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On the reaction of perfluoroalkyl halides in the presence of alcohols and bases

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Abstract

Perfluoroalkyl halides react in the presence of bases and alcohols to give the corresponding 1*H*-perfluoroalkanes. The kinetics of the reaction were studied. The mechanism seems to involve perfluoroalkyl radicals and anions.

Introduction

Perfluorooctyl bromide is used as an oxygen carrier in blood substitutes [1]. For this purpose, it has to be free of impurities such as 1*H*-perfluoroalkanes. For chemical purification, the stability of perfluorooctyl bromide is important. The stability of perfluoroalkyl halides in the presence of bases and alcohols has been examined. For this purpose, the amount of perfluoroalkyl halide consumed (conversion) and the formation of 1*H*-perfluoroalkanes were monitored.

Compounds of the 1*H*-perfluoroalkane type have been described in the literature since 1952 [2]. They are often stated as being by-products of different reactions of perfluoroalkyl halides [3–7]. The electrochemical reduction of perfluoroalkyl halides indicates a single electron-transfer (SET) mechanism for these reactions [8].

Results and discussion

Perfluoroalkyl halides react in the presence of bases and alcohols. Scheme 1 shows the reaction involved. The perfluoroalkyl halide is reduced by the alcohol via a redox reaction to the 1*H*-perfluoroalkane, and the alcohol is oxidized to the corresponding aldehyde or ketone. The reaction stops at the level of the aldehyde or ketone.

Table 1 shows the conversion of perfluoroalkyl halides and the yield of 1*H*-perfluoroalkanes with various alcohols and bases. With alcohols not capable

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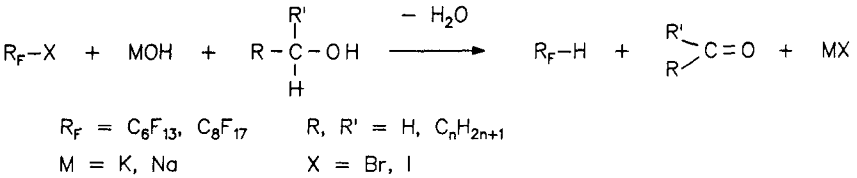

Scheme 1. Reaction of perfluoroalkyl halides with base and alcohol.

TABLE 1

Conversion and yield in the reaction $R_FX \rightarrow R_FH$ with various bases and alcohols at 60 °C

Alcohol	KOH			NaOH		
	$C_8F_{17}I$	$C_6F_{13}I$	$C_8F_{17}Br$	$C_8F_{17}I$	$C_6F_{13}I$	$C_8F_{17}Br$
Methanol	92/31[a]	91/86	–/–[b]	66/65	93/85	–/–
Ethanol	79/64	67/55	5/4	41/40	44/42	3/3
1-Propanol	95/31	97/67	–/–	37/35	45/44	–/–
i-Propanol	100/46	100/88	74/66	97/94	95/94	11/11
1-Butanol	97/95	n.e.[c]	4/2	n.e.	n.e.	7/1
2-Butanol	92/73	n.e.	24/17	n.e.	n.e.	17/17
i-Butanol	89/60	n.e.	18/12	n.e.	n.e.	5/1

[a] Conversion of R_FX (%) yield of R_FH (%). Both were determined by GC methods through comparison with *F*-hexane as an internal standard.

[b] –/– = no reaction occurred.

[c] n.e. = not examined.

of forming carbonyl compounds, such as t-butanol and phenol, no reaction occurred. Conversion depended on the base used. For the stronger base potassium hydroxide, conversion of the perfluoroalkyl halides was greater than with sodium hydroxide, especially for perfluorooctyl bromide. The yield did not necessarily increase with higher conversion. The perfluoroalkyl halides reacted more vigorously in the presence of potassium hydroxide than in the presence of sodium hydroxide. Perfluoroalkyl iodides were more reactive than perfluoroalkyl bromides, as they reacted even at temperatures well below 0 °C.

