

Base Hydrolysis of Dihalobis(acetylacetonato)technetium(IV) Complexes

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Abstract

Reaction mechanism of the dihalobis(acetylacetonato)technetium(IV) complexes $[\text{TcX}_2(\text{acac})_2]$, $\text{X} = \text{Cl}$ and Br was investigated by means of solvent extraction and spectrophotometric methods. $\text{TcX}_2(\text{acac})_2$ is resistant to the attack of acid. In an alkaline solution, however, it liberates first halide ions and then acetylacetonate ions. As a final product, pertechnetate was recognized. The rate equation is expressed as $R = k_1[\text{OH}^-][\text{TcX}_2(\text{acac})_2]$ in a higher concentration of hydroxide ion, whereas it becomes complicated with a decrease in the concentration of hydroxide ion. The respective decomposition rate constants were determined.

Introduction

Technetium-99m labelled complexes have been used widely in the field of nuclear medicine. On the other hand, technetium is a very interesting element in coordination chemistry and during the last five years a variety of complexes have been synthesized and characterized using macroscopic amounts of ^{99}Tc [1]. The established routes for the synthesis of technetium complexes are classified as follows: first is the reduction of pertechnetate to a desired oxidation state and then the complex is synthesized by addition of the ligand; second is the direct synthesis of the desired complex in the presence of both reducing agent and ligand.

However, synthesized technetium β -diketonate complexes are limited. Mazzi *et al.* [2] synthesized first several β -diketonate complexes including tris(acetylacetonato)technetium(III) $[\text{Tc}(\text{acac})_3]$ and dihalobis(acetylacetonato)technetium(IV) $[\text{TcX}_2(\text{acac})_2]$. Recently, a simple method for the synthesis of $\text{Tc}(\text{acac})_3$ has been established by the direct reduction of pertechnetate with dithionite in the presence of acetylacetonate [3]. Tris(benzoylacetonato)technetium(III) and tris(thenoyltrifluoroacetonato)technetium(III) were also synthesized by the latter method [4].

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Kinetic behavior of the technetium(V) complexes has been discussed in terms of the structural *trans* effect (STE) [1, 5]. Tris(acetylacetonato)technetium(III) seems to be inert for the substitution reaction [6]. Furthermore, chromatographic behavior of the tris(β -diketonato)technetium(III) complexes has been compared to that of the corresponding complexes of chromium(III), cobalt(III) and ruthenium(III) [7]. On the other hand, technetium(IV) complexes are generally expected to be substitution inert similar to the complexes of Cr(III) and Re(IV), which should follow from their electronic configuration, d^3 . However, no systematic information of the substitution reaction of these technetium(IV) complexes has been obtained. In the present study, kinetics of the hydrolysis of *cis*- $\text{TcX}_2(\text{acac})_2$ ($\text{X}^- = \text{Cl}^-$ or Br^-) will be examined.

Experimental

Ammonium pertechnetate was obtained from the Radiochemical Centre, Amersham. All the other reagents used were of guaranteed reagent grade.

cis-Dihalobis(acetylacetonato)technetium(IV) complexes were synthesized by the method described in the literature [2]. The complexes synthesized were assigned to the *cis*-form [2].

Kinetic runs were performed by the following procedures. In the solvent extraction method, an aqueous solution of sodium hydroxide was added to a chloroform solution containing a desired concentration of $\text{TcX}_2(\text{acac})_2$ to initiate the reaction. All the solutions had previously been maintained at 25 °C. The ionic strength of the aqueous solution was adjusted to 1.0 M with sodium chloride. Kinetic runs were carried out at 25.0 ± 0.5 °C in air unless otherwise stated. Aliquots were taken from the reaction mixture at suitable intervals. The concentration of technetium in the organic phase was determined by measuring the radioactivity. The absorbance was also measured with a spectrophotometer when necessary.

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In the homogeneous phase system, 0.5 ml of an acetonitrile solution of $\text{TcX}_2(\text{acac})_2$ and 10 ml of an aqueous solution of sodium hydroxide were mixed with a magnetic stirrer at $25.0 \pm 0.5^\circ\text{C}$ in air. The absorbance of the solution was measured at appropriate time intervals. The wave length measured was varied on the basis of the chemical species existing during the kinetic run. Furthermore, the concentration of the chloride ion liberated from the complex was determined by means of an electrochemical method using an ion selective electrode and a colorimetric method [8].

