THE QUESTION OF THE OXIDATION OF α-HYDROXYPYRIDINE AND NICOTINIC ACID BY FENTON'S REAGENT

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The oxidation of nicotinic acid and α-hydroxypyridine by Fenton's reagent ($H_2O_2 + Fe^{++}$) takes place with the decomposition of the pyridine ring to form oxalic acid. In this process, half the label from the α-hydroxypyridine passes into one of the oxygen atoms of the oxalic acid and the other oxygen atoms are derived from the hydrogen peroxide. The oxalic acid isolated from the oxidation of the nicotinic acid contains oxygen from the oxidizing agent. The results obtained show that the hydroxylation of the pyridine ring, apparently preceding its decomposition, takes place with the addition of an OH group containing oxygen from the oxidizing agent to the nucleus.

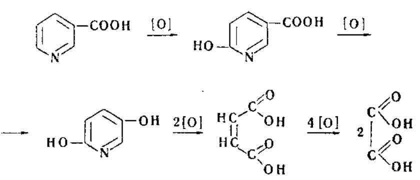
In the oxidation of aqueous solutions of nicotinic acid with oxygen in the presence of the bacterium Pseudomonas fluorescens, 6-hydroxynicotinic acid is formed which then hydroxylates again and decarboxylates with subsequent decomposition to form simpler acids, fumaric or oxalic acid [1]. Using the label ^{18}O, it has been found [2] that the hydroxyl group of $C_6H_3N(OH)(COOH)$ contains oxygen from the water. This was explained by the stability of compounds of pyridine to the electrophilic attack of the intermediate particles formed in the reaction [3]. It appeared of interest to study, using ^{18}O, the oxidation of pyridine derivatives by Fenton's reagent ($H_2O_2 + Fe^{++}$), which has been suggested as a source of hydroxyl radicals possessing electrophilic properties. The oxidation of nicotinic acid and α-hydroxypyridine was studied.

Preliminary experiments showed that the substances selected do not exchange oxygen with water at 100° C in a neutral medium but do so in an acid medium at 23° C over several hours. Hydrogen peroxide also does not exchange oxygen with water [4].

We did not succeed in isolating products of the hydroxylation of the pyridine ring from the reaction mixture. The oxidation of both substances led to oxalic acid. The latter was identified by a mixed melting point and by the elementary analysis of its dihydrate.

The oxidation of nicotinic acid in $H_2{}^{18}O$ (4.05 at.-% of ^{18}O) with hydrogen peroxide of the natural isotopic composition gave oxalic acid containing 0.48 at.-% of ^{18}O, which amounts to 12% of oxygen from the water. The involvement of the water is explained by its exchange with the oxalic acid. Raising the temperature or prolonging the experiment led to an increase in the amount of ^{18}O in this acid. It was established by control experiments that under conditions close to those of the oxidation (23° C, 1hr), oxalic acid undergoes about 10% exchange with a half-period of exchange of about 9 hr.

The results obtained show that, in the oxidation of nicotinic acid, oxygen from the hydrogen peroxide passes into the product. It may be assumed that this reaction takes place by a mechanism formally analogous to that of the biochemical oxidation but further to the more stable oxalic acid:



In the passage into the oxalic acid of the oxygen of the hydroxy group of the 6-hydroxynicotinic acid, the latter is diluted by the oxygen atoms present in the product to 1/8, or 12%, of the original isotopic composition taking into account the decomposition of the maleic acid into two molecules of oxalic acid. This is confirmed by experiments on the oxidation of [^{18}O]-α-hydroxypyridine (1.64 at.-% of ^{18}O), an analog of 6-hydroxynicotinic acid, which produced oxalic acid containing 0.15 at.-% of ^{18}O, which corresponds to 9% of the initial amount.

The oxidation of α-hydroxypyridine by $H_2{}^{18}O_2$ (0.87 at.-% of ^{18}O) in water of the usual isotopic composition gave oxalic acid containing 75% (0.65 at.-% of ^{18}O) of oxygen from the peroxide. The fact that the results of analysis are lower than the calculated figures is again explained by partial exchange of the reaction products with water.

Experiments in $H_2{}^{18}O$ (1.28 at.-% of ^{18}O) with α-hydroxypyridine and H_2O_2 gave oxalic acid containing 9% (0.115 at.-% of ^{18}O after 1 hr) and more of O^{18} from the water as a result of exchange between them, depending on the time.