The kinetics of the reaction of perfluorooctyl bromide with potassium hydroxide and alcohols were studied by GC methods. The progress of the reaction was monitored by the decrease of perfluorooctyl bromide and the increase of 1*H*-perfluorooctane. The concentrations were determined against perfluorohexane as an internal standard. Figure 1 shows the dependence of the yield of 1*H*-perfluorooctane derived from perfluorooctyl bromide on the amount of potassium hydroxide and i-propanol at 70 °C. When the amount of these two compounds was less than that of perfluorooctyl bromide, the yield depended linearly on the amount of potassium hydroxide and i-propanol employed. None of these compounds acted as a catalyst because they reacted

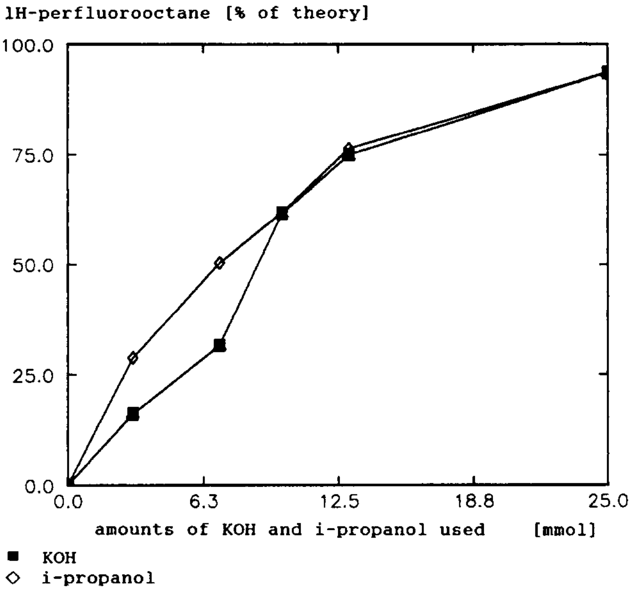

Fig. 1. Dependence of the yield of 1*H*-perfluorooctane on the amount of potassium hydroxide and i-propanol employed in the reaction with 8 mmol of perfluorooctyl bromide. Yield of 1*H*-perfluorooctane given as a percentage of the theoretical value for complete conversion of the perfluorooctyl bromide used (detection by GC methods and expressed in area %).

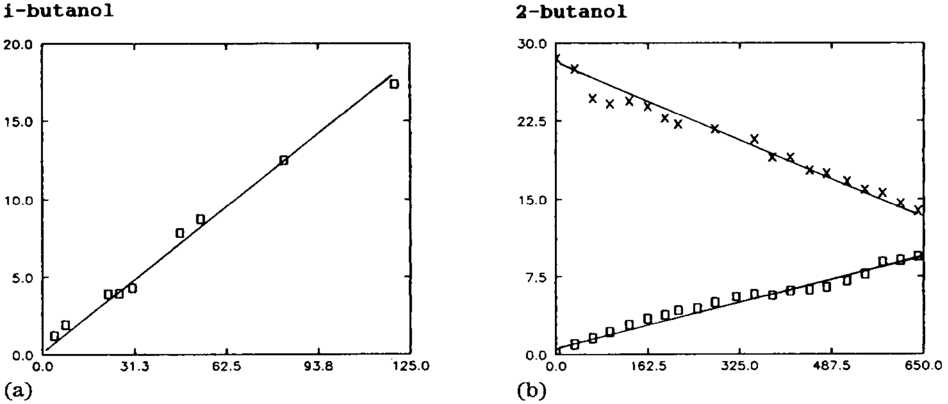

Fig. 2. Kinetics of the reaction of (a) i-butanol and (b) 2-butanol with KOH and perfluorooctyl bromide at 20 °C. Concentrations of 1*H*-perfluorooctane and perfluorooctyl bromide were determined by GC methods using *F*-hexane as a standard (area %). Perfluorooctyl bromide was not determined in the reaction with i-butanol. □ 1*H*-perfluorooctane, × perfluorooctyl bromide.

in equimolar amounts with perfluorooctyl bromide. Excess of either of these compounds raised the yield of 1*H*-perfluorooctane.

