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REACTIVITY OF TETRAALKYL AMMONIUM FLUORIDES

IN APROTIC SOLVENTS

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It is known that the overall solvation envelope of the fluoride hydrate anion contains $12 \text{ H}_2\text{O}$ molecules; the energy of hydration amounts to 107 kcal/mole [1, 2], as a result of which $F^- \cdot nH_2O$ (n = 12) in an aqueous medium is quite a weak nucleophilic and base. The weakly hydrated anion $F^- \cdot nH_2O$ (n = 2.4) becomes one of the strongest nucleophiles [3-5] in an aprotic medium and a strong base capable of detaching H^+ even from weak CH acids [6-8].

It is shown in this paper that the fluoride hydrate anion in an aprotic medium can serve as a source of the hydroxyl anion through the rupture of H^+ from a H_2O molecule on its solvation envelope and the formation of HF. Thus, tetramethyl ammonium fluoride dihydrate (I) quickly reacts with $AgClO_4$ in anhydrous CH_3CN forming a black Ag_2O precipitate: The pH of the solution changes at this time from strongly basic to acidic

$$\begin{array}{c} (\mathrm{CH}_3)_4\mathrm{NF}\cdot 2\mathrm{H}_2\mathrm{O} + \mathrm{AgClO}_4 \rightarrow (\mathrm{CH}_3)_4\mathrm{NClO}_4 + \mathrm{AgOH} + \mathrm{HF}\cdot \mathrm{H}_2\mathrm{O} \\ 2\mathrm{AgOH} \rightarrow \mathrm{Ag}_2\mathrm{O} + \mathrm{H}_2\mathrm{O} \end{array}$$

Compound (I) in anhydrous CH_3CN furnishes OH^- ions which react with perfluoroaromatic compounds. Heating (I) and perfluorotoluene (II) in CH_3CN [mole ratio (I): (II) = 5:1] led to the nucleophilic substitution of F by OH forming the perfluoro-p-cresolate (III). When the ratio of reagents (I): (II) = 2:1, (III) forms a complex with cresol (IV) under these conditions. Similar nucleophilic substitution forming complex (V) is also observed during the reaction of (I) with perfluoropyridine



The hydroxylation reaction detected shows that the fluorine anion in the $F^-(H_2O)_2$ dihydrate is formally capable of detaching H^+ from a H_2O molecule in its solvation envelope forming OH^- and HF

Institute of Heteroorganic Compounds, Academy of Sciences of the USSR, Moscow. Translated from Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya, No. 9, pp. 2048-2052, September, 1976. Original article submitted June 13, 1975.

This material is protected by copyright registered in the name of Plenum Publishing Corporation, 227 West 17th Street, New York, N.Y. 10011. No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, microfilming, recording or otherwise, without written permission of the publisher. A copy of this article is available from the publisher for \$7.50. $R_4NF \cdot 2H_2O \rightleftharpoons R_4N^+ + OH^- + HF \cdot H_2O$

It is quite probable that $F^{-}(H_2O)_2$ is an ambidentate ion (AI) in an aprotic medium with a bridge proton between the F^{-} and OH^{-}

$$HOH...F^-...H \rightarrow OH \leftrightarrow HOH...F \rightarrow H...OH^-$$

The reactivity of the AI is governed by the nature of the reagents used and the stability of the reaction products. Thus, when a halogen is nucleophilically substituted at a saturated C atom, the $F^- \cdot nH_2O$ (n = 2.4) ions are solely the sources of F^- [4]. Similarly electrochemically generated radical cations selectively react with $R_4NF \cdot 2H_2O$ in CH_3CN forming a C - F bond [9]. If the reaction with F^- is reversible, the AI can be the source of the OH⁻ ion, which is observed in the reactions between AgClO₄ and perfluoroaromatic compounds.

