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## Nucleosides, Nucleotides and Nucleic Acids

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Koichiro Fukuoka<sup>a</sup>; Fuminori Suda<sup>a</sup>; Masahide Ishikawa<sup>a</sup>; Tsujiaki Hata<sup>a</sup>

<sup>a</sup> Department of Life Chemistry, Tokyo Institute of Technology, Yokohama, Japan

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## A CONVENIENT METHOD FOR THE SYNTHESIS OF ATP AND $\text{Ap}_4\text{A}$ .

Koichiro Fukuoka, Fuminori Suda, Masahide Ishikawa, and Tsujiaki Hata\*.

Department of Life Chemistry, Tokyo Institute of Technology, Nagatsuta, Midoriku,  
Yokohama 227, Japan

**Abstract:** A bifunctional phosphorylating reagent, *O*-8-(5-chloroquinolyl) *S*-phenyl phosphorothioate (**1**) was employed for the synthesis of adenosine 5'-triphosphate(ATP) and diadenosine 5'-tetraphosphate( $\text{Ap}_4\text{A}$ ) from adenosine 5'-phosphate(AMP) on a large scale.

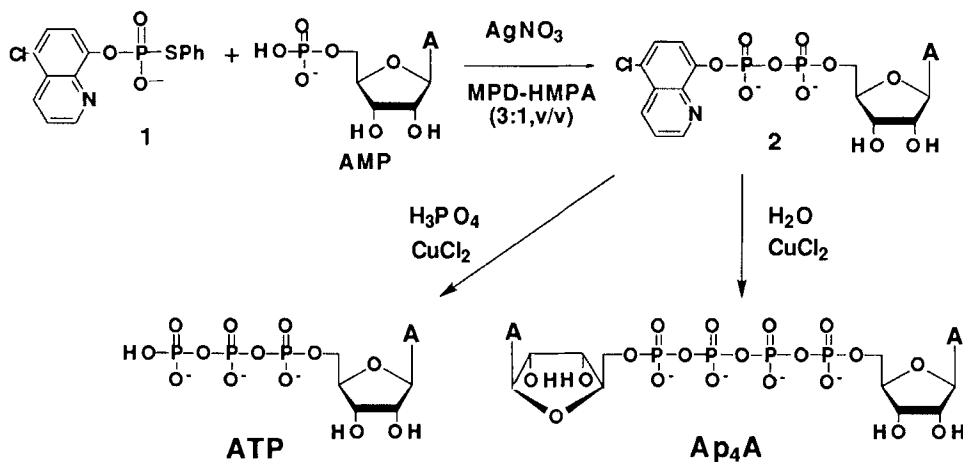
Nucleoside polyphosphates, such as ATP,  $\text{Ap}_4\text{A}$  and the cap structure,  $\text{m}^7\text{G}^5\text{pppN}$  ( $\text{N}=\text{A}$  or  $\text{G}$ ) in eukaryotic mRNA, play important roles in various biological processes. These polyphosphates and their analogues have been synthesized in order to elucidate their biological functions. ATP and  $\text{Ap}_4\text{A}$  were synthesized enzymatically or chemically from activated AMP and pyrophosphate.<sup>1</sup> In the latter, it was difficult to separate ATP or  $\text{Ap}_4\text{A}$  from pyrophosphate by anion exchange column chromatography. Therefore, a convenient method for the synthesis of these polyphosphates is required.

Recently, we have reported the new bifunctional phosphorylating reagent **1** was available for the one-pot synthesis of the cap structure,  $\text{m}^7\text{G}^5\text{pppN}$  ( $\text{N}=\text{A}$  or  $\text{G}$ ).<sup>2</sup> Compound **1** has two different leaving groups, which are activatable selectively. The phenylthio group can be activated by silver ion,<sup>3</sup> and the 5-chloro-8-quinolyloxy group can be activated by copper(II) ion.<sup>4</sup> Therefore, compound **1** would be widely applicable to the convenient synthesis of ATP and  $\text{Ap}_4\text{A}$ .

First, compound **1** was used for the synthesis of ATP. A 1:1 mixture of **1** and AMP was allowed to react with 1.2 equiv of silver nitrate in 1-methylpyrrolidone(MPD)-HMPA(3:1,v/v) at room temperature for 30 min. As a result, the diphosphate intermediate (**2**) was formed along with  $\text{AgSPh}$ . Without isolating **2**, the mixture was treated with 5 equiv of phosphoric acid and 5 equiv of anhydrous copper(II) chloride. The resulting mixture was stirred at room temperature for 24 h. Column chromatography using DEAE Sephadex A-25 gave ATP in 64% yield (92 mg).

Next, compound **1** was also used for the synthesis of Ap<sub>4</sub>A. When 10 equiv of H<sub>2</sub>O were employed in place of phosphoric acid in the above reactions, ADP was formed by partial hydrolysis from **2**. Subsequent reaction between ADP and **2** afforded Ap<sub>4</sub>A. After purification by DEAE Sephadex A-25 column chromatography, Ap<sub>4</sub>A was obtained in 54% yield (62 mg).

In conclusion, it is noteworthy that ATP and Ap<sub>4</sub>A were prepared in high yields by use of **1** in a one-pot reaction without activating AMP. All the above reactions proceeded smoothly to give simple reaction mixtures at room temperature under neutral conditions. Therefore, isolation of ATP and Ap<sub>4</sub>A can be facilitated compared with the known methods. The reagent **1** would be further applicable to the synthesis of other polyphosphate derivatives.



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## REFERENCES

1. Townsend, L. B. "Chemistry of Nucleosides and Nucleotides Volume 2", Plenum Press, New York, **1991**, pp81-160 and references cited therein.
2. Fukuoka, K.; Suda, F.; Suzuki, R.; Takaku, H.; Ishikawa, M.; Hata, T. *Tetrahedron Lett.*, **1994**, *35*, 1063-1066. Fukuoka, K.; Suda, F.; Suzuki, R.; Takaku, H.; Ishikawa, M.; Hata, T. *Nucleosides and Nucleotides*, **1994**, *13*, 1557-1567.
3. Hata, T.; Nakagawa, I.; Shimotono, K.; Miura, K. *Chem. Lett.*, **1976**, 987-990.
4. Takaku, H.; Konishi, T.; Hata, T. *Chem. Lett.*, **1977**, 655-658.