

## Kinetics of Oxidation of Heterocyclic Compounds by Quinolinium Dichromate

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**Abstract.** Quinolinium dichromate in sulfuric acid oxidized heterocyclic aldehydes (to the corresponding acids) and heterocyclic carboxylic acids (to the corresponding hydroxy-substituted acids) in acetic acid-water medium (vol. ratio,  $v(\text{water})/v(\text{acetic acid}) = 50:50$ ). The kinetic results supported a mechanistic pathway proceeding *via* a rate-determining decomposition of the chromate ester.

**Keywords:** kinetics, oxidation, heterocyclic compounds, quinolinium dichromate

### INTRODUCTION

In the oxidation of heteroaldehydes and heteroacids, there exists the distinct possibility of the reaction occurring either at the heteroatom or at the carbonyl function. With a view to establish the site of reaction in the oxidation of heterocyclic compounds, we have focused attention on the oxidation of heteroaldehydes (2-furaldehyde, 2-pyrrolicarbaldehyde, 2-thiophenecarbaldehyde, pyridine-2-aldehyde and pyridine-3-aldehyde) and heteroacids (pyridine-2-carboxylic acid, pyridine-3-carboxylic acid and pyridine-4-carboxylic acid) by quinolinium dichromate [QDC,  $(\text{C}_9\text{H}_7\text{NH}^+)_2\text{Cr}_2\text{O}_7^{2-}$ ], in acid medium, in acetic acid-water (50:50,  $v/v$ ), under nitrogen. This investigation forms part of our sustained efforts to use QDC for a variety of organic transformations.<sup>1</sup>

### EXPERIMENTAL

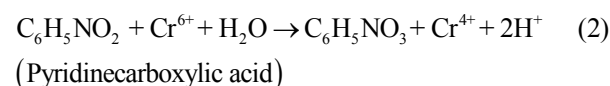
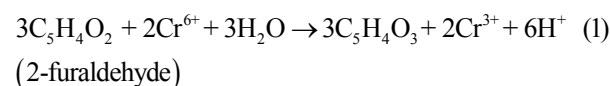
#### Materials, methods and stoichiometry

2-Furaldehyde, 2-thiophenecarbaldehyde, pyridine-2-aldehyde and pyridine-3-aldehyde (Aldrich) were purified by distillation under reduced pressure. Pyridine-2-carboxylic acid, pyridine-3-carboxylic acid, pyridine-4-carboxylic acid (Spectrochem) and 2-pyrrolicarbaldehyde (Aldrich) were recrystallized before use. Quinolinium dichromate [QDC,  $(\text{C}_9\text{H}_7\text{N}^+\text{H})_2\text{Cr}_2\text{O}_7^{2-}$ ], was prepared by the reported method;<sup>2</sup> the infrared spectrum (KBr) exhibited bands at 930, 875, 765 and 730  $\text{cm}^{-1}$ , characteristic of the dichromate ion. Acetic acid (A.R. grade, S.d. fine-chem. Ltd.) was distilled before use, and the fraction distilling at 116 °C was used. Sulfuric acid

(E. Merck) was used after checking its physical constants. IR spectra were recorded on FT-IR (DA-8, Bomem) spectrophotometer, and NMR spectra recorded on FT-NMR (300 MHz, Bruker) spectrometer.

Pseudo-first-order conditions were used for all the kinetic runs ( $[\text{substrate}] \gg [\text{QDC}]$ ). All the reactions were performed at constant temperature ( $\pm 0.1$  K), under nitrogen, and followed by monitoring the absorption band at 440 nm, spectrophotometrically (Systronics, Model-108), as described earlier.<sup>3</sup> Rate constants were evaluated from the linear ( $r > 0.996$ ) plots of  $\log [\text{QDC}]$  against time. The values reported were the mean of two or more runs (reproducibility  $\pm 3\%$ ). The reactions were carried out in aqueous medium, and water-acetic acid mixtures were used for studying the effect of dielectric constants on the rates of the reactions.

