI}}{CF_3CXYZ} + Zn + CO_2 \xrightarrow[2.\ H_2O/H^+]{1.\ DMF,\ ((\cdot} \underset{\text{VII-X, XII}}{CF_3CXYCO_2H} + \underset{\text{XI - XIII}}{CF_3CXHCO_2H} + \underset{\text{XIV}}{CF_3CH_2CO_2H}$$

Starting ethane CF_3CXYZ				Products (%) [a]		
No.	X	Y	Z	CF_3CXYCO_2H	CF_3CXHCO_2H	$CF_3CH_2CO_2H$
I	F	F	Br	VII (35.2)		
II	F	Cl	Br	VIII (38.3) (46.9)[b]	XI (1.4) (2.4)[b]	
III	F	Br	Br	IX (42.8) (47.2)[b]	XI (4.9) (15.2)[b]	
IV	Cl	Cl	Cl	X (13.6)	XII (2.1)	
V	Br	Br	Br		XIII (1.0)	XIV (0.1)
VI	Cl	H	Br	XII (7.2)		

[a] For compounds VII-X and XII from VI, isolated yields are quoted; for XI-XIV yields were calculated from ^{19}F NMR spectra.

[b] Zn/ethane ratio 2:1

In reactions of ethanes II-IV, acids XI-XIV were detected as minor products. These compounds were formed despite the careful separation of the excess of zinc before the acid decomposition of the reaction mixture, which suggests their formation during the course of the sonochemical reaction. The amount of hydrogeno acid XI in reactions of ethanes II and III depended on the initial ratio Zn/ethane (Table 1).

N,N-Dimethylformamide (DMF) was earlier found to be the best solvent for the carboxylation reaction [5]. Experiments using N,N-dimethylacetamide or N-methylpyrrolidinone afforded lower yields of the acids. In dioxane, dimethoxyethane or tetrahydrofuran only reduction or decomposition of starting ethanes occurred and no carboxylic acids were isolated.

The acid hydrolysis of the reaction mixture after the sonochemical carboxylation and its extraction by ether yielded in all cases after distillation 1:1 complexes of an acid and dimethylformamide. These complexes could be distilled without any change in composition at boiling points higher than those of both their components. Very pure free acids were isolated by distillation of the complexes with concentrated sulphuric acid [11]. In Table 2, comparison of boiling points of the free acids and the /acid.DMF/ complexes is given. With other N,N-dialkylamides (N,N-dimethylacetamide, N-methylpyrrolidinone) analogous complex formation was observed.

The mechanically stirred reaction of 1,1-dibromotetrafluoroethane (III) with Zn and CO_2 without the use of ultrasound yielded the acid IX in substantially lower yield (25.2 %) than the sonochemically promoted reaction (42.8 %), along with the minor acid XI (6.0 %).

Simultaneous action of CO_2 and ultrasound on the reaction mixture was found to be necessary for the sonochemical carboxylation to proceed. 'Blank' experiments, when the reaction mixture was irradiated by ultrasound without introducing CO_2 and only then treated with it, gave no carboxylic acid at all. Also, decomposition of the ultrasonically irradiated reaction mixture of Zn and the ethane III in DMF by water led to recovery of a substantial part (85 %) of the starting ethane.

Results of the carboxylation of the low boiling (-20°C) bromopentafluoroethane (I) under atmospheric pressure illustrate the reactivity in the sonochemical reaction and offer an alternative synthesis of pentafluoropropionic acid (VII).

The sonochemically prepared 2-chloro- and 2-bromo-tetrafluoropropionic acids (VIII and IX) were smoothly converted to 2,3,3,3-tetrafluoropropionic acid (XI) by their reduction using zinc and diluted hydrochloric acid.

$$CF_3CFYCO_2H \xrightarrow{Zn/HCl} CF_3CFHCO_2H$$

VIII Y=Cl
IX Y=Br

XI

TABLE 2

Boiling points of fluoropropionic acids and their complexes with dimethylformamide

Compound	Boiling point (°C/mm Hg)			
	free acid			/acid.DMF/
	found	reported	Ref.	found
$CF_3CF_2CO_2H$ (VII)	98	95.5	[12]	188
$CF_3CFClCO_2H$ (VIII)	45/12	134-6	[13]	103/15
$CF_3CFBrCO_2H$ (IX)	53/12	60/22	[14]	115/18
$CF_3CCl_2CO_2H$ (X)	57/12	156/625	[15]	113/17
CF_3CFHCO_2H (XI)	55/17	130/600	[16]	94/12
$CF_3CClHCO_2H$ (XII)	56/15	(nc)		98/17

TABLE 3

NMR spectral data of fluoropropionic acids

Compound	^{19}F (ppm, r.i., J in Hz)		^{1}H (δ ppm, r.i., J in Hz)	
	CF_3	CFY	CXH	CO_2H
VII	83.6 3F s 83.6^a	122.8 2F s 122.1^a		7.52 s 15.02^a s
VIII	80.1 3F d J=7 80.1^a	133.9 1F q J=7 131.6^a		11.48 broad s 15.20^a s
IX	78.4 3F d J=9 78.4^a	136.9 1F q J=9 134.1^a		11.78 broad s 15.25^a s
X	76.7 s			11.85 broad s
XI	76.8 3F dd J_1=12 76.6^a J_2=6	206.8 1F dq J_d=46 204.4^a J_q=12	5.20 1H dq J_d=46 5.03^a J_q=6	11.34 broad s 13.80^a s
XII	72.2^a d J=6		4.75^a 1H q J=6	13.63^a s
XIII	69.9^a d J=7		4.59^a 1H q J=7	13.60^a s
XIV	64.4 t J=9.5		3.21 2H q J=9.5	10.28 s

