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# Facile Cleavage of Adenosine 2',3'-Cyclic Phosphate at pD 7 Catalyzed by Co(III)-Triethylenetetramine Complex

Yoichi MATSUMOTO, Makoto KOMIYAMA,* and Kazuhiko TAKEUCHI†
Institute of Materials Science, University of Tsukuba,
Tsukuba, Ibaraki 305
†National Chemical Laboratory for Industry, Tsukuba, Ibaraki 305

Adenosine 2',3'-cyclic phosphate is efficiently cleaved to adenosine by the [Co(triethylenetetramine)(OH)($H_2O$)]$^{2+}$ complex at pD 7.0, 20 °C. The cleavage (the rate constant 1.9 x $10^{-2}$ $min^{-1}$) in the presence of the complex (0.05 mol $dm^{-3}$) is nearly $10^6$ fold faster than the hydrolysis in the absence of the complex.

Preparation of catalysts for the selective cleavage of nucleic acids has been attracting much interest.[1] A considerable number of successes have been made on the fission of deoxyribonucleic acids. However, information on the cleavage of ribonucleic acids (RNAs) has been relatively scarce.

Previously the present authors succeeded in the regioselective cleavage of RNAs by use of cyclodextrins as catalysts.[2,3] The intermediate for the hydrolysis, 2',3'-cyclic phosphate of ribonucleoside, is selectivity cleaved to either 2'-phosphate or 3'-phosphate. Attachment of catalytic residues to cyclodextrins promoted the catalytic activity still more.[4]

Furthermore, Chin and coworkers showed that Co(III) complexes are quite active for the cleavage of various phosphodiesters.[5] Significant rate acceleration was reported. However, no attempts to cleave RNAs by the complexes have been made yet.

This communication describes that the [Co(trien)(OH)($H_2O$)]$^{2+}$ complex (trien: triethylenetetramine) shows a remarkable catalysis for the cleavage of adenosine 2',3'-cyclic phosphate (A>p). Efficient cleavage of A>p to adenosine is achieved under mild conditions (pD 7.0, 20 °C).

[Co(trien)(OH)($H_2O$)]$^{2+}$ was prepared in situ by the hydrolysis of cis-[Co(trien)$Cl_2$]Cl according to the literature.[5] To 0.05 mol $dm^{-3}$ solution of [Co(trien)$Cl_2$]Cl in $D_2O$, 1.5 equivalents of sodium hydroxide were added. After 10 min, the pD of the solution was adjusted to 7.0. The reaction at 20 °C was initiated by adding A>p to the solution, and was followed by $^1$H-NMR spectroscopy (a Bruker AC200 NMR spectrometer). The initial concentration of A>p in the reaction mixture was 0.01 mol $dm^{-3}$.

As the reaction proceeds, the signal at $\delta$6.27 ppm (assignable to the $C_1$-H proton of the ribose residue of A>p) gradually weakens, with the simultaneous increase of the peak area for the $C_1$-H proton of adenosine ($\delta$6.07 ppm). This

change definitely confirms that A>p is rapidly cleaved to adenosine.

Figure 1 depicts the first-order plot using the peak area for the signal at δ6.27 ppm. The linearity is fair, and the first-order rate constant is determined to be $1.9 \times 10^{-2}$ $min^{-1}$. This value is $7 \times 10^5$ times as large as the rate constant ($2.8 \times 10^{-8}$ $min^{-1}$) for the hydrolysis of A>p to adenosine monophosphate in the absence of the complex at pH 7. The second rate constant has been evaluated from the pH-rate constant profile in a previous paper,[3] which is a fairly straight line of slope unity from pH 12 down to pH 8.5. Thus, 0.05 mol $dm^{-3}$ $[Co(trien)(OH)(H_2O)]^{2+}$ decreases half-life of A>p from 47 years to 36 min!

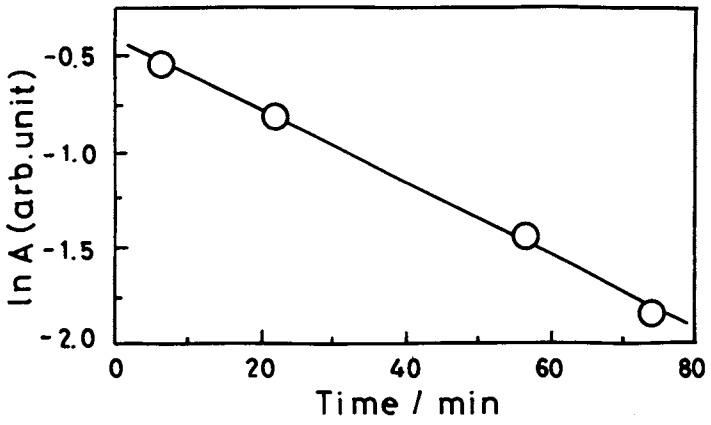


Fig. 1. First-order plot using the peak area (A) at δ6.27 ppm for the $[Co(trien)(OH)(H_2O)]^{2+}$-catalyzed cleavage of A>p at pD 7.0, 20 °C.

The catalytic cleavage probably proceeds via the $[Co(trien)(OH)(A>p)]^{2+}$ complex, formed by the anation of $[Co(trien)(OH)(H_2O)]^{2+}$.[5] Nucleophilic attack by the hydroxide ion toward the phosphorus atom of A>p is quite efficient, since both of them are coordinating to the same Co(III) ion and thus the reaction takes place intramolecularly. The resultant adenosine monophosphate complexing with the Co(III) ion is promptly converted to the final product adenosine.

In conclusion, the Co(III) complex exhibits a remarkable catalysis for the cleavage of A>p. The acceleration is much larger than any of the catalysts previously studied, to the best knowledge of the authors. Study on the catalysis of the complex for the cleavage of ribonucleotide dimers and RNAs is currently under way, and is published in the near future.

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