Radioactivity of ^{99}Tc was measured with a liquid scintillation counter.

Results and Discussion

In the kinetic study, characterization of the chemical species concerned is required. In order to confirm the chemical form of $\text{TcCl}_2(\text{acac})_2$ in the organic phase, measurements of the molar extinction coefficient were made on chloroform solutions ranging in concentration from $5.26 \times 10^{-6}\text{ M}$ to $1.2 \times 10^{-4}\text{ M}$. A constant molar extinction coefficient ($\epsilon = 14800 \pm 200\text{ M}^{-1}\text{ cm}^{-1}$ at 281 nm) was obtained in this concentration range. Therefore, $\text{TcCl}_2(\text{acac})_2$ exists in chloroform as the monomer at least below $1.2 \times 10^{-4}\text{ M}$.

In an acid solution, $\text{TcX}_2(\text{acac})_2$ is stable. No detectable change in the distribution ratio of ^{99}Tc , which is defined as the ratio of the concentration of technetium in the organic phase to that in the aqueous phase, was observed over the period of 24 h, when the chloroform solution of $\text{TcCl}_2(\text{acac})_2$ was shaken with 1.0 M hydrochloric acid solution. The same situation was found when a 4 M perchloric acid solution was used instead of hydrochloric acid. Thus, the distribution ratio can be replaced by the distribution coefficient, which is defined by the ratio of the concentration of $\text{TcCl}_2(\text{acac})_2$ in the organic phase to that in the aqueous phase. The distribution coefficient, D , was determined to be 170 ± 40 at 25°C .

A preliminary experiment showed that the technetium(IV) complexes can be backextracted into the aqueous alkaline solution with decomposition. Finally, quantitative formation of pertechnetate was confirmed by means of spectrophotometry. Thus, the decomposition rates of $\text{TcX}_2(\text{acac})_2$ as a function of the concentration of hydroxide ion were examined in detail.

A plot of the logarithmic concentration of technetium in the organic phase against time shows a straight line. A spectrophotometrical study also revealed a decrease in the absorbance at 281 nm in chloroform during the kinetic run, but no change in the UV-Vis spectrum was observed, showing that

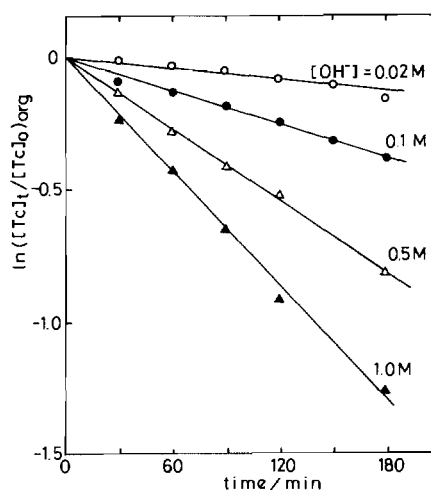


Fig. 1. $\ln\{[\text{TcCl}_2(\text{acac})_2]_t/[\text{TcCl}_2(\text{acac})_2]_0\}$ vs. time at 25°C .

the technetium complex remaining in the organic phase is $\text{TcX}_2(\text{acac})_2$. Typical results for the base hydrolysis of $\text{TcCl}_2(\text{acac})_2$ are shown in Fig. 1. When the kinetic run was carried out in an atmosphere of nitrogen, the apparent decomposition rate accords to that in air within the experimental error. Therefore, oxygen does not participate in the process of solvent extraction, though the final product is pertechnetate which should be formed through air oxidation. Thus, the reaction rate of the base hydrolysis of $\text{TcCl}_2(\text{acac})_2$ is expressed as

$$-\frac{d[\text{TcCl}_2(\text{acac})_2]}{dt} = k_{\text{app}}[\text{TcCl}_2(\text{acac})_2] \quad (1)$$

and the apparent first-order rate constant, k_{app} , can be obtained from the gradient values of straight lines.

