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Reduction of Alloxan by Cyanide Ion. Isolation of Alloxan Radical Anion Salts and Alloxantin

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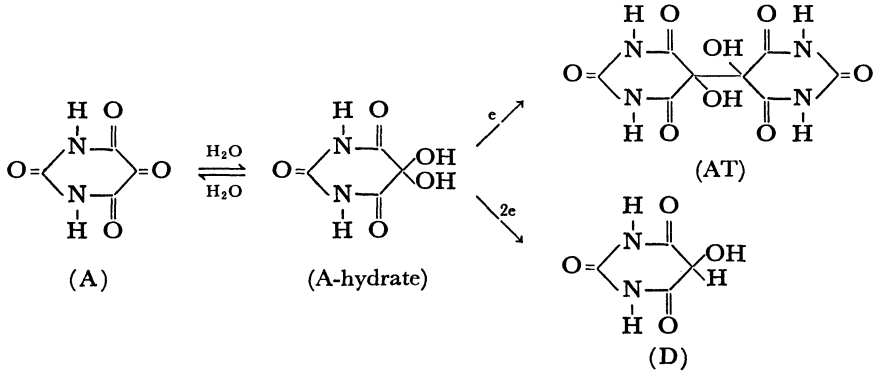
Synopsis. Potassium or pyridinium salts of alloxan radical anion were isolated by the one-electron reduction of alloxan monohydrate with potassium cyanide or 1-benzyl-4-cyano-1,4-dihydronicotinamide at room temperature, respectively.

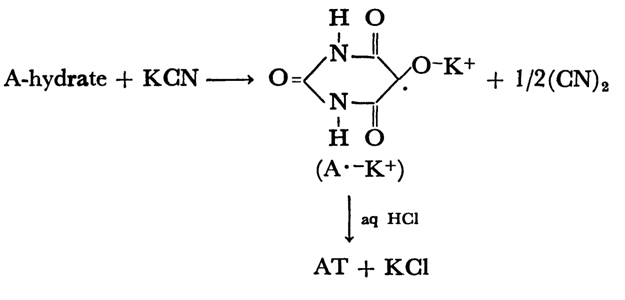
Alloxan(A) is known as one of vicinal tricarbonyl compounds, of which central carbonyl group activated by adjacent two carbonyl groups is so reactive that easily combines one mole of water to form hydrate (A-hydrate).[1] It has been also reported that A-hydrate can be easily reduced by hydrogen sulfide[2] or 1-alkyl-1,4-dihydronicotinamide[3] (NADH model) to obtain AT and dialuric acid(D) by one-electron or two-electron reduction of A-hydrate, respectively.



A is also known as one of "reductones" as same as ascorbic acid which plays important roles in the biological oxidation-reduction system.

In this paper, we wish to report the isolation of alloxan radical anion salts obtained by the reduction of A-hydrate with potassium cyanide and 1-benzyl-1,4-dihydronicotinamide.

Reduction of A-Hydrate by Potassium Cyanide. The reduction of nitro compounds[4] and sulfoxides[5] by cyanide ion have been reported. We found that A-hydrate could be reduced by potassium cyanide in water (pH 6.8) at room temperature to give a yellow precipitate in good yield. The esr spectrum of the precipitate in bulk showed the broad singlet line at 25 °C, as shown in Fig. 1. The precipitate was shown to be the 1 : 1 salt of potassium ion and alloxan radical anion by elemental analyses. Upon treating the precipitate with aq hydrochloric acid, AT was obtained in excellent yield. Based on the results described above, the reasonable structure of the precipitate is considered to the salt ($A^{\cdot-}$ K^+) of potassium ion and alloxan radical anion.



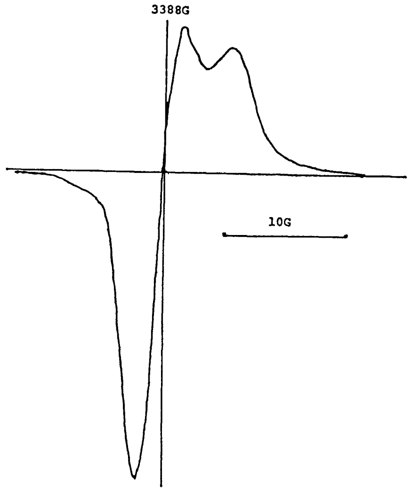
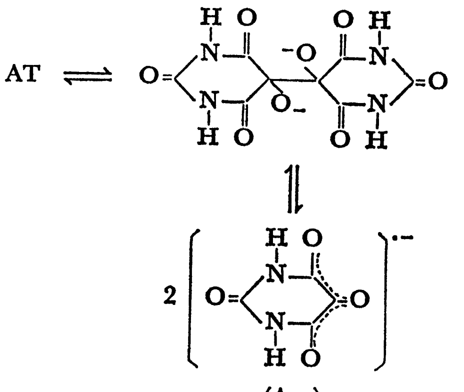


Fig. 1. ESR spectrum of potassium salt ($A^{\cdot-}K^+$) of alloxan radical anion (bulk, 25 °C).

Cyanogen (bp −21.2 °C, mp −27.9 °C[6]) could be also detected by IR (2200 cm^{-1}) qualitatively by trapping in ethanol by bubbling nitrogen gas into the reaction mixture during the reaction.

The formation of alloxan radical anion ($A^{\cdot-}$) has been observed by the reduction of A-hydrate with sodium dithionite in water or methylsulfinylmethanide ($CH_3SOCH_2^-$) in dimethyl sulfoxide (DMSO), and the esr was analyzed in detail. Further, $A^{\cdot-}$ was effectively produced by the dissociation of AT in DMSO.[7]

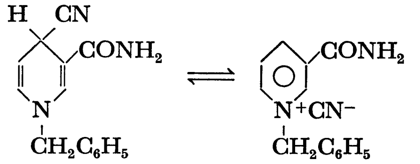


(A·−)

$A^{\cdot -}$ K^+ was also prepared by treating AT with triethylamine in the presence of excess potassium chloride.

