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Determination by Multi-NMR Studies of New Stable Aluminum Complexes with Pyrophosphate and Fluoride in Aqueous Solution

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Multi-NMR studies (^{27}Al, ^{19}F, ^{31}P) show that, in the presence of pyrophosphate at pH 7, fluoride and aluminum (Al^{3+}) ions combine in aqueous solution, to generate a wide variety of ternary complexes. Among the latter, a new class of stable complexes, showing J_{FF} and J_{FP} coupling constants, has been identified in which two octahedral aluminum cations are bound by two pyrophosphate moieties, with a common fluorine atom bridging the two aluminum ions. Both the pyrophosphate groups and the fluoride ion contribute to the stability of these molecules. The existence of J_{FF} couplings provides evidence for the octahedral coordination of aluminum in these complexes.

Introduction

The biological importance of fluorometallic complexes such as fluoroaluminates and fluoroberyllates has been recognized in so far as they act as phosphate analogues in enzymic reactions, possibly mimicking either the γ-group of a nucleoside triphosphate when a nucleoside diphosphate is present[1] or an inorganic phosphate in the absence of any nucleotide.[2]

In the former case, the inhibitory effect of these fluorometallic complexes was originally explained by (i) the monodentate binding of the fluorometal to the β-phosphate of the nucleotide and (ii) the assumed tetrahedral geometry that was analogous to that of a γ-phosphate (see ref 3).

Later, it was shown that, in aqueous solution, a mixture of ADP, beryllium (Be^{2+}), and fluoride ions gives rise to ternary complexes wherein the fluoroberyllate binds only to the polyphosphate chain, in a bidentate fashion.[4] On the other hand, although evidence has been found supporting the existence of a tetrahedral structure for the AlF_4^- anion in organic solvents,[5,6] we have been able to show that all fluoroaluminate complexes formed in aqueous solution, at pH 7, are hexacoordinated, with an octahedral geometry.[7]

Crystallographic evidence for the octahedral coordination of the aluminum cation, in the presence of nucleotides and fluoride, was obtained when the metal interacts with the active sites of proteins, such as the G-protein Giα_1,[8] transducin,[9] nucleoside diphosphate kinase,[10] nitrogenase,[11] the Ras−RasGAP complex,[12] and the G-protein RhoA.[13] In these cases, the fluoroaluminate complex mimics the pentavalent transition state of the phosphoryl transfer reaction (see ref 14).

For studying complexes containing ADP, fluoride, and beryllium (Be^{2+}), we previously used pyrophosphate (PPi) as a simpler analogue of a dinucleotide.[4] In the present work, we describe a parallel study, using multi-NMR, of ternary complexes formed among pyrophosphate, aluminum (Al^{3+}), and fluoride in aqueous solution at pH 7.

Previous studies with phosphatidic compounds[15−17] have already shown the diversity of aluminum−phosphorus complexes, even in the absence of fluoride. In particular, ^{27}Al NMR experiments have been performed on aluminum−pyrophosphate complexes in aqueous solution at pH 2, showing that several Al−pyrophosphate complexes exist, which exchange slowly with $Al(H_2O)_6^{3+}$ on the ^{27}Al NMR time scale.[18] Moreover, the complexity of the spectra increases when the pH of the solution is close to 7. Nevertheless, we have focused our attention on this pH value because of its physiological importance with respect to the analogy with ADP, and because of the diversity

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of interactions among aluminum (Al^{3+}), pyrophosphate, fluoride, and hydroxy/water that lead to the formation of such a large number of complexes.

Experimental Section

Materials. Aluminum nitrate (Merck), sodium fluoride (Riedel DeHaen), and anhydrous disodium pyrophosphate (Sigma) were used as sources of aluminum, fluoride, and pyrophosphate, respectively. Aqueous solutions contained 30% D_2O. The pH of all samples was adjusted to within ±0.1 unit using a pH meter (corrected for D_2O). Measurements were made at least 1 h after mixing of the ions, to ensure that complete thermodynamic equilibrium has been attained.

NMR Measurements and Data Analysis. NMR spectra were obtained using Varian U 600 or U^+ 500 and Bruker AM 400 spectrometers for ^{31}P and ^{19}F, and using a Bruker DSX 500 or AM 400 spectrometer for ^{27}Al.

^{27}Al NMR spectra were run either at 130.30 MHz with a selective probe or at 104.26 MHz with a multinuclear probe (10 mm). Chemical shifts are given relative to a 0.1 M aluminum nitrate solution as external reference (pH 1; $T = 295$ K).