As Fig. 2 shows, a first-order dependence of the apparent rate constant on the hydroxide ion appears above 0.02 M; that is, the rate constant can simply be explained as

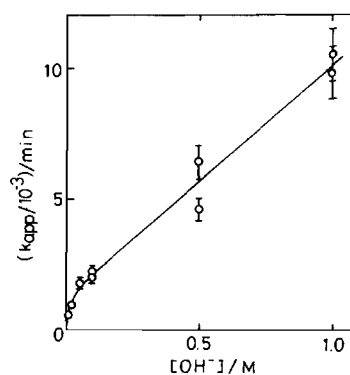


Fig. 2. Dependence of the apparent decomposition rate constant of $\text{TcCl}_2(\text{acac})_2$ on the concentration of hydroxide ion at 25°C . Solid line was calculated by eqn. (9).

$$k_{\text{app}} = k_1 [\text{OH}^-] \quad (2)$$

and k_1 was determined to be $(1.5 \pm 0.2) \times 10^{-4} \text{ M}^{-1} \text{ s}^{-1}$ at 25 °C. However, in the concentration range below 0.02 M, complicated reaction processes may be suggested. This is also confirmed by an Arrhenius plot of k_{app} . At $[\text{OH}^-] = 1.0 \text{ M}$, a plot of $\ln(k_{\text{app}})$ against T^{-1} gives a straight line and the activation energy for k_1 was determined to be 80.4 kJ/mol. On the other hand, such a plot does not give a straight line at $[\text{OH}^-] = 0.002 \text{ M}$. In the low $[\text{OH}^-]$ range, therefore, the decomposition reaction differs from that expressed as eqn. (2). Prior to discussing the reaction mechanism, let us consider the fate of the species extracted into the aqueous phase.

It is impossible to describe the whole reaction processes in terms of the distribution ratio obtained from the solvent extraction method, because the decomposition processes should require several steps until pertechnetate is formed as the final product. In order to obtain information of complete decomposition processes, the kinetic behavior of the species which was backextracted into the aqueous phase was examined by spectrophotometry. The absorption maxima of $\text{TcCl}_2(\text{acac})_2$ in a chloroform solution are at 281, 314(sh), 340(sh), 382 and 420 nm. On the other hand, the spectrum of the aqueous phase exhibits absorption maxima at 292, 350 and 540 nm. The absorbances at 350 and 540 nm increase with time, but then decrease after reaching maxima. This suggests that a chemical species which is formed by the backextraction of $\text{TcCl}_2(\text{acac})_2$ decomposes with reaction time. A further spectrophotometric study was carried out in the homogeneous system, taking into consideration that determination of the chloride ion liberated from the complex by means of the electrochemical method is difficult even in the presence of a trace amount of chloroform.

$\text{TcCl}_2(\text{acac})_2$ is stable in acetonitrile. On addition of an aqueous solution of sodium hydroxide, however, the solution turned immediately from brown to red-violet, exhibiting absorption maxima at 292, 350 and 540 nm. The red-violet solution was gradually decolorized and finally the spectrum of pertechnetate which is characterized by maxima at 244 and 287 nm was obtained. On the other hand, exactly twice as much free chloride ion as technetium was found in the earliest stage and its concentration remained constant during the kinetic run. These features indicate that the red-violet species is a bis-(acetylacetonato)technetium complex splitting off the chloride ion.

Figure 3 shows decreases in the absorbances at 350 and 540 nm with time. The decomposition rate of the complex can be regarded as simple first-order kinetics without respect to the concentration of hydroxide ion. Thus, the decomposition rate constant, k_{M} , was shown to be $(3.6 \pm 0.4) \times 10^{-4} \text{ s}^{-1}$.

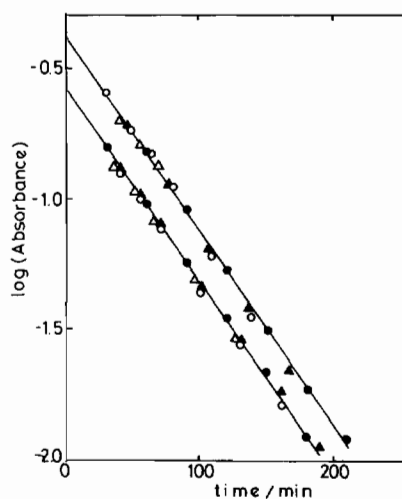


Fig. 3. Time dependence of the absorbance of the bisacetylacetonate complex in the acetonitrile solution at 25 °C. Δ : $[\text{OH}^-] = 0.1 \text{ M}$, \circ : $[\text{OH}^-] = 0.25 \text{ M}$, \blacktriangle : $[\text{OH}^-] = 0.5 \text{ M}$, \bullet : $[\text{OH}^-] = 1.0 \text{ M}$. Upper line: 350 nm, lower line: 540 nm.