Plots necessary for the determination of the reaction order for perfluorooctyl bromide and 1*H*-perfluorooctane are given in Fig. 2. The reaction was performed at 20 °C and 70 °C with i-butanol and 2-butanol, using potassium hydroxide as the base. These investigations led to unexpected results. Thus, the decrease in the concentration of perfluorooctyl bromide and the increase in that of 1*H*-perfluorooctane was linear. This implies that the reaction is zero order for both perfluorooctyl bromide and 1*H*-perfluorooctane.

Perfluoroalkyl halides are soluble in alcohols. Addition of a base lowers this solubility and phase separation occurs, resulting in a system with three different phases, i.e. an alcoholic phase with base and perfluoroalkyl halide, a perfluoroalkyl halide phase with some alcohol and no base and a solid phase. The rate of reaction was determined by the constant concentration of base and perfluoroalkyl halide in the alcoholic phase.

Table 2 lists the influence of different reaction conditions on the ratio of 1*H*-perfluorooctane to perfluorooctyl bromide in a system with i-propanol and potassium hydroxide. For a constant reaction time, the ratio is somewhat higher with ultrasonic treatment and much lower on reaction with an 8 N solution of potassium hydroxide in water. Ultrasonic treatment increased the interfacial area of all three phases and hence the reaction proceeded somewhat faster. The addition of water drastically lowered the solubility of the perfluoroalkyl halides in the alcohols and thus the reactions proceeded more slowly.

Two different mechanisms are discussed in the literature for perfluoroalkyl halides [4, 9] and these are shown in Fig. 3. The first step in both mechanisms is a single electron transfer (SET) to form a perfluoroalkyl halide radical anion. This perfluoroalkyl halide radical anion has two possible pathways for reaction: (i) release of a halide anion, leaving a perfluoroalkyl radical behind; and (ii) release of a halogen radical, leaving a perfluoroalkyl anion behind. In 1990, Rozhkov [9] described the anionic pathway for the reaction of tertiary perfluoroalkyl bromides. The reaction via perfluoroalkyl radicals is that usually described as the mechanism for n-perfluoroalkyl halides [4, 10].

To distinguish between the two mechanisms, reactions were performed with different additives. The results obtained are listed in Table 3. The SET step was demonstrated by the partial suppression of the reaction with

TABLE 2

Dependence of the $C_8F_{17}H/C_8F_{17}Br$ ratio[a] for the reaction $C_8F_{17}Br \rightarrow C_8F_{17}H$ on various conditions at 60 °C

Conditions	$C_8F_{17}H$	$C_8F_{17}Br$
$C_8F_{17}Br$, KOH, i-propanol	200	100
$C_8F_{17}Br$, KOH, i-propanol, $\gg$[b]	250	100
$C_8F_{17}Br$, KOH, 8 N, i-propanol	260	100

[a] Estimated by GC methods (area %).

[b] Ultrasound.

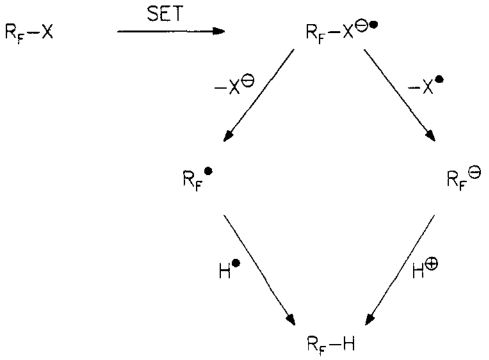

Fig. 3. Two possible pathways for the reaction of perfluoroalkyl halides.

TABLE 3

Dependence of the $C_8F_{17}H/C_8F_{17}Br$ ratio[a] for the reaction $C_8F_{17}Br \rightarrow C_8F_{17}H$ on additives

Conditions	$C_8F_{17}H$	$C_8F_{17}Br$
$C_8F_{17}Br$, KOH, i-propanol	200	100
$C_8F_{17}Br$, KOH, i-propanol, *p*-DNB[b]	4	100
$C_8F_{17}Br$, KOH, i-propanol, hex-1-ene	80	100
$C_8F_{17}Br$, KOH, i-propanol, $CaCl_2$	60	100

[a] Estimated by GC methods (area %).
[b] *p*-DNB = *p*-dinitrobenzene.