^{19}F NMR spectra were run at either 564.31 or 470.26 MHz using a 5 mm indirect detection probe. Heteronuclear ^{31}P decoupling was performed using the WALTZ16 sequence. Chemical shifts were measured relative to trifluoroacetic acid (external reference; $T = 295$ K) and are given relative to the $CFCl_3$ standard reference (−76.6 ppm relative to $CFCl_3$).

Typical acquisition and processing parameters for ^{27}Al and ^{19}F were as described previously[7] (^{27}Al, pulse width corresponding to 60°, relaxation delay 0.3 s, acquisition size (104.26 MHz) 8 K, spectral width 200 ppm; ^{19}F, pulse width corresponding to 50°, relaxation delay 0.3 s, acquisition size (470,26 MHz) 6 K, spectral width 50 ppm). Prior to Fourier transform, zero filling and linear prediction followed by apodization were carried out.

^{31}P NMR spectra were run at 242.90 MHz using a 5 mm multinuclear or indirect detection probe, or at 202.42 or 161.98 MHz (10 mm multinuclear probe). Heteronuclear ^{19}F decoupling was performed using the GARP1 sequence. Typical acquisition parameters were as follows: pulse width corresponding to 60°, relaxation delay 0.6 s, acquisition size (202.42 MHz) 8 K, spectral width 5 ppm. Prior to Fourier transform, zero filling and linear prediction followed by apodization were carried out. Chemical shifts were measured relative to an external 85% solution of H_3PO_4 ($T = 295$ K).

Results

An extensive study of aluminum, PPi, and fluoride mixtures in aqueous solution at neutral pH, for different concentrations (from 2.5 to 50 mM) and temperatures (from 5 to 80 °C) was carried out, and monitored using ^{27}Al, ^{31}P, and ^{19}F NMR.

I. ^{27}Al NMR Spectra. ^{27}Al NMR of aluminum with PPi in aqueous solution gave two broad (∼500 and 1300 Hz) overlapping resonances (Figure la), labeled $\mathbf{a_1}$ and $\mathbf{a_2}$, located at 0 and −3.5 ppm, respectively. When the [PPi]/[Al] ratio increased, the intensity of $\mathbf{a_1}$ decreased monotonically to zero (when the [PPi]/[Al] ratio $\approx$ 3), whereas $\mathbf{a_2}$ increased to a maximum when the [PPi]/[Al] ratio $\approx$ 2.5−3.0. When fluoride was added, a broad (∼1500 Hz) absorption band ($\mathbf{a_3}$, Figure 1b) was observed in the same chemical shift range ($\delta \approx -4$ ppm).

II. ^{31}P NMR Spectra. II.1. Aluminum−Pyrophosphate Complexes. ^{31}P NMR spectra of a mixture of aluminum and pyrophosphate in aqueous solution showed the following (Figure 2a): two broad signals ($\mathbf{b_1} = -6.2$ ppm; $\mathbf{b_4} = -8.8$ ppm) which were not coupled, a poorly resolved pair of doublets ($\mathbf{b_2} = -6.5$ and −8.1 ppm; $J_{PP} = \sim 13$ Hz), as confirmed by a COSY experiment, and a singlet band ($\mathbf{b_3}$) located at −7.4 ppm.

An increase in the [PPi]/[Al] ratio resulted in an increase in $\mathbf{b_3}$ and a concomitant decrease in the $\mathbf{b_1}$ and $\mathbf{b_4}$ lines as well as in the $\mathbf{b_2}$ substructure. When the [PPi]/[Al] ratio was increased to 2, the latter resonances disappeared, and $\mathbf{b_3}$ increased to a maximum value, corresponding to a ratio of ∼2 PPi per aluminum atom. Concomitantly, a continuous increase in the free PPi resonance was observed at $\delta = -5.8$ ppm.