The basic properties of the $F^{-}(H_2O)_2$ anion are extremely strongly expressed since HF, which is a weak acid in aprotic solvents, is formed when an H^+ is split off

$$R_4N^+ + F^-(H_2O)_2 + BH \rightleftharpoons R_4N^+ + B^- + HF(H_2O)_2$$
⁽¹⁾

At first glance the surprising existence of carbanions of weak CH-acids in the presence of water is explained by the fact that the H₂O molecules are held extremely strongly both by the F⁻ anion and by the HF formed. The F⁻(H₂O)₂ anion can split H⁺ from CH-acids having a pK_a ≤ 25 [8]. The formation of cresol and the absence of cyanomethylation products in the reaction of (II) with (I) in CH₃CN indicate that the acid – base equilibrium [Eq. (1)] for the CH-acids with a pK_a ≥ 25 is shifted to the left and, accordingly, the concentration of anion B⁻ is very low. The formation of cyanomethylation products of benzophenone [8] is evidently explained by the reversibility of the addition of the ambidentate F⁻(H₂O)₂ ion at the carbonyl bond and the irreversibility of the addition of the CH₂CN⁻ anion. When a stronger CH-acid (pK_a < 25) is added to the (I) – CH₃CN system, the acid – base equilibrium [see Eq. (1)] is shifted to the right, the concentration of carbanion B⁻ increases sharply at this time, and it becomes the principal agent governing the course of the process. For example, when (I) and (II) are heated in CH₃CN in the presence of acetophenone (pK_a 19) [10], nucleophilic substitution with the participation of OH⁻ is practically unobserved. The principal course of the reaction is the nucleophilic substitution of F by the acetophenone carbanion. Benzofuran derivatives (VI) are formed as a result of a series of successive substitution reactions:



Analogously the nucleophilic substitution of F in the case of other stronger acids proceeds through their anions. Thus (II) in a solution of (I) in CH_3CN smoothly reacts with succinimide forming N-(heptafluoro-p-tolyl)succinimide (VII)



Under similar conditions C_6F_6 forms the mono- and disubstitution products (VIII) and (IX) with β -naphthol

$$C_{6}F_{6} + C_{10}H_{7}OH \xrightarrow{(CH_{3})_{1}NF \cdot 2H_{2}O}{CH_{3}CN} C_{6}F_{5}OC_{10}H_{7} + C_{10}H_{7}OC_{6}F_{4}OC_{10}H_{7}$$
(VIII) (IX)

We also studied the feasibility of employing KOH to generate carbanions to substitute nucleophilically F in polyfluoroaromatic compounds. Compound (II) reacts only with the substitution of F by OH and the formation only of polycondensation products (III). With less reactive compounds (C_6F_6 , C_6F_5Cl , C_6F_5H), not only are phenolates formed but one also succeeds in obtaining products (X) and (XI) in which F has been substituted by the corresponding carbanions:

 $C_{6}F_{5}X \xrightarrow{\text{CH}_{3}\text{COCH}_{3}} (p-XC_{6}F_{4})_{2}\text{CHCOCH}_{3} + p-XC_{6}F_{4}\text{OH}} (X) X = F, 22\% X = F, 28\% X = H, 21\% X = H, 47\% X = H, 21\% X = H, 47\% X = H, 47\% (XI) X = F, Cl, H$

EXPERIMENTAL

The ¹⁹F NMR spectra were run on a Hitachi H-60 spectrometer and the PMR spectra on a Perkin – Elmer P-12 spectrometer. The chemical shifts are given in ppm (δ scale) from CF₃COOH and tetramethylsilane (external standards).

<u>Tetramethyl Ammonium Fluoride Dihydrate (I).</u> Into a 1 m × 18 mm column was placed 200 g of Amberlite IRA-400; it was flushed with a 5% NaF solution in water (20 liter) to the disappearance of traces of the halide in the eluate. The column was washed with 3 liters of water, then a solution of 20 g of tetramethyl ammonium iodide in 350 ml of H₂O was passed through and the fluoride formed was washed out with water to the appearance of the first drops of eluate containing iodine (AgNO₃ test). The solution obtained was evaporated in vacuo and the residue dried for 30 h (50°C at 10^{-3} mm). A total of 11 g (85% yield) of (I) was obtained as white, extremely hygroscopic crystals. Found: F 14.41; N 10.56%. C₄H₁₆FO₂N. Calculated: F 14.73; N 10.85%.

