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# Synthesis and Characterization of Cetylpyridinium Hexafluorosilicate as New Potential Caries Protecting Agent

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## ABSTRACT

The present investigation is mainly on the synthesis, characterization and determination of some properties of new compound cetylpyridinium hexafluorosilicate for his potential use as caries-preventive and antibacterial agent. Hexafluorosilicate of the composition $(C_{21}H_{38}N)_2SiF_6$ was separated as crystalline product of interaction of hexafluorosilicic acid with the methanol solution of cetylpyridinium chloride. This complex was characterized by elemental analysis, IR, $^1$H and $^{19}$F NMR, mass-spectrometry, differential thermal analysis, and solubility data. The IR spectral data indicates on absence of noticeable distortion of the symmetry of $SiF_6^{2-}$ anion with regard to $O_h$. The studied compound is characterized by the predicted tendency to hydrolyze in dilute aqueous solutions with the formation of silica and fluoride anions.

**Keywords:** Hexafluorosilicate, IR spectra, NMR, solubility, hydrolysis.

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## INTRODUCTION

In recent years, several research groups demonstrated the possible usage of ammonium hexafluorosilicate (AHF) and amino acids hexafluorosilicates as caries-protectors and hyposensitive agents in the practice of dentistry[1-10]. In particular, AHF is proposed as a possible alternative to the known drug silver diamine fluoride, $[Ag(NH_3)_2]F$[11], which, while having an effective remineralizing and bactericidal action, causes an undesirable darkening of the treated hard dental tissues[12]. AHF solution does not produce tooth staining, but large amounts of precipitates form at the tooth surface compared with other fluoride compounds[1-3]. In addition, continuous dentin tubule occlusion and covering of the dentin surface can be expected. Besides being stable, the precipitate formed after AHF treatment induces calcium phosphate precipitation from saliva[4], because silica works as a catalyst for the formation of calcium phosphate from simulated body fluids[13]. It was also concluded[7] that AHF treatment increased the crystallinity of apatite powder and repaired the demineralized enamel surface with formation of fluoridated apatite and/or calcium fluoride-like precipitate regardless of the concentration of fluorine. AHF treatment would thus be useful against the formation dental caries. For the prevention of dental caries, it seems that the tooth surface should be covered with highly antibacterial materials[14], including *e.g.* guanidine derivatives, phenolic antiseptics, triclosan, quaternary ammonium compounds such as cetylpyridinium chloride (CPC). As it follows from the data[6], AHF with the addition of CPC was the most effective for reducing the adherence of bacteria and inhibiting the formation of biofilm, showing the same level as $[Ag(NH_3)_2]F$. The aim of this work is the synthesis, the study of the structure and properties of cetylpyridinium hexafluorosilicate – the fluoride containing salt with cation, exhibiting antibacterial activity.

## MATERIALS AND METHOD

The commercial fluorosilicic acid (45 %) and CPC (Hangzhou dayangchem Co., Ltd, China) were used. The IR-absorption spectra were recorded on a spectrophotometer Spectrum BX II FT-IR System (Perkin-Elmer) (range 4000 – 350 $cm^{-1}$, samples as tablets with KBr). The EI mass spectra were recorded on MX-1321 spectrometer (direct input of a sample in a source, the energy of ionizing electrons 70 eV). $^1H$, $^{19}F$ NMR spectra were recorded on a spectrometer Varian VXR-300 (299.94, 282.20 MHz, solvent $CDCl_3$, TMS and $CFCl_3$ as standards, respectively). Thermogravimetric analysis was performed on a Q-1500 D derivatograph of F. Paulik – J. Paulik – L. Erdey’s system (platinum crucible, sample 100 mg, temperature range 20 – 800 ° C, the sample heating rate 10 °/min, $Al_2O_3$ as standard). The isothermal conditions of experiments on detection of solubility ($t = 25 \pm 0.2$ °C) were provided with the help of an ultra-thermostat U15.pH values of aqueous solutions were determined using an EV-74 universal ionomer.

**Synthesis of cetylpyridinium hexafluorosilicate (I)**

The synthesis of **I** was performed by ion exchange reaction between a methanol solution of cetylpyridinium chloride (CPC) and a solution of 45 % fluorosilicic acid (molar ratio of CPC : $H_2SiF_6$ = 1 : 2):

$$2(C_{21}H_{38}N)Cl + H_2SiF_6 \rightarrow (C_{21}H_{38}N)_2SiF_6 + 2HCl \qquad (1)$$

The reaction mixture was kept at room temperature to evaporate the solvents and a colorless crystalline product was obtained with an approximately qualitative yield. The carbon, hydrogen and nitrogen content were determined using a CHN elemental analyzer and silicon was quantified by photocolorimetric method.