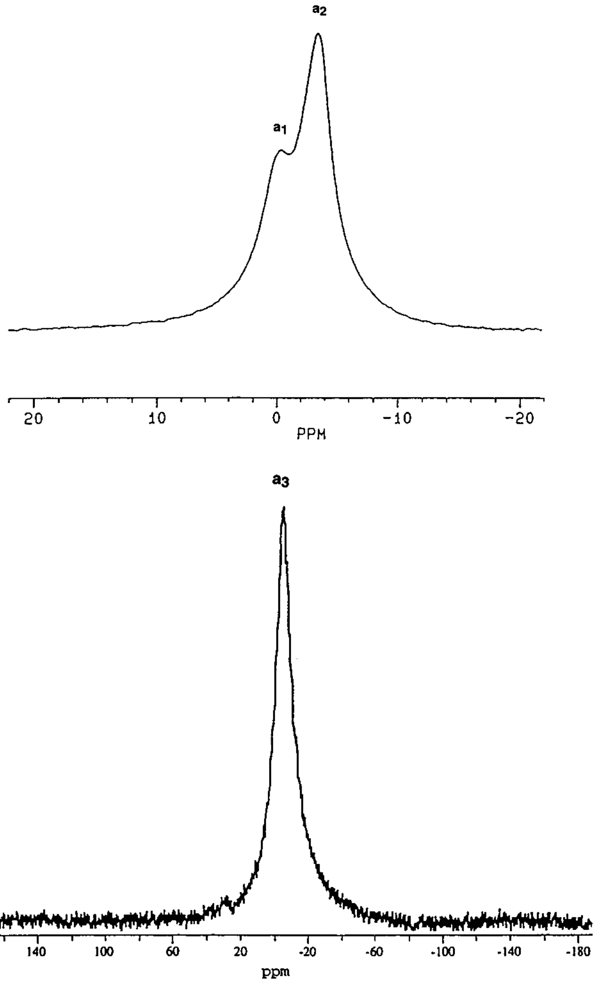

Figure 1. ^{27}Al NMR spectra at pH 7 of (a, top) (104.26 MHz) an Al−PPi (5 mM/8 mM) mixture and (b, bottom) (130.30 MHz) an equimolar Al−PPi−F mixture (10 mM each).

II.2. Effect of Fluoride Addition. The addition of fluoride anions to aluminum−pyrophosphate complexes yielded two types of spectra depending on the [PPi]/[Al] ratio. When the [PPi]/[Al] ratio was lower than 2, a very complex spectrum was observed. ^{19}F decoupling revealed a simpler spectrum comprising multiple resonances (Figure 2b, where [Al] = [PPi] = [F] = 30 mM).

Among the above, it was possible to distinguish several AB/AX type subspectra ($J_{PP} = 6.5$ Hz), as confirmed by a COSY experiment (Table 1). Following an increase in the [F]/[Al] ratio, the intensities of these signals decreased to zero (at [F]/[Al] ratios greater than 6) and the intensity of the free PPi signal increased. Signal $\mathbf{b_3}$ (located at −7.4 ppm, cf. section II.1), which was very weak in the absence of fluoride (when [PPi]/[Al] = 1), increased in intensity with increasing fluoride concentration.

When the [PPi]/[Al] ratio was about 2, the fluoride dependence of this signal differed slightly. The $\mathbf{b_3}$ signal, which was also present without fluoride (see the previous paragraph) exhibited a rather unusual dependence on fluoride concentration (Figure 3): its intensity initially decreased until [F]/[Al] $\approx$ 2, then increased to a maximum (for [F]/[Al $\approx$ 4), and finally decreased to zero with higher fluoride concentrations, concomi-

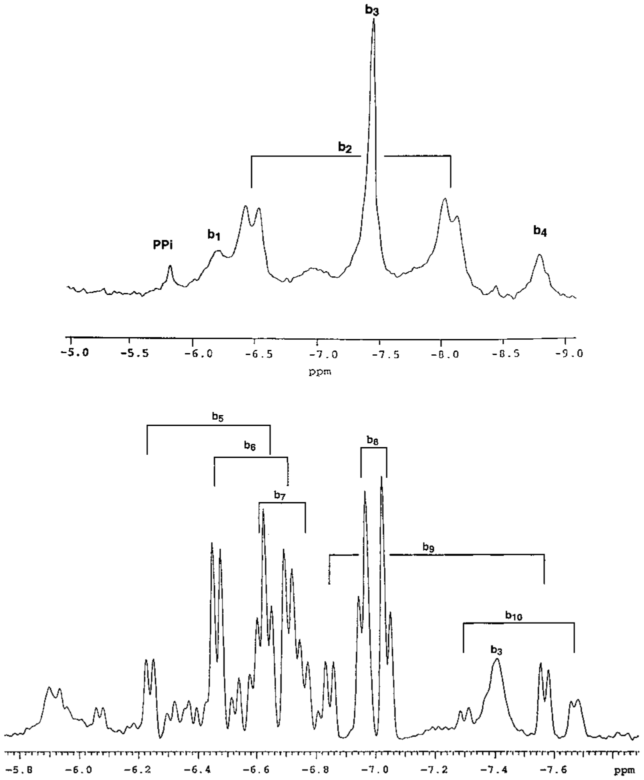

Figure 2. ^{31}P NMR spectrum at pH 7 of (a, top) (161.98 MHz) an Al−PPi (5 mM/6 mM) mixture and (b, bottom) (242.90 MHz) an equimolar Al−PPi−F mixture (30 mM each).