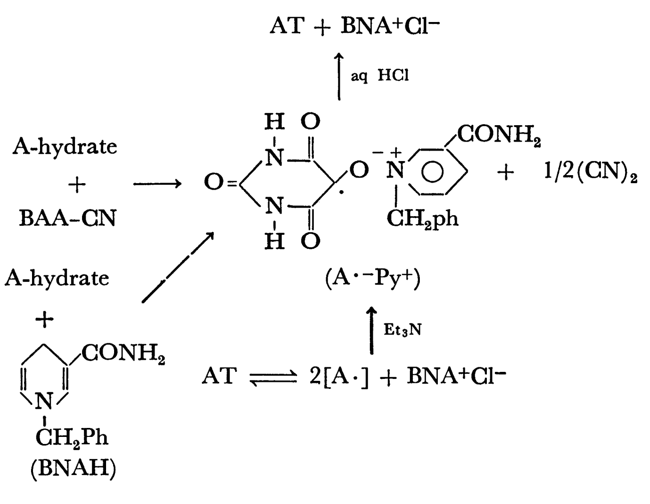
$$AT \rightleftharpoons 2[A\cdot] + 2KCl \xrightarrow{Et_3N} 2A^{\cdot -}K^+ + 2Et_3N\cdot HCl$$

Reduction of A-Hydrate by 1-Benzyl-4-cyano-1,4-dihydronicotinamide. Whereas 1-benzyl-4-cyano-1,4-dihydronicotinamide (BNA–CN) shows the absorption maximum at 333—337 nm (dihydro form) in acetonitrile or dichloromethane, it exhibits both 337 (BNA–CN) and 265 nm (BNA^+CN^-) bands in methanol or ethanol, indicating the presence of equilibrium between BNA–CN and BNA^+CN^-.



(BNA-CN) (BNA^+CN^-)

The reaction of A-hydrate and BNA–CN was tried in ethanol at room temperature to yield a yellow precipitate in a good yield. The yellow precipitate was found to be the pyridinium salt ($A^{\cdot -}Py^+$) of alloxan radical anion which was obtained by the reduction of A-hydrate with 1-benzyl-1,4-dihydronicotinamide (BNAH) or the reaction of AT and 1-benzyl-3-carbamoylpyridinium chloride (BNA^+Cl^-) in the presence of triethylamine.³⁾ The production of cyanogen during the reaction was also detected by IR spectrum qualitatively. $A^{\cdot -}Py^+$ was treated with aq. HCl to give and BNA^+Cl^- in excellent yields. $A^{\cdot -}K^+$ and $A^{\cdot -}Py^+$ are insensitive to oxygen in solid state, but they are easily oxidized in solution to give alloxan.



Experimental

Materials. Alloxan monohydrate(A-hydrate) (mp 253 °C (dec)) was prepared by the oxidation of barbituric acid with chromium trioxide.⁸⁾ Alloxantin(AT) (mp 230—231 °C) used in this study was prepared by the reduction of A-hydrate with hydrogen sulfide.⁹⁾ 1-Benzyl-3-carbamoylpyridinium chloride (BNA^+Cl^-) (mp 230—232 °C)¹⁰⁾ was synthesized by the reaction of benzyl chloride and nicotinamide in *N,N*-dimethylformamide. 1-Benzyl-4-cyano-1,4-dihydronicotinamide (BNA–CN) was prepared by the reaction of BNA^+Cl^- and potassium cyanide in water and recrystallized from acetonitrile. Mp 113—133 °C (dec).¹¹⁾

The Reaction of A-Hydrate and Potassium Cyanide. To a solution of 0.8 g (5 mmol) of A-hydrate in 30 ml of water (buffer solution; pH 6.8), was added a solution of potassium cyanide (0.39 g, 6 mmol) in 10 ml of distilled water with stirring at room temperature to yield a precipitate immediately. After stirring for 2 h, the precipitate was filtered off and dried in vacuo to give alloxan radical anion salt ($A^{\cdot -}K^+$) in 65% yield. Mp 270—273 °C (dec). IR (KBr, cm^{-1}): 3250 (N–H), 1670 (C=O). Found: C, 26.31; H, 1.61; N, 15.26%. Calcd for $C_4H_2O_4N_2K_1$: C, 26.50; H, 1.67; N, 15.46%.

AT (mp 229—231 °C) was also isolated from the filtrate in 15% yield.

The Reaction of AT and Potassium Chloride in the Presence of Triethylamine. To a solution of 1.6 g (5 mmol) of AT and 1.8 g (25 mmol) of potassium chloride in 100 ml of water, was added a solution of 1 g (10 mmol) of triethylamine dropwise with stirring at room temperature to obtain $A^{\cdot -}K^+$ (5.6 g, 70%).

The Reaction of A-Hydrate and BNA–CN. To a solution of 0.8 g (5 mmol) of A-hydrate in 20 ml of ethanol, was added a solution of 1.2 g (5 mmol) of BNA–CN in 20 ml of ethanol in the atmosphere of nitrogen at room temperature to give 1.1 g (70%) of pyridinium salt ($A^{\cdot -}Py^+$) of alloxan radical anion. IR (KBr, cm^{-1}): 3350, 3180 (N–H), 1700, 1590 (C=O). Found: C, 57.30; H, 4.57; N, 15.72%. Calcd for $C_{17}H_{15}O_5N_2$: C, 57.25; H, 4.52; N, 15.46%.

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