A Kinetic Study of the Isotopic Exchange of Lutetium between the Lutetium Ion and its Ethylenediamine-N, N, N', N'-Tetra Acetate

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The isotopic exchange reaction of lutetium between the uncomplexed lutetium ion and its EDTA complex has been kinetically studied in a pH region from 6.5 to 5.5 by using lutetium-177 as a tracer. The rate is proportional to the first order of the concentration of both uncomplexed lutetium and its EDTA complex. The dependence of hydrogen ion concentration on the rate is very complicated. In the pH region from 6.5 to 6.0, the rate is independent on the concentration of hydrogen ion, and in the pH region below 6.0, clearly dependent on the hydrogen ion concentration. It may be supposed, therefore, that a possible mechanism for the exchange reaction in neutral solution is a simple displacement of the lutetium from the chelate compound by a collision with an uncomplexed lutetium.

The rate of exchange is given by the expression:

$$R = 2.2 \times 10^{-2} [\text{Lu-EDTAOH}_2^-] [\text{Lu}^{3+}] \text{mole } l^{-1} \cdot \text{min}^{-1}.$$

In acid solution, the acid catalized reaction may compete with the bimolecular reaction.

1. Introduction

The lutetium ions in aqueous solution form very strong complex with ethylenediamine tetra-acetic acid (EDTA). Its relative stability has been studied on the basis of the measurements of chemical equilibrium¹⁾. Nevertheless, there is no data obtained from the view point of kinetic stability. The present report concerns with extending the knowledge of the exchange reaction between the uncomplexed lutetium ion and its EDTA complex by using lutetium-177 as a tracer. Separation of the uncomplexed lutetium ion from the complex ion was carried out by precipitation with oxalate anion. The mechanism and the influence of the reactants for the exchange reaction will be discussed.

2. Experimental

2.1 Preparation of the tracer

Lutetium-177 (half-life 6.8d) was produced by neutron irradiation of the commercial lutetium oxide for 5 hrs in the JRR-1 reactor. The neutron flux was $(1\sim 5) \times 10^{11}$ n/cm²/sec. Radiochemical purity of the tracer obtained was examined by γ -ray spectrometry and decay analysis.

2.2 Preparation of uncomplexed lutetium

solution

Lutetium oxide was dissolved in nitric acid, the excess of which was removed by evaporation of the solution to dryness. Lutetium nitrate thus obtained was dissolved in water. Generally, this lutetium solution was labelled with lutetium-177.

2.3 Preparation of lutetium EDTA complex solution

Na₂-EDTA (Wako Pure Chemical Ind., Ltd., Extra pure grade) was purified by the usual method²⁾. Lutetium EDTA complex was formed instantaneously on mixing lutetium nitrate solution with equivalent amount of Na₂-EDTA solution.

3. Procedure

The reaction mixture was obtained by mixing both solutions of uncomplexed lutetium and the chelate compound. All the experiments were made in the buffer solutions containing 0.01 M ammonium acetate. The pH was adjusted as required by addition of ammonia. The temperature of the solutions was controlled to

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$25.0 \pm 0.1^\circ\text{C}$. At appropriate interval after mixing, saturated sodium oxalate solution, the amount of which is 1.5 times equimolar to the lutetium ion was added to an aliquot of the reaction mixture to precipitate the uncomplexed lutetium ion as lutetium oxalate³⁾. The pH of sodium oxalate solution was adjusted in advance to be equal to that of the reaction mixture. The precipitates settle rapidly in the pH region from 6.5 to 4.0. The precipitates were centrifuged, separated by decantation, washed twice with buffer solution, and dissolved in nitric acid. During the procedure, the precipitates were diminished by about 10% in quantity, hence, correction for the amount of activity measured was necessary.

Although this separation method may tend to have some disadvantages such as occlusion of undesired complex, dissolution of precipitate, and zero-time exchange due to separation induced exchange, the preliminary experiments established that this technique was satisfactory applicable.

Fig.1 is the yield curves of precipitates obtained at various molar equivalent ratio of oxalic acid to lutetium ion. The reproducibility was found to be satisfactory.

Fig.1 The yield of precipitate at various molar equivalent ratio of oxalic acid to lutetium ion.

4. Measurement of radioactivity

Activity was measured by the single channel γ -spectrometer providing well-type NaI (TI) crystal. The pulse was biased so as to produce an integrated count of the photopeaks more

than 113 keV of lutetium-177. The usual correction for radioactive decay and background was made.

Run No.	pH	$\text{Lu} \cdot \text{EDTA} \cdot \text{OH}_2^- (M)$	$\text{Lu}^{3+} (M)$
22	5.5	9.09×10^{-3}	4.54×10^{-3}
40	6.0	9.09×10^{-3}	4.54×10^{-3}
28	6.5	9.09×10^{-3}	4.54×10^{-3}
10	5.5	2.27×10^{-3}	2.27×10^{-3}
29	6.0	2.27×10^{-3}	2.27×10^{-3}
33	6.5	2.27×10^{-3}	2.27×10^{-3}

Fig.2 Variation of fractional exchange with time.

5. Results

According to McKay⁴⁾, the exchange rate is expressed by

$$R = -2.303 \frac{1}{t} \frac{ab}{a+b} \log(1-F) \quad (1)$$

where a and b represent the concentrations of uncomplexed lutetium and lutetium EDTA complex respectively, F the fractional exchange at time t .