<u>Reaction of Tetraethyl Ammonium Fluoride Dihydrate (XII) with $AgClO_4$.</u> Compound (XII), 0.92 g, was dried for 20 h over P_2O_5 in vacuo at 10^{-3} mm, then in a stream of dry Ar was dissolved in 10 ml of anhydrous CH_3CN , and 1.65 g of $AgClO_4$ · $3CH_3CN$ (XIII), obtained by the method in [11], in 10 ml of CH_3CN was added. The pouring together of the solutions was accompanied by a brownish-black precipitate. Within 1 h the pH of the reaction mixture reached 4 (by universal indicator paper). The reaction mixture was filtered and the residue was dried in vacuo. A total of 0.29 (50%) of blackish-brown Ag_2O crystals was obtained.

<u>Tetramethyl Ammonium Perfluoro-p-cresolate (III)</u>. A mixture of 7.7 g (60 mmole) of (I) and 2.85 g (12 mmole) of (II) in 30 ml of anhydrous CH_3CN was boiled for 6 h, then evaporated in vacuo. The residue was extracted with acetone, the solvent evaporated off, and the residue was recrystallized from $CHCl_3$ – acetone. A total of 1.7 g of (III) was obtained, mp 155.5–158°C. Found: C 42.68; H 3.87; F 43.32; N 4.40%. $C_{11}H_{12}F_7NO$. Calculated: C 42.99; H 3.90; F 43.32. N 4.56%. ¹⁹F NMR spectrum (acetone): -26.2 (CF₃); 74.0 (m-F); 92.8 (o-F).

<u>Complex between (III) and Perfluoro-p-cresol (IV).</u> A mixture of 7 g (54 mmole) of (I) and 5.9 g (25 mmole) of (II) in 30 ml of anhydrous acetonitrile was boiled for 6 h, evaporated in vacuo, to the residue was added H₂O, the residue was isolated and recrystallized (CH₂Cl₂). A total of 2.5 g of (IV), mp 133-135°C. Found: C 39.61; H 2.45; F 48.61; N 2.65%. C₁₈H₁₃F₁₄O₂N. Calculated: C 39.92; H 2.40; F 49.17; N 2.58%. ¹⁹F NMR spectrum (acetone): -24.3 (CF₃); 70.2 (m-F); and 86.4 (o-F). Mass spectrum: m/e 234 (C₇F₇OH). IR spectrum at 20°C: 1540, 1660, and 3060 cm⁻¹; in addition a broad band with a center at 3160 cm⁻¹, which is characteristic for perfluorocresol [12], appears at -180° C.

The Complex between γ -Hydroxyperfluoropyridine and the Tetramethyl Ammonium Salt of γ -Hydroxyperfluoropyridine (V). Analogously from 3.1 g (24 mmole) of (I) and 5.6 g (33 mmole) of perfluoropyridine was obtained 3.2 g (65%) of (V), mp 189-195°C (CCl₄ - C₂H₅OH). Found: C 41.51; H 3.02; F 37.44; N 10.35%. C₁₄H₁₃F₈N₃O₂. Calculated: C 41.27; H 3.19; F 37.35; N 10.32%. ¹⁹F NMR spectrum (pyridine): two multiplets with centers at 22.0 and 92.9. IR spectrum at 20°C: 1549, 1650, and 3060 cm⁻¹; a broad band with a center at 3160 cm⁻¹ appears at -180°C.

 $\frac{2-\text{Phenyl-3-p-perfluorotolyl-4,5,7-trifluoro-6-trifluoromethylbenzo[b]furan (VI, X = H). A mixture of 3.5 g (27 mmole) of (I), 4.5 g (37 mmole) of acetophenone, and 4.4 g (18.6 mmole) of (II) in 15 ml of CH₃CN was boiled for 6 h, evaporated in vacuo, H₂O was added, and the mixture was extracted with CH₂Cl₂. After evaporating the solvent the residue was recrystallized from CH₃CN. A total of 0.8 g of (VI), X = H, mp 158.5-160°C was obtained. Found: C 49.81; H 1.01; F 45.98%. C₂₂H₅F₁₃O. Calculated: C 49.62; H 0.94; F 46.42%.$

 $\frac{2-p-Fluorophenyl-3-p-perfluorotolyl-4,5,7-trifluoro-6-trifluoromethylbenzo[b]furan (VI, X = F).$ Analogously from 3.7 g of (I), 9.45 g (40 mmole) of (II), and 5.5 g (40 mmole) of p-fluoroacetophenone was obtained 0.6 g (VI, X = F) with a mp 169-172°C (cyclohexane). Found: C 47.99; H 0.92; F 48.42%. C₂₂H₅F₁₄O. Calculated: C 48.00; H 0.73; F 48.36%.

