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SYNTHESIS OF MODEL COMPOUND OF COENZYME I
2-(ADENIN-9-YL)ETHYL 3-CARBAMOYL PYRIDINIUM CHLORIDE

T. Okubo and N. Ise

Department of Polymer Chemistry,

Kyoto University, Kyoto, Japan

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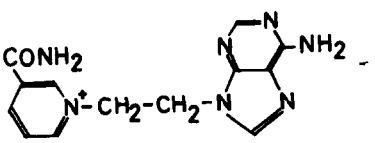
The studies on the syntheses of model compounds of nicotinamide adenine dinucleotide (NAD^+) and on their reactivities or physical properties are useful in understanding of the enzyme action. Three types of the model compounds of NAD^+ have been reported, namely (1) compounds having substituents other than carbamoyl group at the 3-position of the pyridine ring,[1] (2) 3-carbamoyl pyridinium compounds quaternized with various groups without adenine base,[2] (e.g., 1-methylnicotinamide) and (3) compounds in which purine and/or carbohydrate moieties are modified.[3] We wish to report here on the preparation of a model compound of the second type, i.e., 3-carbamoyl pyridinium salts quaternized with groups, which lack both phosphate and carbohydrate residues but contain the base only.

The preparation of 2-(adenin-9-yl)ethyl 3-carbamoyl pyridinium chloride (I) was carried out by Menschutkin reaction of nicotinamide (II) with 9-(2-chloroethyl)adenine (III). The latter was prepared by chlorination of 9-(2-hydroxyl ethyl)adenine with thionyl chloride which in turn was obtained from adenine and ethylene carbonate in dimethylformamide according to the reported methods.[4,5]

The reaction of III (4g) with II (3g) was performed in dimethylformamide



(I)

(20 ml) at 100° for 24 hrs. The solvent was then eliminated by heating in vacuum. The residue was completely washed with ethanol, dissolved into water (10 ml) and then recrystallized with ethanol. I was obtained as hygroscopic white powder. Anal. calcd. for $C_{13}H_{14}N_7OCl$ C, 48.8% ; H, 4.4% ; N, 30.7% ; Cl, 11.1%. Found C, 48.4% ; H, 4.7% ; N, 30.2% ; Cl, 11.0%.

Addition of cyanide ion to the model compound resulted in formation of 1,4-adduct exhibiting an absorption peak at 338 nm (ϵ, 6320). The second-order rate constant ($\vec{k}$) and association equilibrium constant (K) for I have been determined in alkaline aqueous solutions at 25° to be 0.79 $M^{-1}sec^{-1}$ and 173 M^{-1}, respectively, at KCl concentrations of 0.002~0.02 M and a I concentration of 2×10^{-4}M. The equilibrium was reached within 30 min after mixing the model compound with KCN under the experimental conditions investigated. Both the rate and equilibrium constants were found to be independent of the concentration of KOH in the range of $10^{-4} \sim 10^{-2}$M. The $\vec{k}$ and K values of nicotinamide adenine dinucleotide (β isomer)(β-NAD^+) and the corresponding α isomer (α-NAD^+) were reported by Lindquist and Cordes[6] to be 0.18 $M^{-1}sec^{-1}$ and 164 M^{-1}, and 0.075 $M^{-1}sec^{-1}$ and 16.7 M^{-1}, respectively, at 25° and at ionic strength 0.5. The $\vec{k}$ and K values of 3-carbamoyl 1-alkyl(methyl, ethyl, propyl)pyridinium chlorides are much smaller compared with those of α-NAD^+.[6] It is interesting to note that the $\vec{k}$ and K values of our model compound are fairly close to those of β-NAD^+. This indicates that the electron withdrawal by adenine from the ring nitrogen of pyridine is strong. Similar model compounds containing thymine and theophylline were also prepared. The details of the work will be reported shortly.

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