

QUINOLINIUM DICHROMATE OXIDATION OF HETEROCYCLIC CARBOXYLIC ACIDS

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Abstract. Heterocyclic carboxylic acids were oxidized to the corresponding hydroxy-substituted acids by quinolinium dichromate in sulfuric acid, in 50% (v/v) acetic acid-water as solvent. The kinetic results supported a mechanistic pathway proceeding via a rate-determining decomposition of the chromate ester.

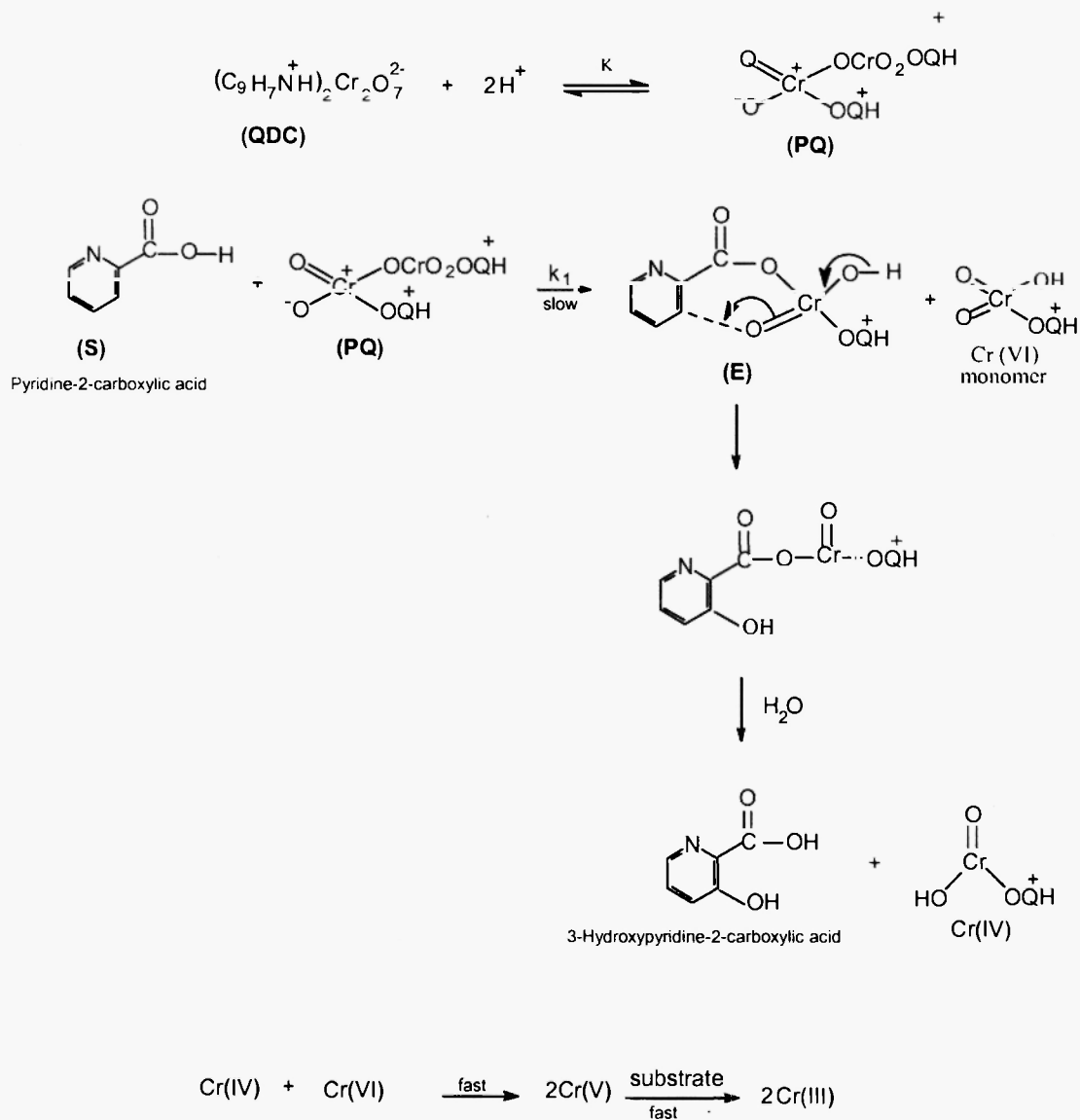
Introduction

Quinolinium dichromate [QDC, $(C_9H_7NH^+)_2Cr_2O_7^{2-}$] has been used for diverse transformations such as the oxidation of hydrocarbons,¹ oxidative cleavage of unsaturated compounds,² oxidation of cyclic and bicyclic alcohols,³ amino acids,⁴ diols,⁵ α -hydroxy acids,⁶ ketones,⁷ and aldehydes.^{8,9} There have been earlier reports of the decarboxylation of pyridinecarboxylic acids¹⁰⁻¹² and pyrimidinecarboxylic acids.¹³ With a view to establish the site of reaction in heterocyclic carboxylic acids, we have carried out a kinetic study on the oxidation of heterocyclic carboxylic acids (pyridine-2-carboxylic acid, pyridine-3-carboxylic acid and pyridine-4-carboxylic acid) by QDC, in acid medium, in 50% acetic acid-water (v/v), under nitrogen.