Table 1. Main AB/AX Subspectra Observed by ^{31}P{^{19}F} NMR of an Equimolar Al−PPi−F Mixture (10 mM Each)

	b_5	b_6	b_7	b_8	b_9	b_{10}
δ (ppm)	−6.24 −6.63	−6.46 −6.71	−6.61 −6.76	−6.95 −7.04	−6.85 −7.57	−7.30 −7.67

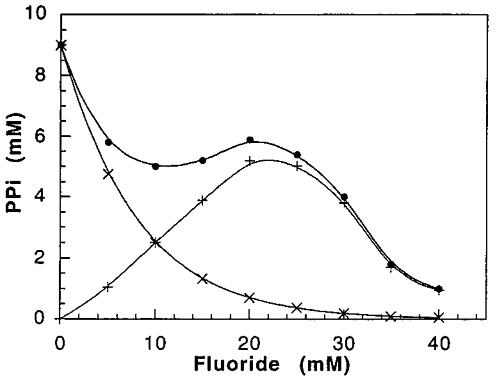

Figure 3. Intensity of the experimental ^{31}P NMR signal $\mathbf{b_3}$ (●) versus fluoride concentrations of 10 mM PPi and 5 mM Al. Simulated evolution of intensities for $\mathbf{b_{3a}}$ (+) and $\mathbf{b_{3b}}$ (×) so that their sum corresponds to $\mathbf{b_3}$ (see the text).

tantly with all the other resonances. The intensity values for signals $\mathbf{b_5}$−$\mathbf{b_{10}}$, which were very weak, followed a bell-shaped dependency curve with respect to fluoride concentration, with the maximum value occurring for [F]/[Al] ≈ 2.

At a [PPi]/[Al] ratio higher than 2, only two resonances remained: the $\mathbf{b_3}$ signal and the free PPi resonance, the latter increasing concomitantly when the [F]/[Al] ratio became higher than 3, while the former decreased monotonically.

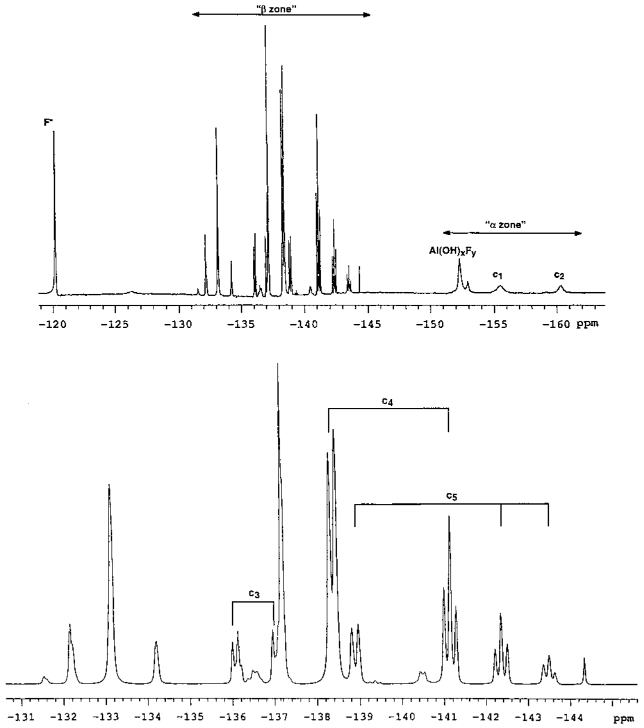

Figure 4. ^{19}F NMR (564.31 MHz) spectrum at pH 7 of an equimolar Al−PPi−F mixture (30 mM each): (a, top) whole spectrum including α range and β range (see the text); (b, bottom) enlargement showing only the β range.

Table 2. Chemical Shifts and Heteronuclear J_{FP} Values for the α Range (See the Text) of an Equimolar Al−PPi−F Mixture (30 mM Each)[a]

	c_1	c_2
δ (ppm)	−155.4	−160.3
J_{FP} (Hz)	∼8^t	∼9^t

[a] Superscript letter t = triplet.

III. ^{19}F NMR Spectra. The addition of fluoride ions to an aqueous solution of aluminum (Al^{3+})−pyrophosphate led to the appearance of complex ^{19}F NMR spectra. A careful examination of these spectra allowed their division into two distinct groups of resonances (Figure 4a), one of them being located between −162 and −151 ppm (the "α range") and the other between −145 and −131 ppm (the "β range").[19]

The α range included four resonances. Two of them (−152.2 and −152.8 ppm) have been described previously and have been assigned to hydroxyfluoroaluminate complexes.[7] The other two lines, $\mathbf{c_1}$ and $\mathbf{c_2}$ (Table 2), had a maximum intensity at a [PPi]/[Al] ratio ≈ 1, and at low temperatures (5−10 °C), they showed triplet structures corresponding to J_{FP} couplings, as confirmed by a ^{31}P decoupling experiment. Increasing the temperature to 80 °C induced broadening of all the resonances by exchange between the complexed fluorine and free fluoride. Irrespective of the [PPi]/[Al] ratio, the [F]/[Al] ratio dependency of all resonances in the α range was similar to that previously observed for hydroxyfluoroaluminate complexes.[7]

The β range was characterized by many resonances (Figure 4b), some of which were multiplet structures resulting from J_{FF} couplings (Table 3) as confirmed by a COSY experiment. All the lines showed poorly-resolved heteronuclear multiplet structures, as confirmed by ^{31}P decoupling experiments. Their coupling values were slightly greater than those observed in the α range (Table 2).