Stoichiometric ratios,  $\Delta[\text{QDC}]/\Delta[\text{substrate}]$ , in the range 0.66 to 0.69 (for heteroaldehydes) and 1.02 to 1.05 (for heteroacids) were obtained,<sup>1</sup> which conformed to the following overall equations:



#### Product analysis

Doubly distilled water (30 ml) was taken, cooled in ice, and concentrated  $\text{H}_2\text{SO}_4$  (7.9 g, 0.08 mol) was added slowly with constant cooling. After the acid solution

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had cooled to room temperature, QDC (9.52 g, 0.02 mol) was added and the mixture was warmed to 323 K for complete dissolution of the QDC. To this mixture, 0.015 mol of the substrate (1.45 g of 2-furaldehyde, 1.43 g of 2-pyrrolicarbaldehyde, 1.69 g of 2-thiophenecarbaldehyde, 1.61 g each of pyridine-2-aldehyde and pyridine-3-aldehyde, and 0.18 g each of the pyridinecarboxylic acids), taken in 25 ml of acetic acid-water solution ( $v/v = 50:50$ ), was added. The reaction mixture was stirred at 323 K for 48 h under nitrogen. The organic layer was extracted three times with diethyl ether (25 ml each time), and the combined organic extracts were washed with water and dried over anhydrous  $\text{Na}_2\text{SO}_4$ . The oxidized products were obtained after complete removal of ether (yields:  $\approx 85\text{--}90\%$ ), subjected to IR (KBr) and  $^1\text{H}$  NMR ( $\text{CDCl}_3$  / 1 drop  $\text{DMSO-d}_6$ ) analyses, and characterized as follows:

- (i) 2-furancarboxylic acid (from 2-furaldehyde) :  $\nu/\text{cm}^{-1}$ : 3000, 2860 (br, s, -OH), 2583, 1690 (s, C=O), 1470, 1305, 1245, 1020, 930, 760  $\text{cm}^{-1}$ ;  $\delta/\text{ppm}$ : 10.5 (s, 1H, COOH), 7.9 (d, 1H, 5-H), 7.3 (d, 1H, 3-H), 6.7 (t, 1H, 4-H);
- (ii) 2-pyrrolicarboxylic acid (from 2-pyrrolicarbaldehyde):  $\nu/\text{cm}^{-1}$ : 3000, 2850 (br, s, -OH), 1692 (s, C=O), 1545, 1355, 1105, 925, 750  $\text{cm}^{-1}$ ;  $\delta/\text{ppm}$ : 10.2 (s, 1H, COOH), 6.9 (d, 1H, 5-H), 6.7 (d, 1H, 3-H), 6.2 (t, 1H, 4-H);
- (iii) 2-thiophenecarboxylic acid (from 2-thiophenecarbaldehyde):  $\nu/\text{cm}^{-1}$ : 3090, 2850 (br, s, -OH), 2621, 1690 (s, C=O), 1530, 1350, 1100, 910, 750  $\text{cm}^{-1}$ ;  $\delta/\text{ppm}$ : 11.4 (s, 1H, COOH), 7.8 (d, 1H, 5-H), 7.5 (d, 1H, 3-H), 7.1 (t, 1H, 4-H);
- (iv) pyridine-2-carboxylic acid (from pyridine-2-aldehyde):  $\nu/\text{cm}^{-1}$ : 3030 (br, s, -OH), 2500, 1720 (s, C=O), 1590, 1305, 1255, 1040, 830, 680  $\text{cm}^{-1}$ ;  $\delta/\text{ppm}$ : 8.9 (s, 1H, COOH), 8.3 (d, 1H, 6-H), 8.1 (d, 1H, 3-H), 7.7 (m, 2H, 4,5-H);