[a] Data obtained from the /acid.DMF/ complex

EXPERIMENTAL

General procedures

Boiling points are uncorrected. All prepared compounds were characterized by NMR (^{19}F and ^{1}H) and infrared spectroscopy and by elemental analyses. NMR spectra were recorded in deuteriochloroform on Varian XL-100/15 and Tesla BS 567 spectrometers. ^{1}H chemical shifts are quoted in δ units using tetramethylsilane, and ^{19}F chemical shifts in ppm positive to high field of trichlorofluoromethane, both internal references. Infrared spectra were obtained by use of the Perkin-Elmer 325 instrument.

Sonochemical reactions were carried out with an ultrasonic laboratory cleaner (25 kHz, 160 W, Tesla UC002 BM-1, 4 litres) in glass vessels. Commercially available zinc powder (Lachema) was used. Solvents (DMF, N,N-dimethylacetamide and N-methylpyrrolidinone) were dried by azeotropic distillation with benzene and stored over molecular sieves. Carbon dioxide for carboxylation reactions was prepared by the evaporation of dry ice and dried by passing it through a tube filled with anhydrous $CaCl_2$. Fluorohalogenoethanes I-VI were prepared or purchased as described [6].

Sonochemically promoted carboxylation reactions

Gaseous carbon dioxide was bubbled into a suspension of Zn (3.9 g, 60 mmol), fluorohalogenoethane (60 mmol) and dry dimethylformamide (60 ml) in a flask under the dry ice reflux condenser for 15 minutes. The flask was then immersed into the water bath of a laboratory ultrasonic cleaner and irradiated by ultrasound with continuous bubbling of CO_2 until condensation of the starting ethane ceased (usually 6 hours). In the case of bromopentafluoroethane (I) (b.p. -20°C), the weighed amount of the compound was evaporated from another flask and introduced into the suspension simultaneously with CO_2 by the same procedure. The solution was then separated from unreacted zinc, and 100 ml of diluted (1:4) hydrochloric acid was added. Extraction by ether, drying of the ether solution by anhydrous $MgSO_4$ and

TABLE 4

Elemental analyses of fluoropropionic acids and the /acid.DMF/ complexes

	% Found Calcd.					
Compound	C	H	F	Cl	Br	N
VII	21.61 21.97	0.89 0.61	57.66 57.91			
/VII.DMF/	30.46 30.39	3.65 3.40	39.70 40.06			5.54 5.91
VIII	20.15 19.96	0.87 0.56	41.94 42.11	19.40 19.64		
/VIII.DMF/	28.46 28.42	3.43 3.18	30.51 29.97	13.74 13.98		5.28 5.52
IX	15.87 16.02	0.60 0.45	34.23 33.78		35.95 35.52	
/IX.DMF/	23.85 24.18	2.58 2.71	25.90 25.50		26.58 26.81	4.40 4.70
X	18.04 18.30	0.87 0.51	28.62 28.94	36.31 36.01		
/X.DMF/	26.96 26.69	2.79 2.99	21.04 21.11	26.15 26.26		5.37 5.19
XI	25.02 24.67	1.71 1.38	51.83 52.03			
/XI.DMF/	32.51 32.88	4.10 4.14	34.57 34.68			6.56 6.39
XII	22.45 22.17	1.51 1.24	34.91 35.07	22.05 21.82		
/XII.DMF/	30.50 30.59	3.82 3.85	24.36 24.19	15.16 15.05		5.68 5.94

evaporation of ether yielded crude /acid.DMF/ complexes, which were purified by vacuum fractionation. Yields of the experiments are summarized in Table 1, boiling points, spectral data and elemental analyses in Tables 2,3 and 4.

Free fluoropropionic acids were isolated by careful mixing of the /acid.DMF/ complex with an equal volume of concentrated sulphuric acid and by following distillation [11].

Mechanically stirred reaction of CF_3CFBr_2 (III) with zinc and carbon dioxide

A suspension of Zn (3.9 g, 60 mmol), III (15.6 g, 60 mmol) and dry DMF (60 ml) was saturated by introducing dry CO_2 (15 minutes) and then stirred by a magnetic stirrer in a flask fitted with a dry-ice cooled reflux condenser, in a bath at 60°C. Gaseous CO_2 was continuously introduced by a tube to the bottom of the flask. After 6 hours of reaction, the dark brown solution was separated from unreacted zinc, and acids IX and XI were isolated by the above described procedure. Yields of acids IX and XI were 3.4 g (25.2 %) and 0.52 g (6.0 %), respectively.

2,3,3,3-Tetrafluoropropionic acid (XI)

To a stirred solution of 8.2 g (27.5 mmol) of the /IX.DMF/ complex (or 6.2 g, 27.5 mmol of the free acid IX) in 100 ml of diluted (1:4) HCl was added 3.3 g (50 mmol) of Zn powder in four portions. Within 2 hours Zn dissolved completely and the clear solution was extracted by ether. After evaporation of dried ($MgSO_4$) ether solution, 2,3,3,3-tetrafluoropropionic acid (XI) (b.p. 55°/17 mm Hg, yield 3.5 g, 87 %) was isolated by fractionation. The same procedure starting from VIII (4.7 g, 26 mmol) yielded 3.6 g (94.8 %) of XI.

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