## RESULTS AND DISCUSSION

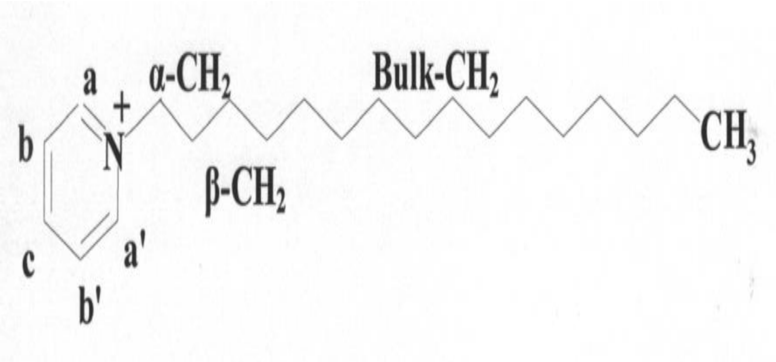
The composition of isolated compound **I** was established by elementary analysis data.

Found, %: C – 68.09; N – 3.85; H – 9.75; Si – 3.60.

For $(C_{21}H_{38}N)_2SiF_6$ (**I**) calculated, %: C – 67.16; N – 3.73; H – 10.20; Si – 3.74.

Mass spectrum of **I** shows an intense peak of cetylpyridinium ion $[C_{21}H_{38}N]^+$ ($m/z = 304$, $I = 100$ %), a peak of ion $[SiF_3]^+$ ($m/z = 85$, $I = 59$ %) – characteristic product of fragmentation of $SiF_6^{2-}$ and peaks of ions $[C_5H_5N+H]^+$($m/z = 80$, $I = 21$ %), $[C_5H_5N]^{+\cdot}$ ($m/z = 79$, $I = 7$ %).

The characteristics of IR spectra of the compounds **I** and CPC[15] are presented in Table 1. Vibration rating is carried out using published data[16, 17]. The IR spectra of **I** and CPC exhibit bands of stretching and deformation vibrations $\nu$ (CH) and $\delta$(CH) near 3050 and 1206, 1178 $cm^{-1}$ respectively. In spectrum of **I** the stretching vibrations of methylene groups $\nu_{as}(CH_2)$ and $\nu_s(CH_2)$ were registered at 2911.33 and 2850.76 $cm^{-1}$, respectively; these positions being characteristic and very close to positions of corresponding bands in spectrum of CPC. In the case of spectrum **I**, three $\nu_{ring}$ vibrations at 1637.55, 1577.26 and 1487.54 $cm^{-1}$ are observed. The strong $\nu$(SiF) and $\delta(SiF_2)$ stretches of $SiF_6^{2-}$ anion are observed for **I** in their characteristic regions at 739.48 and 482.16 $cm^{-1}$ respectively[17]. The singlet character of $\nu$ (SiF) and $\delta(SiF_2)$ vibrations is in agreement with proximity of anions structure to the idealized $O_h$- symmetry. Possibly, it can reflect the absence of strong interionic H-bonds in the structure **I**, the presence of which can result in distortion of anion structure. The $^1H$ NMR spectrum of **I**, using $CDCl_3$ as solvent, shows seven sets of multiplets (Figure 1, table 2). The presented $^1H$ NMR spectrum is typical for the salts of cetylpyridinium cation[18]:



In the $^{19}$F NMR spectrum of **I** (Figure 2) in the solution of $CDCl_3$ singlet signal with chemical shift –133.79 ppm is observed. The resonance is in accordance with the published chemical shifts for $SiF_6^{2-}$ anions[19]. Endothermic effects on the curve DTA of **I** at $t_M$ = 48 and 104 °C for which *no mass loss* is observed may be related to phase transition and melting of salt, respectively. Exothermic effect at $t_M$ = 358 °C and endothermic effect at 474 °C may be attributed to the thermal decomposition processes. Table 3 summarizes the solubility data for the newly synthesized salt **I** in comparison with the previously reported hexafluorosilicates[20, 21]. It has been previously shown[20] that for the substituted pyridinium hexafluorosilicates their water solubility correlates with parameter *h* defined as

$$h = n/d(D\cdots A)_{av.}, \qquad (2)$$

where n is the number of short inter-ionic contacts (that include strong and medium H-bonds, $D\cdots A \leq 3.2$ Å[22]), $d(D\cdots A)_{av.}$is an average donor-acceptor distance in the complex structure. The solubility of pyridinium salts tends to decrease with increasing number of H-donors in the pyridinium moieties. In the case of salt **I** the strong inter-ionic H-bonds must be absent (weak interactions between $SiF_6^{2-}$ anion and $sp^2$-hybridized C–H groups can be observed[23]) and the relatively low solubility of **I** can be explained by the substantial lipophilic effect of cetylic radical $–C_{16}H_{33}$.