- (v) pyridine-3-carboxylic acid (from pyridine-3-aldehyde):  $\nu/\text{cm}^{-1}$ : 3030 (br, s, -OH), 2445, 1720 (s, C=O), 1590, 1300, 1195, 830, 680  $\text{cm}^{-1}$ ;  $\delta/\text{ppm}$ : 9.1 (s, 1H, COOH), 8.8 (s, 1H, 2-H), 8.2 (d, 1H, 6-H), 7.5 (m, 2H, 4,5-H);
- (vi) 3-hydroxypyridine-2-carboxylic acid (from pyridine-2-carboxylic acid),  $\nu/\text{cm}^{-1}$ : 3080 (b, s, -OH), 2500 (O-H, str.), 1710 (s, C=O), 1610, 1410, 1389 (O-H bend.), 1250 (C-O, str.), 950 (O-H, str.), 720  $\text{cm}^{-1}$ ;
- (vii) 2-hydroxypyridine-3-carboxylic acid (from pyridine-3-carboxylic acid),  $\nu/\text{cm}^{-1}$ : 3060 (b, s, -OH), 2510 (O-H, str.), 1690 (s, C=O), 1610, 1420, 1370 (O-H bend.), 1248 (C-O, str.), 946 (O-H, str.), 745  $\text{cm}^{-1}$ ;
- (viii) 3-hydroxypyridine-4-carboxylic acid (from pyridine-4-carboxylic acid),  $\nu/\text{cm}^{-1}$ : 3075 (b, s, -OH), 2505 (O-H str.), 1700 (s, C=O), 1610, 1410, 1385 (O-H bend.), 1245 (C-O, str.), 950 (O-H, str.), 740  $\text{cm}^{-1}$ .

## RESULTS AND DISCUSSION

### Kinetic Results

The observed pseudo-first-order rate constants for the oxidation of heterocyclic compounds did not alter appreciably with changing QDC concentrations (10-fold range), at constant substrate concentration (large excess); this indicated a first-order dependence on QDC (Tables 1 and 2). In the range of substrate concentrations (10-fold), at constant acidity, the order of the reaction with respect to [substrate] was unity (Tables 1 and 2). In the range of acid concentrations used (0.5–1.5 mol  $\text{dm}^{-3}$  for the oxidation of heteroaldehydes, and 3.0–5.0 mol  $\text{dm}^{-3}$  for the oxidation of heteroacids), the observed pseudo-first-order rate constants showed a first-order dependence on [acid]. It could be suggested that in the

**Table 1.** Rate data for oxidation of heteroaldehydes at 313 K

$\frac{c(\text{Substrate})}{10^{-2} \times \text{mol dm}^{-3}}$	$\frac{c(\text{QDC})}{10^{-3} \times \text{mol dm}^{-3}}$	$\frac{c(\text{H}_2\text{SO}_4)}{\text{mol dm}^{-3}}$	$10^4 k_{\text{ex}}/\text{s}^{-1}$		
			2-Furaldehyde	2-Pyrrole-carbaldehyde	2-Thiophene-carbaldehyde
1.0	1.0	0.5	1.25	1.18	1.14
2.5	1.0	0.5	3.12	2.91	2.83
5.0	1.0	0.5	6.21	5.90	5.67
10.0	1.0	0.5	12.5	11.8	11.2
1.0	0.75	0.5	1.22	1.15	1.14
1.0	0.50	0.5	1.25	1.18	1.13
1.0	0.25	0.5	1.24	1.19	1.15
1.0	0.10	0.5	1.27	1.14	1.12
1.0	1.0	0.75	1.88	1.75	1.64
1.0	1.0	1.0	2.50	2.36	2.20
1.0	1.0	1.25	3.20	2.90	2.70
1.0	1.0	1.50	3.80	3.55	3.40