When comparison is made with the α range, two important differences are apparent: (i) The β range is prevalent for [PPi]/

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(19) The fluoride ion is still present at −120.2 ppm.

Table 3. Chemical Shifts and Multiplicities Observed in the β Range by ^{19}F NMR of an Equimolar Al−PPi−F Mixture (30 mM Each)[a]

	c_3	c_4	c_5
δ (ppm)	−136.15(1)^{d} −137.15(1)^{d}	−138.40(2)^{d} −141 .20(1)^{t}	−138.95(2)^{d} −142.40(2)^{t} −143.40(1)^{t}
J_{FF} (Hz)	78	82	83 (mean value)
J_{FP} (Hz)	∼12^{t}	∼12^{t}	∼12^{pr}

[a] Values in parentheses correspond to the number of equivalent nuclei. Multiplicities corresponding to homonuclear or heteronuclear couplings are indicated by superscript letters, d = doublet, t = triplet, and pr = poorly resolved.

[Al] ratios ≈ 1, particularly when Al, PPi, and F are in equimolar concentrations, and vanishes at [PPi]/[Al] > 2. It also vanishes at higher fluoride concentrations. (ii) Hyperfine structures (both homonuclear J_{FF} and heteronuclear J_{FP}) are still observable at temperatures as high as 80 °C.

Discussion

It is well known[20,21] that the aluminum chemical shift is directly related to its degree of coordination. All the ^{27}Al resonances currently observed at neutral pH are in the 0 ppm/−10 ppm range, indicating the hexacoordinated nature of the aluminum in these species. Similar results have been deduced with fluoroaluminate compounds.[7]

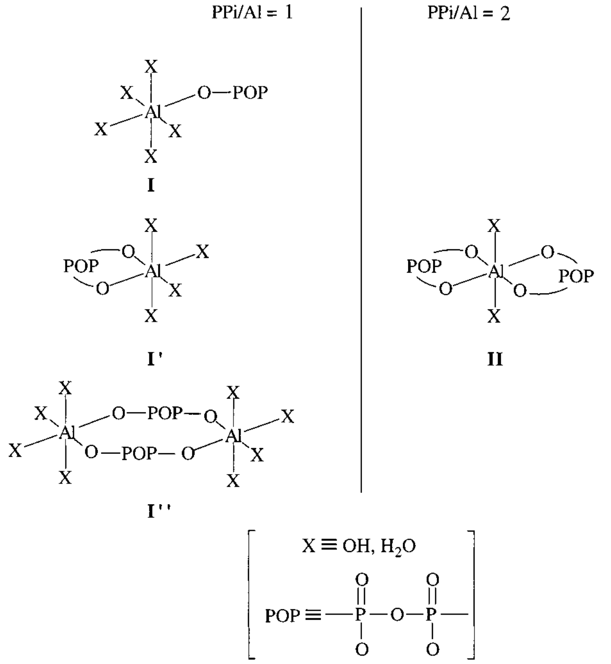
Due to its 5/2 spin and quadrupole moment ($Q_{Al} = 0.149 \times 10^{-28}$ m^2), the line width of aluminum drastically increases when the geometry of the nucleus diverges from cubic symmetry and masks the observation of possible heteronuclear couplings (J_{AlP}, J_{AlF}). Aluminum resonances corresponding to octahedral geometry are close together, and often overlap, as shown in Figure 1b, where the line located at −4 ppm has a line width of 1500 Hz and corresponds to two overlapping Lorentzian lines (see below). Consequently, the analytical information obtained by ^{27}Al NMR, except for the geometry of aluminum, is relatively poor.

Assignment of the Aluminum−Pyrophosphate Species. The observed similarities in the evolution of the ^{27}Al NMR and the ^{31}P NMR spectra help to determine which species are present when aluminum is bound to pyrophosphate in aqueous solution. The $\mathbf{a_1}$ (^{27}Al) and $\mathbf{b_1}$, $\mathbf{b_2}$, and $\mathbf{b_4}$ (^{31}P) signals exhibit a similar intensity dependence (decreasing when [PPi]/[Al] > 1 to zero for [PPi]/[Al] ≈ 2), and the $\mathbf{a_2}$ (^{27}Al) and $\mathbf{b_3}$ (^{31}P) signals also increase with the [PPi]/[Al] ratio, with a maximum being reached for [PPi]/[Al] ≈ 2.