Following correction may be made for an apparent zero-time exchange⁵⁾, if the exponential exchange law is also applied to this zero-time exchange reaction.

$$\ln(1-F') = -\frac{a+b}{ab} R t + \ln(1-F_0) \quad (2)$$

where F' is the apparent fractional exchange at time t , F_0 the fractional exchange observed after separation at time 0.

Fig. 2 shows typical applications of eq. (2) to this experimental system. The straight lines obtained indicate eq.(2) to be applicable. R was calculated from the half-time of the exchange.

R has a dimension of mole $l^{-1} \cdot \text{min}^{-1}$. Reproducibility of R was $\pm 10\%$ and was mainly resulted from the fluctuation of pH adjustment (± 0.03).

$$[\text{Lu}^{3+}] = 4.54 \times 10^{-3} M$$

—×—: pH 6.5; —●—: pH 6.0;
—○—: pH 5.5

Fig. 3 Effect of concentration of $\text{Lu} \cdot \text{EDTA}$ complex on rate.

First, the relationships between R and a , and also between R and b were examined, the results being shown in Figs. 3 and 4 respectively. R is clearly proportional to the concentrations of the complex and of the lutetium ion respectively. The pH dependence of R is also shown in Fig. 5 and a complicated pattern is observed with respect to pH. In the pH region from 6.5 to 6.0, the rate is unaffected by the change in pH, but in the pH from 6.0 to 5.5 the rate increases with increasing hydrogen ion concentration. The following kinetic expression with the limited pH region from 6.5 to 6.0 describes the results:

$$R = k[\text{Lu} \cdot \text{EDTAOH}_2^-][\text{Lu}^{3+}] \text{ mole } l^{-1} \cdot \text{min}^{-1} \quad (3)$$

In Fig. 6, the values of R are plotted against the $[\text{Lu} \cdot \text{EDTAOH}_2^-][\text{Lu}^{3+}]$, where the linear relationship is seen within the pH region examined. From the slope in Fig. 6, the average reaction rate constant, k at $25.0 \pm 0.1^\circ \text{C}$ was calculated to be $(2.2 \pm 0.2) \times 10^{-2} l \cdot \text{mole}^{-1} \cdot \text{min}^{-1}$.

6. Discussion

In the pH region from 6.5 to 6.0, the rate

$$[\text{Lu} \cdot \text{EDTAOH}_2^-] = 4.54 \times 10^{-3} M$$

—×—: pH 6.5; —●—: pH 6.0;
—○—: pH 5.5

Fig. 4 Effect of concentration of lutetium ion on rate.

$[\text{Lu} \cdot \text{EDTAOH}_2^-] (M)$	$[\text{Lu}^{3+}] (M)$
1: 9.09×10^{-3}	4.54×10^{-3}
2: 4.54×10^{-3}	4.54×10^{-3}
6: 1.14×10^{-3}	4.45×10^{-3}
3: 2.27×10^{-3}	4.54×10^{-3}
4: 2.27×10^{-3}	3.13×10^{-3}
5: 2.27×10^{-3}	2.27×10^{-3}

Fig. 5 Effect of concentration of hydrogen ion on rate.

of exchange reaction is proportional to the first order of the uncomplexed lutetium and its EDTA complex, and is independent on the concentration of hydrogen ion. It appears probable that the isotopic exchange reaction proceeds predominantly by the mechanism of

Fig. 6 Relationship between R and $[\text{Lu} \cdot \text{EDTAOH}_2][\text{Lu}^{3+}]$ at pH 6.0 and 6.5. simple bimolecular reaction.

When the hydrogen ion concentration is higher, the rate is still proportional to the first order of $[\text{Lu} \cdot \text{EDTAOH}_2]$. While, the dependence of the rate on the lutetium concentration shows the appreciable decrease from the first order relationship and the pH dependence appears considerably.

In the pH region below 6.0, therefore, the exchange reaction will be complicated with several paths, bimolecular reaction, acid catalyzed dissociation reaction of lutetium EDTA complex. It is interesting to examine the exchange reaction in the pH region below 5.5.

要 旨

Lu-Lu·EDTA 系交換反応の研究

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放射性ルテチウムをトレーサーとするルテチウム EDTA 錯塩とルテチウムイオン間のルテチウム交換反応の研究をおこない, 反応速度と反応機作について検討した。反応物質の分離は, シュウ酸による沈殿法を用いた。

反応次数は, pH 6.5~5.5 では錯塩濃度とルテチウムイオン濃度についてともに一次であった。しかしながら, 水素イオン濃度については pH 6.5~6.0 では依存性が認められず, pH 6.0~5.5 において約 0.6 次の依存性が現われてきた。ゆえに中性付近では単純な 2 分子反応で交換反応が進

But because the solubility of lutetium oxalate increases in stronger acid solution, further kinetic study could not be performed with good precision.

A detailed study of isotopic exchange reaction of Lu-EDTA-Lu has been made in this laboratory by using the separation method with cation exchange resin. The results which will appear in the near future support the mechanism discussed above, if the difference between the concentrations of the solutions in both experiments is taken into consideration.

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むが、酸性度が増してくると次第に酸触媒解離機作による交換反応が増してくるものと思われる。

なお、pH 6.5~6.0における反応速度式として

$$R = 2.2 \times 10^{-2} [\text{Lu} \cdot \text{EDTAOH}_2] [\text{Lu}^{3+}] \text{ mole} \cdot \text{l}^{-1} \cdot \text{min}^{-1} \quad (25.0 \pm 0.1^\circ \text{C})$$

がえられた。