The occurrence of $SiF_6^{2-}$ hydrolysis in water solutions of **I** according to reaction scheme (3) is confirmed by the expected development of yellow-colored solution after addition of $(NH_4)_2MoO_4$:

$$SiF_6^{2-} + 4H_2O \rightleftarrows Si(OH)_4 + 6F^- + 4H^+ \qquad (3)$$

However, attempting to determine the extent of the hydrolysis of **I** at $1\cdot10^{-4}$ M of aqueous solution with the use of spectrophotometric method[24] failed due to intense opalescence of the solution. The pH value of a 0.001 M aqueous solution of **I** (3.25) is close to the similar values for AFS[4] and pyridinium hexafluorosilicates[20] (3.09 – 3.33). The acidic character of this dilute solutions provides the etched of dentine and calcium phosphate precipitation[4, 6].

**Table 1: IR spectral data ($cm^{-1}$) for cetylpyridinium hexafluorosilicate and cetylpyridinium chloride**

| I | CPC | Assignment |
|---|---|---|
| 3054.53 w. | 3049.11 w. | $\nu(CH)$ |
| 2911.33 v.s. | 2912.30 s. | $\nu_{as}(CH_2)$ |
| 2850.76m. | 2848.65m. | $\nu_s(CH_2)$ |
| 1637.55 m. | 1637.44 m. | $\nu_{ring}$ |
| 1577.26 w. | | $\nu_{ring}$ |
| 1487.54 m. | 1508.22 m. | $\nu_{ring}$ |
| 1472.87 m. | | $\delta_s(CH_2)$ |
| 1375.72 w. | | $\delta_s(CH_3)$ |
| 1206.14 w. | 1209.28 w. | $\delta(CH)$ |
| 1178.13 w. | 1178.42 w. | $\delta(CH)$ |
| 777.62 s. | 783.04 s. | $\rho(CH_2)$ |
| 739.48 v.s. | | $\nu(SiF)$ |
| 482.16 m. | | $\delta(SiF_2)$ |

Note: w = weak, m = medium, s = strong, v = very.

**Table 2: $^1$H NMR spectrum of cetylpyridinium hexafluorosilicate**

| Assignment | $CH_3$, 3H | Bulk-$CH_2$, 26H | β-$CH_2$, 2H | α-$CH_2$, 2H | b,b´-CH, 2H | c-CH, 1H | a,a´-CH, 2H |
|---|---|---|---|---|---|---|---|
| δ, ppm | 0.87 | 1.24 | 1.90 | 4.70 | 8.05 | 8.49 | 8.95 |
| J(HH), Hz | 7.0 | – | – | – | – | – | – |

**Table 3: Solubility of pyridinium hexafluorosilicates in water**

| Compound | Solubility, mol. %, 25 °C |
|---|---|
| $(2\text{-}CH_3C_5H_3NH)_2SiF_6$ | 11.60 |
| $[2,6\text{-}(CH_3)_2C_5H_3NH]_2SiF_6$ | 9.90 |
| $[2\text{-}HO(O)CC_5H_4NH]_2SiF_6$ | 5.33 |
| $[3\text{-}HO(O)CC_5H_4NH]_2SiF_6$ | 3.33 |
| $[2,6\text{-}(HOCH_2)_2C_5H_3NH]_2SiF_6$ | 2.52 |
| $[2\text{-}CH_3\text{-}3\text{-}OH\text{-}4,5\text{-}(HOCH_2)C_5HNH]_2SiF_6$ | 0.89 |
| $(2\text{-}H_2NC_5H_3NH)_2SiF_6$ | 5.60 |
| $[2,6\text{-}(H_2N)_2C_5H_3NH]_2SiF_6$ | 0.06 |
| $(C_{21}H_{38}N)_2SiF_6$ | 0.15 |
| $CPC\cdot H_2O$ | 0.2 |