The nonequivalence of the two phosphorus nuclei, in the $\mathbf{b_2}$ line set, corresponding to an AB/AX substructure, allows us to assign it to molecules of structural type **I** (Chart 1). Evidence for this assignment is strengthened by the rapid collapse of both the $\mathbf{a_1}$ and $\mathbf{b_2}$ signals as soon as fluoride is added to the solution, in a manner similar to that of the beryllium−pyrophosphate complexes studied previously.[4] The existence of isomers differing in the relative position of the X ligands (OH or H_2O) may account for the poorly resolved doublets.

No coupling was observable between the $\mathbf{b_1}$ and $\mathbf{b_4}$ signals, and no coupling was detected in a COSY experiment. These signals arise when PPi and Al are equimolar and probably correspond to pyrophosphate complexes in which the phosphorus atoms are equivalent, i.e., bound in a bidentate fashion to aluminum. The **I′** and/or **I″** structural types (Chart 1), which include many possible isomers, may satisfy these conditions and thus give poorly resolved ^{31}P NMR resonances. The existence of structures **I′** and **I″** is supported by the results obtained with fluoro complexes (see below).

Chart 1. Possible Structures Corresponding to the ^{27}Al and ^{31}P NMR Resonances of the Al−PPi Complexes



The couple $\mathbf{a_2}$/$\mathbf{b_3}$ corresponds to complexes with a [PPi]/[Al] ratio of 2. The singlet $\mathbf{b_3}$ corresponds to molecule(s) in which bidentate pyrophosphate is bound to the aluminum. The ^{19}F NMR spectra help in the assignment of the $\mathbf{b_3}$ signal, and its puzzling behavior in the ^{31}P NMR spectrum, which is a function of fluoride concentration, may be explained if the assumption is made that this signal actually corresponds to two closely-overlapping resonances ($\mathbf{b_{3a}}$ and $\mathbf{b_{3b}}$), due to the poor resolution of the ^{31}P NMR spectra. One of these ($\mathbf{b_{3a}}$), which is present even in the absence of fluoride, disappears at higher fluoride concentrations and is assigned to Al−PPi$_2$ species of the **II** type (Chart 1) in which the two PPi ligands are bound in a bidentate fashion to Al. The second, which exists only with fluoride ($\mathbf{b_{3b}}$), is assigned to ternary Al−PPi−F complexes where one PPi ligand is bound in a bidentate fashion to Al (see below). The intensity of the latter signal would follow a classical bell-shaped variation versus fluoride concentration, with a maximum [F]/[Al] ratio close to 4. The experimentally observed intensity corresponds to the sum of both the $\mathbf{b_{3a}}$ and $\mathbf{b_{3b}}$ signals (Figure 3), with a minimum at [F]/[Al] ≈ 1. Such a coincidence in chemical shifts has already been found in the case of beryllium−pyrophosphate−fluoride complexes, in which two signals differed by only 0.03 ppm.[4]

Assignments of the Aluminum−Pyrophosphate−Fluoride Species. The presence of two sets of fluorinated compounds revealed by ^{19}F NMR (α and β ranges, as defined in the Results) is confirmed by ^{27}Al NMR (Figure 1b, in which curve analysis could be used to estimate the $\mathbf{a_3}$ resonance as a ∼30/70 mixture of two different sets of octahedral aluminum complexes, located at −11 and −3 ppm, respectively). However, the chemical shifts of the ^{31}P NMR resonances do not allow discrimination of the α and β ranges (Figure 2b).

The presence of a poorly resolved triplet corresponding to heteronuclear coupling J_{PF} on both $\mathbf{c_1}$ and $\mathbf{c_2}$ lines clearly

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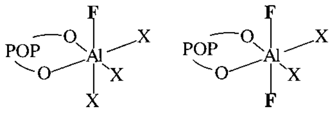
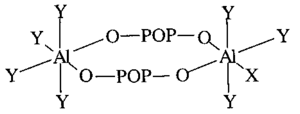
Chart 2. Structures Corresponding to the ^{31}P and ^{19}F Resonances of the α Range of the Al−PPi−F Complexes



III **IV**

Chart 3. Structural Type Corresponding to the ^{19}F Resonances of the β Range of the Al−PPi−F Complexes

[Y ≡ F, OH, H_2O]



V

indicates that the corresponding compounds possess one PPi unit that is bidentately bound to one aluminum. The fact that their intensities reached a maximum for a [PPi]/[Al] ratio ≈ 1 strengthens this assumption. The 0.5 ppm shift between them is on the same order of magnitude as the shift measured previously for fluoroaluminate complexes $AlF_1(H_2O)_5^{2+}$ and $AlF_2(H_2O)_4^{+}$.[7] Thus, structures **III** and **IV** should correspond to the $\mathbf{c_1}$ and $\mathbf{c_2}$ lines, respectively (Chart 2). They derive from structure **I′** which has been described previously.