Results and Discussion

The method used for the kinetic measurements has been described earlier.⁵ The rate of oxidation of heterocyclic carboxylic acids was found to be dependent on the first powers of the concentrations of each - substrate, oxidant and acid (Table 1). In the range of acid concentrations used, the dichromate ion (or its protonated form) has been shown to be the predominant species.⁹ The observed order of reactivity was : pyridine-2-carboxylic acid > pyridine-4-carboxylic acid > pyridine-3-carboxylic acid. The presence of the carboxylic group in the 2-position would influence the distribution of charge as a result of the steric configuration. This steric arrangement would not be possible either with 3-carboxylic or with 4-carboxylic acids. Steric considerations would thus favour the mechanistic pathway for the reaction as proceeding via the formation of a cyclic intermediate involving an attack by the oxygen (of the oxidant) at the position adjacent to the carboxylic group.

The sequence of reactions has been shown in the Scheme. The attack of the protonated QDC (PQ) on the substrate (S) was favoured by the formation of a cyclic chromate ester (E). In order to test the feature of a cleavage of the carbon-hydrogen bond in the rate-determining step of the reaction, an evaluation of the kinetic isotope effect for the hydrogen atom in pyridine-2-carboxylic acid- d_3 was carried out. It was observed that pyridine-2-carboxylic acid reacted faster than pyridine-2-carboxylic acid- d_3 by a factor of 2.4, which indicated that the rate determining step of the reaction involved a cleavage of the carbon-hydrogen bond in pyridine-2-carboxylic acid. The mechanism envisaged the formation of a cyclic intermediate in which the carbon (of the substrate) would be bonded to the oxygen



Scheme

Table 1: Rate constants for the Oxidation of Heterocyclic Carboxylic Acids by QDC, in 50% acetic acid-water at 50°C.

[Substrate] x 10 ² mol dm ⁻³	[QDC] x 10 ³ mol dm ⁻³	[H ₂ SO ₄] mol dm ⁻³	10 ⁴ <i>k</i> / s ⁻¹		
			<i>1</i>	<i>2</i>	<i>3</i>
1.0	1.0	3.0	1.72	1.48	1.64
5.0	1.0	3.0	8.68	7.47	8.20
10	1.0	3.0	17.5	15.0	16.5
1.0	0.75	3.0	1.76	1.49	1.60
1.0	0.50	3.0	1.67	1.46	1.63
1.0	0.10	3.0	1.65	1.47	1.62
1.0	1.0	3.5	2.01	1.71	1.93
1.0	1.0	4.0	2.34	1.96	2.20

Note: *1*: Pyridine-2-carboxylic acid; *2*: Pyridine-3-carboxylic acid;

3: Pyridine-4-carboxylic acid.

(of the oxidant). Such an electrocyclic mechanism involved six electrons; being a Hückel-type system ($4n+2$), this was an allowed process.¹⁴

Experimental

The oxidation of heterocyclic carboxylic acids (pyridine-2-carboxylic acid, pyridine-3-carboxylic acid and pyridine-4-carboxylic acid) by QDC resulted in the formation of the corresponding hydroxycarboxylic acids. The oxidation reactions were carried out as follows: To 15 ml of water cooled in ice, concentrated H_2SO_4 (7.9g, 0.08 mol dm^{-3}) was added slowly, with constant cooling. The acid solution was cooled to room temperature, quinolinium dichromate (4.76 g, 0.01 mol dm^{-3}) was added and the mixture warmed to 50°C for complete dissolution of the QDC. To this mixture, $0.015 \text{ mol dm}^{-3}$ of substrate (0.46 g), taken in 25 ml of 50% acetic acid-water solution, was added. The reaction mixture was stirred at 50°C for 24h under nitrogen. The organic layer was extracted thrice with ether (25 ml each time), and the combined organic extracts were washed with water and dried over anhydrous Na_2SO_4 . The oxidized products (3-hydroxypyridine-2-carboxylic acid from pyridine-2-carboxylic acid; 2-hydroxypyridine-3-carboxylic acid from pyridine-3-carboxylic acid; 3-hydroxypyridine-4-carboxylic acid from pyridine-4-carboxylic acid) were obtained after complete removal of ether (yields $\approx 85\text{-}90\%$).

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