<u>N-(Heptafluoro-p-tolyl)succinimide (VII)</u>. A mixture of 3.3 g of (I), 3.5 g (35 mmole) of succinimide, and 8.4 g (35 mmole) of (II) in 30 ml of anhydrous CH_3CN was boiled for 3 h, evaporated in vacuo, H_2O was added, the residue was recrystallized from CH_3CN , and then from ethanol. A total of 2.1 g of (VII), mp 185-191°C [after sublimation at 100°C (0.1 mm)], was obtained. Found: C 42.01; H 1.54; F 41.88; N 4.39%. $C_{11}H_4F_7O_2$. Calculated: C 41.90; H 1.27; F 42.22; N 4.44%. ¹⁹F NMR spectrum (CF₃COOH): -28.4 (CF₃); 66.2, and 67.7.

<u>Pentafluorophenyl- β -naphthol Ether (VIII) and Bis(β -naphthyloxy)tetrafluorobenzene (IX).</u> A mixture of 2 g of (I), 1.55 g (10.7 mmole) of β -naphthol, and 2.3 g (12.4 mmole) of C₆F₆ in 25 ml of anhydrous CH₃CN was boiled 6 h, evaporated in vacuo, 100 ml of H₂O was added, the residue was isolated and dried. A total of 3.1 g of a white crystalline product was obtained. After a twofold recrystallization from ethyl acetate 0.2 g of (IX), mp 211-213°C, was obtained. Found: C 71.66; H 3.47; F 17.03%. C₂₆H₁₄F O₂. Calculated: C 71.89; H 3.22; F 17.50%. The mother liquors were evaporated and the residue recrystallized from pentane. After sublimation 0.45 g of (VIII), mp 78-79.5°C, was obtained. Found: C 62.18; H 2.24; F 29.75%. C₁₆H₇F₅O. Calculated: C 61.94; H 2.26; F 30.64%. ¹⁹F NMR spectrum (CCl₄): 77.1, 83.7, 86.0.

<u>1,1-Bis (pentafluorophenylacetone (X, X = F).</u> A mixture of 32 g of C_6F_6 , 100 ml of anhydrous acetone, and 40 g of KOH was boiled for 3 h, 1 liter of H₂O was added, it was extracted five times with ether and twice with CH₂Cl₂. The extract was dried, fractionally distilled, and the fraction with a bp of 150-180°C (5 mm) was recrystallized from hexane. A total of 7.4 g (22%) (X, X = F), mp 79-80°C was obtained. Found: C 46.16; H 0.97; F 48.33%. C₁₅H₄F₁₀O. Calculated: C 46.15; H 1.02; F 48.72%. PMR spectrum (CH₂Cl₂): 2.22 (CH₃); 5.47 (CH); ratio of the integrated intensities 3:1. ¹⁹F NMR spectrum: 63.9, 78.3 t, 86.6. The 2,4-dinitrophenylhydrazone was obtained, mp 208-214°C. Found: N 9.65%. C₂₁H₈F₁₀N₄O₄. Calculated: N 9.82%.

The water layer was acidified with conc. HCl, extracted five times with ether, twice with CH_2Cl_2 , and the solvents were fractionally distilled. A total of 10.5 g of pentafluorophenol, bp 62°C (20 mm), was obtained by distilling the remainder. The pentafluorophenol was back-titrated in water with a KOH solution. After evaporation 12.5 g of potassium pentafluorophenolate was obtained, yield 28%. Found: C 32.20%. C_6F_5OK . Calculated: C 32.43%.