The ^{31}P signal $\mathbf{b_{3b}}$ observed at ∼−7.4 ppm, as defined above, corresponds to both structures **III** and **IV**, the phosphorus nuclei of which are equivalent. The number of isomers explains the breadth of this resonance (Figure 2b).

The experimental ^{19}F NMR results, and the existence of heteronuclear J_{PF} triplets for all the ^{19}F resonances in the β range and of homonuclear J_{FF} multiplets for signals $\mathbf{c_3}$ and $\mathbf{c_4}$ (Figure 4b and Table 3) lead us to propose molecules of the type shown by structure **V** (Chart 3), comprising two octahedral aluminums bound together via two common PPi ligands. This structure is derived from structure **I″**, which has been described previously. Such a bidentate connection between two ligands has already been described for fluorogermanium complexes.[22] This kind of double bidentate bond, preventing any intermolecular exchange on the aluminum sites, could explain the exceptional thermodynamic stability in aqueous solution, allowing observation of hetero- and homonuclear couplings at temperatures as high as 80 °C.

Complexes corresponding to these lines or sets of lines[23] can be assumed to be derived from the **V** type of structure, containing various numbers of fluoride ions, as shown in examples given in Chart 4: singlets (e.g., $\delta = -133.2, -134.2$, and -137.2 ppm in Figure 4b) with structures $\mathbf{V_a}$ and/or $\mathbf{V_b}$ and $\mathbf{V_c}$; multiplet $\mathbf{c_3}$ (d, d) with $\mathbf{V_c}$ and/or $\mathbf{V_d}$; multiplet $\mathbf{c_4}$ (d, t) with $\mathbf{V_e}$ and/or $\mathbf{V_f}$.

The large number of possible molecules accounts for the multiplicity of ^{19}F resonances. It also explains the intricacy of the ^{31}P resonances. Therefore, it is impossible to retrieve any heteronuclear J_{FP} coupling in ^{31}P NMR spectra. The various AB/AX subspectra (e.g., $\mathbf{b_5}-\mathbf{b_{10}}$) correspond to the various examples of complexes (i.e., $\mathbf{V_a}$, $\mathbf{V_c}$, $\mathbf{V_d}$, $\mathbf{V_f}$), for which homonuclear J_{PP} couplings could be observed only by ^{19}F decoupling.

Chart 4. Examples of Complexes Deriving from the **V** Structural Type and Corresponding to the ^{19}F Resonances of the β Range

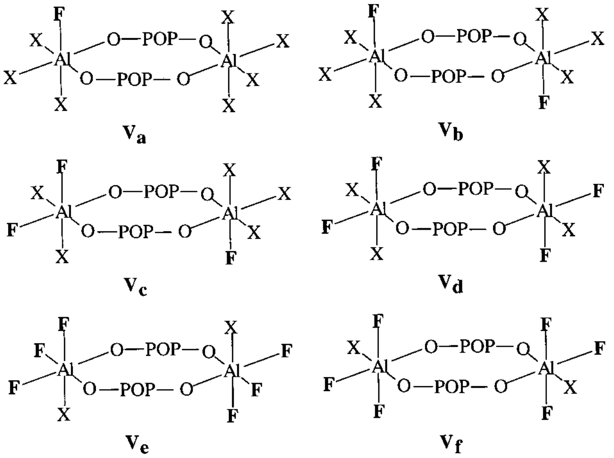
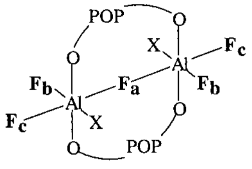


Chart 5. Structure Corresponding to the $\mathbf{c_5}$ Region of the ^{19}F NMR Spectrum