TABLE 4

Fluoride anion analysis of the alcoholic phase for different perfluoroalkyl halides and 1*H*-perfluorooctane

R_FX	R_FX concentration (mol)	Fluoride anion concentration mol
$C_6F_{13}I$	0.02	1.7×10^{-3}
$C_8F_{17}I$	0.02	1.9×10^{-3}
$C_8F_{17}Br$	0.02	1.3×10^{-3}
$C_8F_{17}H$	0.02	n.f.[a]

[a] n.f. = no fluoride anions found.

p-dinitrobenzene as a single electron-transfer scavenger. The addition of hex-1-ene to the reaction of perfluoroalkyl bromide with potassium hydroxide and i-propanol lowered the ratio from about 2:1 to 1:1. The first-formed perfluoroalkyl fragment apparently reacts with hexene and hence can be considered to be a perfluoroalkyl radical. An even greater decrease in the yield of 1*H*-perfluorooctane occurred upon addition of calcium chloride. The formation of calcium fluoride is only possible with a perfluoroalkyl anion.

The results of analyses of the alcoholic phase with a fluoride-sensitive electrode are given in Table 4. The formation of fluoride anions was almost independent of the nature of the halogen. The fluoride anions must therefore originate from a perfluoroalkyl anion since no detectable trace of fluoride anion was found in the formation of 1*H*-perfluorooctane from i-propanol and potassium hydroxide.

The reactions of n-perfluoroalkyl halides are usually described as proceeding by a radical mechanism. However, conversion of perfluoroalkyl halides to 1*H*-perfluoroalkanes in the presence of alcohols and bases occurs via perfluorinated radicals and perfluorinated anions. A comparison of the reactivities of the various perfluoroalkyl halides shows the expected result. Perfluoroalkyl iodides react more readily than the analogous bromides. However, perfluorooctyl bromide cannot be considered to be an inert compound as it reacts readily with bases and alcohols even at 20 °C.

Experimental

Fluoride anions were determined with a Fluorid-Elektrode F500 (WTW GmbH, Weilheim, FRG). NMR spectra were recorded on a Varian EM 360L operating at 60 MHz for ^{1}H and 56.4 MHz for ^{19}F NMR spectroscopy. GC analyses were carried out on a gas chromatograph CAP 12 (Gira, France) equipped with a thermal conductivity detector. The column used was of copper 3 m×6 mm i.d. packed with 30% SE30 on Chromosorb P (60–80 mesh). The perfluoroalkyl halides were a gift from Hoechst AG (Gendorf, FRG).

In a typical reaction, 2 mmol perfluoroalkyl halide, 4 mmol base and 5 ml alcohol were refluxed for 1 h at 70 °C. After neutralization with HCl (aq.), the phases were separated and examined by GC methods. The products were identified by comparison with reference samples using ^{19}F, ^{1}H NMR and IR spectroscopy, and GC methods.

Kinetic studies were carried out in sealed vials using perfluorohexane as the internal standard.

Acknowledgement

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References

1 K. C. Lowe, *Blood Substitutes*, Ellis Horwood, Chichester, 1988.
2 R. N. Haszeldine, *J. Chem. Soc.*, (1952) 3423.
3 W. Y. Huang and H. Z. Zhang, *J. Fluorine Chem.*, *50* (1990) 133.
4 Q. Y. Chen, Z. M. Qin and Z. Y. Yang, *J. Fluorine Chem.*, *36* (1987) 149.
5 Q. Y. Chen and Z. Y. Yang, *J. Fluorine Chem.*, *28* (1985) 399.
6 A. Sekiya and N. Ishikawa, *Chem. Lett.*, (1977) 81.

7 R. N. Haszeldine, *J. Chem. Soc.*, (1952) 3423.

8 C. P. Andrieux, L. Gelis, M. Medebielle, J. Pinson and J. M. Savéant, *J. Am. Chem. Soc.*, *112* (1990) 3509.

9 F. N. Rozhkov, *3rd German–Soviet Symp. Fluorine Chem.*, Schmitten, FRG, 1990, pp. 145–154.

10 M. Yoshida and N. Kamigata, *J. Fluorine Chem.*, *49* (1990) 1.