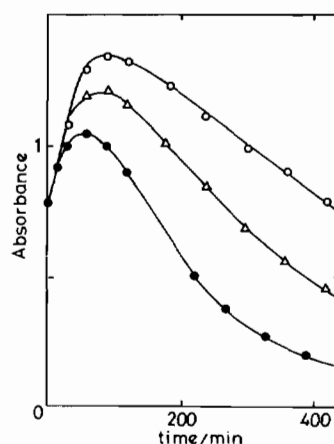


Fig. 4. Time dependence of the absorbance at 292 nm in the acetonitrile solution at 25 °C. \circ : $[\text{OH}^-] = 0.25 \text{ M}$, Δ : $[\text{OH}^-] = 0.5 \text{ M}$, \bullet : $[\text{OH}^-] = 1.0 \text{ M}$. Solid lines were calculated by eqn. (6).

On the other hand, the absorbance at 292 nm varies in a complicated manner. As is shown in Fig. 4, the absorbance increases at first, reaches a maximum and decreases gradually. The maximum absorbance depends on the concentration of hydroxide ion. This fact can be reasonably explained by the assumption that an increase in the absorbance corresponding to the decomposition of the bisacetylacetonate complex and a decrease is due to the decomposition of a free acetylacetonate molecule. In fact, a separate experiment showed that decomposition of acetylacetonate takes place in an alkaline solution and its rate can be expressed as

$$-\frac{d[\text{acac}^-]}{dt} = k_d [\text{OH}^-] [\text{acac}^-] \quad (3)$$

in which k_d is the decomposition rate constant of the acetylacetonate ion and is determined as follows

$$k_d = 1.2 \times 10^{-4} \text{ M}^{-1} \text{ s}^{-1} (25^\circ \text{C})$$

Since the formation rate of the free acetylacetonate ion is given by

$$\frac{d[\text{acac}^-]}{dt} = k_M[\text{Tc}(\text{acac})_2^{2+}] - k_d[\text{OH}^-][\text{acac}^-] \quad (4)$$

integration of eqn. 4 gives the following equation

$$[\text{acac}^-] = \frac{2k_M}{k_d - k_M} [\text{Tc}(\text{acac})_2^{2+}]_0 (e^{-k_M t} - e^{-k_d t}) \quad (5)$$

where k_M is the decomposition rate constant of the bisacetylacetonate complex. Thus, the following equation giving the absorbance at 292 nm, A_{292} , can be derived as a function of time

$$A_{292} = [\text{Tc}(\text{acac})_2^{2+}]_0 \times \left(\epsilon_{\text{acac}^-} \frac{2k_M}{k_d - k_M} (e^{-k_M t} - e^{-k_d t}) + \epsilon_M e^{-k_M t} \right) \quad (6)$$

where ϵ_{acac^-} and ϵ_M are the molar absorption coefficients of free acetylacetonate ion and the bisacetylacetonate complex at 292 nm, respectively. In eqn. (6), unknown parameters, ϵ_M and k_M , can be determined by analysis of the curve in Fig. 4. The best fit values for ϵ_M and k_M obtained by the non-linear least squares method are $1.3 \times 10^4 \text{ M}^{-1} \text{ cm}^{-1}$ and $(3.8 \pm 0.4) \times 10^{-4} \text{ s}^{-1}$, respectively, using the known parameters ϵ_{acac^-} ($= 1.57 \times 10^4 \text{ M}^{-1} \text{ cm}^{-1}$) and k_d . The value for k_M agrees closely with that obtained by analysis of the variation of absorbances at 350 and 540 nm. In Fig. 4 the solid lines were calculated by eqn. (6).