The results obtained permit the assumption that the oxygen of the hydroxyl group of the 6-hydroxynicotinic acid formed as an intermediate in the oxidation of nicotinic acid comes from the peroxide. Otherwise the oxalic acid formed by the oxidation of the nicotinic acid would contain not less than 22% of oxygen from the water (12% through the OH group of the 6-hydroxynicotinic acid and not less than 10% because of exchange with the water).

EXPERIEMTNAL

Oxidation of nicotinic acid. A solution of 4 mM of the substance in 20 ml of water acidified with a drop of conc H_2SO_4 was treated with 0.02 mole of 79% H_2O_2 and a solution of 0.36 mM of $FeSO_4 \cdot 7H_2O$ in 5 ml of water. The mixture was shaken in a sealed vessel for 30 min and was left in ice for 1.5 hr. Then the water was evaporated off in vacuum and the residue was sublimed. In order to avoid exchange with water in experiments with an isotopic label, the oxalic acid obtained in small amount, sufficient for determining the isotopic composition and melting point, was not crystallized from water but was purified by resublimation in vacuum and was analyzed for its content of ^{18}O in the anhydrous state; mp 194° C.

Oxidation of α-hydroxypyridine. To a solution of 2.6 mM of substance in 10 ml of water acidified with a drop of conc H_2SO_4 was added 0.02 mole of 79% hydrogen peroxide and a solution of 0.36 mM of $FeSO_4 \cdot 7H_2O$ in 2 ml of water. The mixture, which had become dark, was shaken in a sealed vessel for about 1 hr, after which it had become lighter, and then the water was evaporated off in vacuum, and the residue was sublimed. After resublimation in vacuum, mp of the $C_2H_2O_4$ 194° C.

The ^{18}O label was introduced into the water, the hydrogen peroxide, or the α-hydroxypyridine. The latter was prepared by the diazotization of α-aminopyridine with subsequent decomposition of the diazonium salt in $H_2{}^{18}O$. α-Hydroxypyridine with mp 105–106° C was obtained. The isotopic analysis of the α-hydroxypyridine, oxalic acid, $H_2{}^{18}O$, and $H_2{}^{18}O_2$ was carried out by known methods [5]. The accuracy of the analysis, including the errors in isolating the samples, was 5%. The isotopic results obtained are given as atomic excess percentages over the natural content of the isotope.

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LETTERS TO THE EDITOR

KINETIC CONFIRMATION OF THE PRESENCE OF ISOMERS OF THE COLORED FORM OF 2H-BENZOPYRAN-2-SPIRO-2'-INDOLINES

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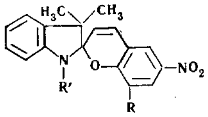
It has been reported [1] that the kinetics of the dark decoloration of the photochromic spiropyrans is described by a first-order equation. We have studied the kinetics of the dark decoloration of the spiropyrans I–III in 95% ethanol at 20° C by the method of Berman [1] et al.



I $R = H$, $R' = CH_3$; mp 179–180,5°; [2] λ_{max} 540 nm
II $R = OCH_3$, $R' = CH_3$; mp 152,5–153,5°; [1] λ_{max} 560 nm
III $R = Br$, $R' = C_6H_5$; mp 165,5–166° [3] λ_{max} 580 nm

It was found that the dependence of the logarithm of the optical density on the time deviates considerably from linearity in the initial section but is linear in the final section. By treating the curves obtained according to Brown and Fletcher's method [5], we have established that the process studied can be described by two parallel first-order reactions of dark decoloration. For the spiropyran I, $K_1 = (3.8 \pm 0.3) \cdot 10^{-3}$ sec^{-1}, $K_2 = (1.80 \pm 0.05) \cdot 10^{-4}$ sec^{-1}; for II, $K_1 = (6.1 \pm 0.2) \cdot 10^{-3}$ sec^{-1}, $K_2 = (1.4 \pm 0.2) \cdot 10^{-3}$ sec^{-1}; and for III, $K_1 = (1.5 \pm 0.5) \cdot 10^{-2}$ sec^{-1}, $K_2 = (2.6 \pm 0.2) \cdot 10^{-3}$ sec^{-1}.

Apparently, in the irradiation of solutions of the spiropyrans with UV light at room temperature, just as is the case at low temperatures [5–7], a mixture of at least two isomers with a colored merocyanin structure is formed which take part in the dark decoloration reaction at different rates.

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