<u>1,1-Bis-(2,3,5,6-tetrafluorophenyl)acetone (X, X = H).</u> A mixture of 16.8 g of C_6F_5H , 50 ml of anhydrous acetone, and 20 g of KOH was boiled 12 h, 1 liter of water was added, it was extracted five times with ether and twice with CH_2Cl_2 . The extract was dried and fractionally distilled. A total of 3.8 g of (X, X = H), bp 80-85°C (0.1 mm), mp 91-92°C (hexane), was obtained. Found: C 51.01; H 1.97; F 43.09%. $C_{15}H_6F_8O$. Calculated: C 50.84; H 1.69; F 42.94%. PMR spectrum (CCl₄): 2.3 (CH₃), 5.44 (CH), 7.04 m (C_6F_4H); ratio of the integrated intensities 3:2:1. ¹⁹F NMR spectrum (CH₂Cl₂): 63.4 q; 86.4 d.t.; ratio of the integrated intensities 1:1. The 2,4-dinitrophenylhydrazone was obtained, mp 188-189°C. Found: N 10.71%. $C_{21}H_{10}F_8N_4O$.

The water layer was acidified with HCl, extracted with ether and CH_2Cl_2 , the extract was evaporated, and back-titrated with a KOH solution. After evaporating and drying 9.5 g of potassium tetrafluorophenolate was obtained.

<u> α -Pentafluorophenylacetophenone (XI, X = F).</u> A mixture of 18.6 g of C_6F_6 , 11 g of KOH, and 12 g of acetophenone was agitated for 5 h, 150 ml of H₂O was added while cooling, and it was extracted with ether. The extract was washed with water, dried, and the solvent evaporated in vacuo. The residue was recrystallized from methanol, then from CCl₄. A total of 2.1 g of (XI, X = F), mp 115-116°C [13], was obtained. Found: C 58.60; H 2.50; F 33.48%. C₁₄H₇F₅O. Calculated: C 58.74; H 2.45; F 33.22%. IR spectrum: 1692 cm⁻¹ (C = O). PMR spectrum (CCl₄): 4.3 (CH₂); 7.62 and 8.04 (C₆H₅). ¹⁹F NMR spectrum: 64.9, 78.0, and 85.0.

 $\frac{\alpha-(2,3,5,6-\text{Tetrafluorophenyl})\text{acetophenone (XI, X = H)}.$ Analogously from 11 g of KOH, 12 g of acetophenone, and 33.6 g of C₆F₅H was obtained 4.6 g of (XI, X = H), mp 104-106°C (hexane, methanol). Found: C 62.77; H 3.10; F 27.95%. C₁₄H₈F₄O. Calculated: C 62.68; H 2.99; F 28.36%. IR spectrum: 1690 cm⁻¹ (C=O). PMR spectrum (C₆F₆): 4.41 (CH₂); 7.05 (C₆F₄H), and 7.6-7.9 (C₆H₅); ratio of the integrated intensities 2:1:5:3. ¹⁹F NMR spectrum (CCl₄): 62.1 and 65.2.

 $\frac{\alpha-(2,3,5,6-\text{Tetrafluoro-4-chlorphenyl)\text{acetophenone (XI, X = Cl)}}{\alpha-(2,3,5,6-\text{Tetrafluoro-4-chlorphenyl)\text{acetophenone (XI, X = Cl)}}, \text{ mp 139-141°C (CH₃OH)}. Found: C 55.69; H 2.47; F 24.59; Cl 11.48\%. C₁₄H₇ClF₄O. Calculated: C 55.54; H 2.31; F 25.11; Cl 11.37\%. IR spectrum: 1690 cm⁻¹ (C=O). PMR spectrum (C₆F₆): 4.47 (CH₂); 7.63 and 7.97 (C₆H₅). ¹⁹F NMR spectrum: a group of signals at 63.9.$

CONCLUSIONS

1. The fluorine dihydrate anion in an aprotic medium is an ambidentate ion and can serve as a source of both the fluoride anion and the hydroxyl anion (through the splitting of the proton from a water molecule in its solvation envelope and the formation of HF).

2. Tetraethyl ammonium fluoride dihydrate was used to generate the acetophenone and fluoroacetophenone carbanions and the succinimide and naphthol anions during the nucleophilic substitution of fluorine in a series of polyfluoroaromatic compounds.

3. The feasibility of using KOH to generate the acetone and acetophenone carbanions during the nucleophilic substitution of fluorine in polyfluoro aromatic compounds was demonstrated.

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