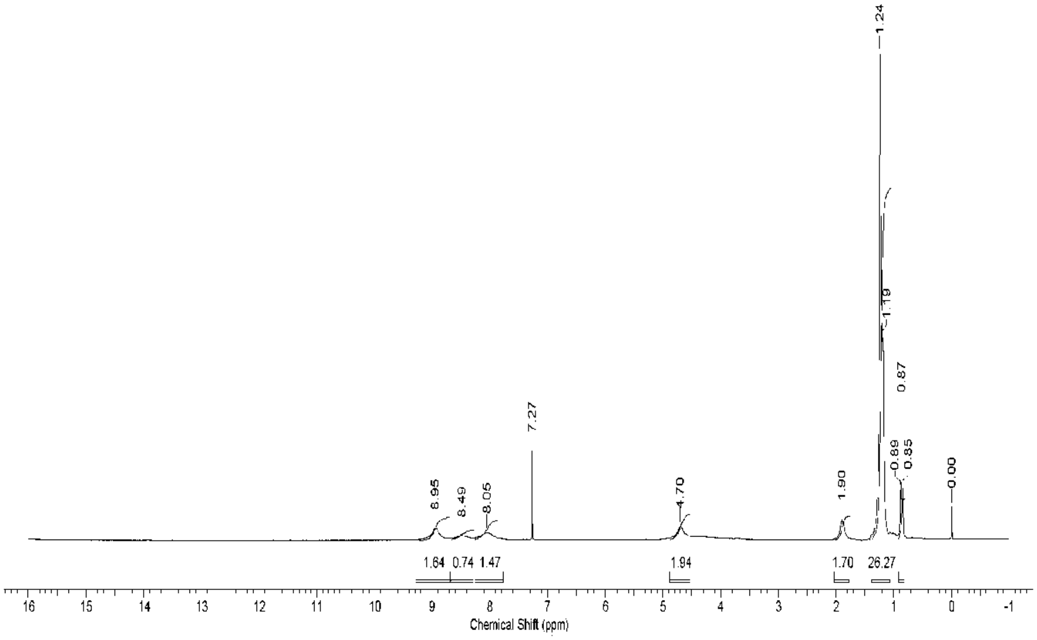


**Figure 1: $^{1}$H NMR spectrum of I**

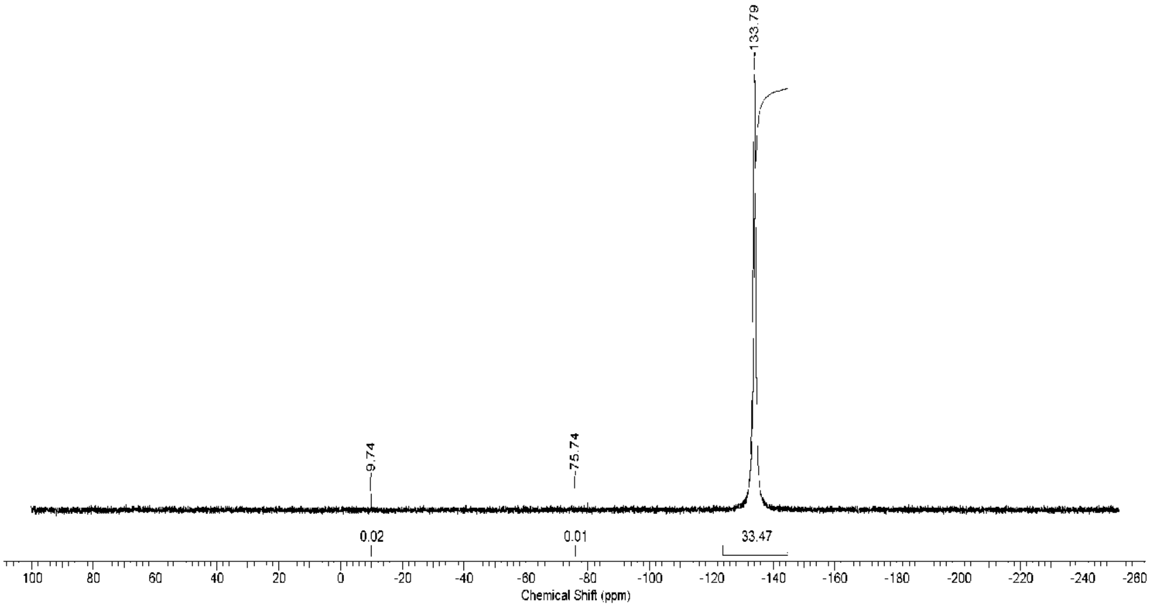


**Figure 2: $^{19}$F NMR spectrum of I**

# CONCLUSION

Cetylpyridinium hexafluorosilicate was synthesized and characterized using various spectral techniques. The IR spectral data demonstrate that the geometry of $SiF_6^{2-}$ anion is near to the idealized $O_h$-symmetry. The solubility data in water (25 ºC) for hexafluorosilicate is 0.15 mol. %. The studied compound is characterized by the predicted tendency to hydrolyze in dilute aqueous solutions with the formation of silica and fluoride anion. The study of biological activity of this compound is the subject of further investigations

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