The base hydrolysis of $\text{TcBr}_2(\text{acac})_2$ was also examined by means of the solvent extraction method. As is shown in Fig. 5, a plot of the logarithmic

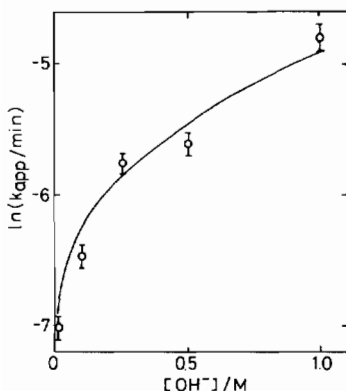
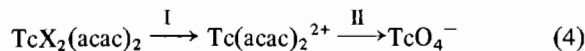


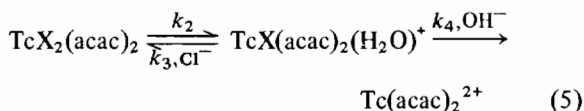
Fig. 5. Dependence of the apparent decomposition rate constant of $\text{TcBr}_2(\text{acac})_2$ on the concentration of hydroxide ion at 25°C . Solid line was calculated by eqn. (9).

apparent rate constant against the concentration of hydroxide ion gives a straight line in the range of concentration over 0.2 M. The absorption spectrum of the species which was extracted into the aqueous phase was the same as that in the $\text{TcCl}_2(\text{acac})_2$ system. This fact provides further evidence to confirm that a bisacetylacetonate technetium complex is present in the aqueous phase.

On the basis of the experimental results described above, the decomposition processes can be described as follows



In process I, the bisacetylacetonate complex which exhibits absorption maxima at 350 and 540 nm is formed by virtue of the attack of hydroxide ion at the higher concentration of hydroxide ion. This process (Ia) may include the substitution reaction of the hydroxide ion for a chloride ion, followed by the instantaneous liberation of the other chloride ion. There remains the question whether the bisacetylacetonate still contains hydroxide ion in the coordination sites or not. In the base hydrolysis of technetium(V) complexes, the corresponding species is considered to be $\text{TcO}(\text{OH})(\text{acac})_2$ [9]. However, it is difficult to obtain definite information on the chemical form of the bisacetylacetonate and the possibility of intramolecular rearrangement of the *cis*-complex to the *trans*-complex. Thus, we express hereafter the bisacetylacetonate complex as $\text{Tc}(\text{acac})_2^{2+}$. On the other hand, in the low $[\text{OH}^-]$ region it might be formed through the formation of an intermediate by taking into consideration the fact that $\text{TcX}_2(\text{acac})_2$ is stable in acid solution. Thus, this process (Ib) may be described as follows



In addition, distribution of $\text{TcX}_2(\text{acac})_2$ between the organic and aqueous phases seems to be rapid in comparison with the decomposition rate. Thus, the decrease in the concentration of $\text{TcCl}_2(\text{acac})_2$ is expressed as

$$\frac{d[\text{TcCl}_2(\text{acac})_2]}{dt} = -(k_1[\text{OH}^-] + k_2)[\text{TcCl}_2(\text{acac})_2] + k_3[\text{Cl}^-][\text{TcCl}(\text{acac})_2(\text{H}_2\text{O})^+] \quad (6)$$

$$\frac{d[\text{Tc}(\text{acac})_2^{2+}]}{dt} = k_{\text{app}}[\text{TcCl}_2(\text{acac})_2] - k_4[\text{OH}^-][\text{Tc}(\text{acac})_2^{2+}] \quad (7)$$

When the steady-state approximation may be applied to the concentrations of $\text{TcCl}(\text{acac})_2(\text{H}_2\text{O})^+$, the following equations can be derived

TABLE I. Rate Constants for the Base Hydrolysis of $\text{TcX}_2(\text{acac})_2$ at 25 °C