VI

Finally, the complex corresponding to the set of lines $\mathbf{c_5}$ cannot be interpreted as deriving from the **V** type of structure. We propose the **VI** structure (Chart 5) to account for its three different multiplicities (Table 3). This structure could fit, assuming that the *trans* $^2J_{FF}$ coupling constants are small compared to the *cis* $^2J_{FF}$ coupling constants (about 83 Hz, see the Results) as is often the case in octahedral complexes.[22,24,25] In the $\mathbf{c_5}$ part of the spectrum, the doublet (−138.95 ppm; 2F) is attributed to $\mathbf{F_c}$, the triplet (−142.40 ppm; 2F) to $\mathbf{F_b}$, and the triplet (−143.40 ppm; 1F) to $\mathbf{F_a}$. A spectral simulation with a value of $^2J_{trans} \approx 15$ Hz gives a spectrum very similar to the experimental $\mathbf{c_5}$ subspectrum. Such a structure, where two octahedral fluoroaluminate complexes are bound by a common fluoride atom at a corner, has already been proposed in hydrogen peroxide solution.[26] Brownstein[22,24] has shown that, with another ligand such as silicon or vanadium, other fluorometallic complexes have similar structures, identified using ^{19}F NMR with observable J_{FF} coupling constants (in SO_2 solution at −75 °C for silicon and in SO_2ClF solution at −100 °C for vanadium). It should be noted that, in these two cases, no *trans* $^2J_{FF}$ coupling has been observed.

For the **VI** fluorocomplex, the central fluoride ($\mathbf{F_a}$), coupled to the four phosphorus atoms of the two equivalent PPi groups, should give rise to a J_{PF} quintet, whereas the other fluoride atoms ($\mathbf{F_b}$ and $\mathbf{F_c}$) give triplets. We have been unable to observe the presence of a quintet in the $\mathbf{F_a}$ resonance. However, the low sensitivity and the poor resolution of the corresponding multiplet do not allow us to exclude the possible existence of a quintet. Moreover, the coupling constant $^3J_{F_aP}$, which is possibly lower

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(22) Brownstein, S. *Can. J. Chem.* **1980**, *58*, 1407.

(23) A careful examination of the $^{19}F\{^{31}P\}$ NMR spectra reveals splittings of several resonances (as $\mathbf{c_3}$ and $\mathbf{c_4}$) of various intensities which may be due to different isomers.

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(26) Kon'shin, V. V.; Chernyshov, B. N.; Ippolitov, E. G. *Izsvest. Akad. Nauk SSSR* **1987**, *8*, 1707.

than the other $^3J_{FP}$ ($\mathbf{F_b}$, $\mathbf{F_c}$), may help to explain the difficulty in experimentally observing such a quintet.

We have performed similar experiments using ADP instead of pyrophosphate to ligate the fluoroaluminate ion. ^{27}Al NMR shows that the aluminum cation is still hexacoordinated. ^{19}F NMR shows that all the signals of the ADP−fluoroaluminate complex spectra are singlets, and located in the α range defined previously.[27] The absence of a β range could be interpreted as resulting from steric hindrance due to nucleotide size and the difference in acidity of the phosphates.

These results confirm that the β range, which exists only with pyrophosphate, is correlated with structures tightly bound by two bidentate pyrophosphate ligands. Similar experimental results, which were published previously, concerning nucleotide−aluminum−fluoride complexes at pH 6, and using multi-NMR (^{1}H, ^{19}F, ^{31}P)[28,29] lacked ^{19}F resonances in the β range, as defined in the present paper.

Conclusion

In a previous study[7] we showed that the aluminum ion is always hexacoordinated in fluoroaluminate complexes that are able to interact with P-type ATPases. This geometry is maintained when the fluoroaluminate, in aqueous solution, is bound to diphosphatidic compounds such as nucleotides or pyrophosphate.

Moreover, multi-NMR shows a large variety of ternary Al−PPi−F complexes. They are characterized by the ability of two fluoroaluminates to bind to each other by an edge or by a corner. Of these complexes, we highlight a new class of very stable complexes in which aluminum binds two pyrophosphate units in a bidentate fashion with, in one case, one central fluoride atom firmly binding the two aluminum ligands. These complexes are characterized by ^{19}F NMR signals, which have a distinctive range of chemical shifts, and by their J_{FF} and J_{FP} couplings. As far as we know, this is the first description of fluorometallic complexes that are sufficiently nonlabile to permit the observation of J_{FF} and J_{FP} couplings by ^{19}F NMR and J_{PP} couplings by ^{31}P NMR in aqueous solutions at temperatures as high as 80 °C. In these complexes, the existence of J_{FF} couplings provides unambiguous evidence for the octahedral geometry of the aluminum center.

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Supporting Information Available: Figures showing NMR intensities of Al−PPi complexes versus [PPi]/[Al], α and β range ^{19}F NMR intensities versus initial NaF concentration, ^{27}Al NMR spectrum of an equimolar Al−PPi−F mixture, and ^{19}F NMR $\mathbf{c_5}$ set of lines and the corresponding simulated spectrum. This material is available free of charge via the Internet at http://pubs.acs.org.

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