Complex	Rate constant			
	k_1 ($\text{M}^{-1} \text{s}^{-1}$)	k_2 (s^{-1})	k_3 ($\text{M}^{-1} \text{s}^{-1}$)	k_4 ($\text{M}^{-1} \text{s}^{-1}$)
<i>cis</i> - $\text{TcCl}_2(\text{acac})_2$	$(1.5 \pm 0.2) \times 10^{-4}$	$(1.5 \pm 0.2) \times 10^{-5}$	$(2.6 \pm 0.7) \times 10^{-3}$	$(4.9 \pm 1.3) \times 10^{-1}$
<i>cis</i> - $\text{TcBr}_2(\text{acac})_2$	$(1.0 \pm 0.1) \times 10^{-4}$	$(2.4 \pm 0.2) \times 10^{-5}$	$(3.0 \pm 1.0) \times 10^{-3}$	$(5.6 \pm 1.9) \times 10^{-1}$

$$\ln \left(\frac{[\text{TcCl}_2(\text{acac})_2]_t}{[\text{TcCl}_2(\text{acac})_2]_0} \right)_{\text{org}} = \left(k_1 [\text{OH}^-] + \frac{k_2 k_4 [\text{OH}^-]}{k_3 [\text{Cl}^-] + k_4 [\text{OH}^-]} \right) t \quad (8)$$

Consequently, k_{app} in eqn. (1) can be expressed as follows

$$k_{\text{app}} = \left(k_1 + \frac{k_2 k_4}{k_3 [\text{Cl}^-] + k_4 [\text{OH}^-]} \right) [\text{OH}^-] \quad (9)$$

$$[\text{Tc}(\text{acac})_2^{2+}] = \frac{k_{\text{app}}}{k_{\text{M}} - k_{\text{app}}} [\text{TcCl}_2(\text{acac})_2] \times (e^{-k_{\text{app}} t} - e^{-k_{\text{M}} t}) \quad (10)$$

Since k_1 has been determined, the rate constants k_2 , k_3 and k_4 can be obtained by the non-linear least squares method from the relationship between k_{app} and the concentration of hydroxide ion as shown in Figs. 2 and 5. The rate constants are summarized in Table I. The solid lines in Figs. 2 and 5 were calculated by eqn. (9).

There seems to be a marked difference between the rate constants of the chloro-complex and those of the bromo-complex. In the process Ia, k_1 may include the term of the distribution coefficient. If the distribution process of $\text{TcX}_2(\text{acac})_2$ between the organic and aqueous phases is taken into account, the concentration of $\text{TcX}_2(\text{acac})_2$ in the organic phase is expressed as follows

$$[\text{TcX}_2(\text{acac})_2] = \frac{D}{1+D} [\text{TcX}_2(\text{acac})_2] e^{-\{k[\text{OH}^-]/(1+D)\}t} \quad (11)$$

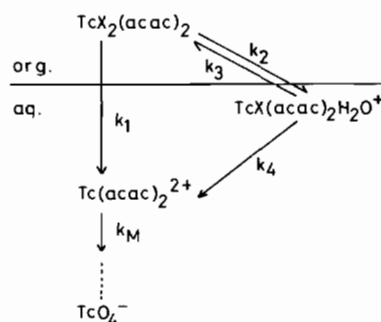
where k is the decomposition rate constant of $\text{TcX}_2(\text{acac})_2$ in the aqueous phase. Thus, k_1 is replaced by

$$k_1 = k/(1+D).$$

If the distribution process is considered, the fact that the decomposition of $\text{TcX}_2(\text{acac})_2$ takes place promptly in an acetonitrile solution may be understood. In the present system, however, the distribution coefficient is evaluated to be high with a rela-

tively large error. Furthermore, all the plots of $\ln\{[\text{TcX}_2(\text{acac})_2]_t/[\text{TcX}_2(\text{acac})_2]_0\}$ against time give straight lines passing through the origin. Suggesting that the term $D/(1+D)$ in eqn. (11) may be taken as unity. Accordingly, the values for k_1 are listed in Table I. In the process Ib, the ease of hydrolysis appears to increase in the order $\text{X} = \text{Cl} < \text{Br}$, reflecting the expected metal-halogen bond strength [10, 11].

In conclusion, $\text{TcX}_2(\text{acac})_2$ is resistant to the attack of water, when it is present in the organic phase. The coordinated halide ion is much more labile than the bidentate ligand against the base hydrolysis. On addition of hydroxide ion, therefore, the labile halide ions are liberated from the coordination sites. The resulted bisacetylacetonate complex decomposes gradually to pertechnetate. These processes are summarized in Fig. 6.

Fig. 6. Mechanism of the base hydrolysis of $\text{TcX}_2(\text{acac})_2$.

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