**Table 2.** Rate data for oxidation of heteroacids at 323 K

$\frac{c(\text{Substrate})}{10^{-2} \times \text{mol dm}^{-3}}$	$\frac{c(\text{QDC})}{10^{-3} \times \text{mol dm}^{-3}}$	$\frac{c(\text{H}_2\text{SO}_4)}{\text{mol dm}^{-3}}$	$10^4 k_{\text{ex}} / \text{s}^{-1}$		
			Pyridine-2-carboxylic acid	Pyridine-3-carboxylic acid	Pyridine-4-carboxylic acid
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

range of acid concentrations used, the oxidant QDC was converted to the protonated  $\text{Cr}^{\text{VI}}$  species, wherein the dichromate ion (or its protonated form) was the predominant species.<sup>1</sup> Earlier reports have established the involvement of a protonated  $\text{Cr}^{\text{VI}}$  species in chromic acid oxidation reactions.<sup>4</sup> The data in Table 2 showed that an increase in  $[\text{H}^+]$  favored a higher rate of oxidation. Such an effect would not support a decarboxylation process. This was similar to the reported behavior of other aromatic acids, where the unionized carboxyl group underwent decarboxylation with great difficulty or not at all.<sup>5-7</sup>

In the experimental range of temperatures used, the dissociation constants of the heteroacids were reported to be: <sup>8(a)</sup> pyridine-2-carboxylic acid =  $3 \times 10^{-6}$  ( $\text{p}K = 5.52$ ); pyridine-3-carboxylic acid =  $1.4 \times 10^{-5}$  ( $\text{p}K = 4.85$ ); pyridine-4-carboxylic acid =  $1.1 \times 10^{-5}$  ( $\text{p}K = 4.96$ ). These values were quite low, indicating

that these substrates remained undissociated in the presence of the high concentrations of mineral acid used.

The reactions were studied in solutions containing varying proportions of water and acetic acid. The dielectric constants ( $\epsilon_r$ ) of water-acetic acid mixtures were calculated from the  $\epsilon_r$  of the pure solvents.<sup>8(b)</sup> A decrease in  $\epsilon_r$  resulted in an increase in the rate (Tables 3 and 4). The magnitude of this effect established that, for the equilibrium  $2\text{HCrO}_4^- \rightleftharpoons \text{Cr}_2\text{O}_7^{2-} + \text{H}_2\text{O}$ , the equilibrium was shifted to the right due to the reduced water activity, thus favoring the dichromate form over the chromate form. The absence of any salt effects indicated that these reactions were not of the ion-ion type. If the reactions were between two neutral molecules, then the plot of  $\log k_{\text{ex}}$  versus  $(\epsilon_r - 1) / (2\epsilon_r + 1)$  would have been linear; this was not found to be so. The plots of  $\log k_{\text{ex}}$  versus  $1/\epsilon_r$  were linear, with positive slopes, which indicated that the reactions were of the ion-dipole type.<sup>9</sup>

**Table 3.** Solvent effect for oxidation of heteroaldehydes at 313 K

$\nu(\text{H}_2\text{O}):\nu(\text{AcOH})$	Dielectric Constant, $\epsilon_r$	$10^4 k_{\text{ex}} / \text{s}^{-1}$		
		2-Furaldehyde	2-Pyrrole-carbaldehyde	2-Thiophene-carbaldehyde
50:50	39.79	1.25	1.18	1.14
45:55	36.44	1.82	1.58	1.41
40:60	33.09	2.51	2.09	1.78
35:65	29.74	3.80	2.95	2.51
30:70	26.39	6.30	4.27	3.55

$c(\text{Substrate}) = 0.01 \text{ mol dm}^{-3}$ ;  $c(\text{QDC}) = 0.001 \text{ mol dm}^{-3}$ ;  $c(\text{H}_2\text{SO}_4) = 0.5 \text{ mol dm}^{-3}$ .

**Table 4.** Solvent effect for oxidation of heteroacids at 323 K

$\nu(\text{H}_2\text{O}):\nu(\text{AcOH})$	Dielectric Constant, $\epsilon_r$	$10^4 k_{\text{ex}} / \text{s}^{-1}$		
		Pyridine-2-carboxylic acid	Pyridine-3-carboxylic acid	Pyridine-4-carboxylic acid
50:50	38.1	1.72	1.48	1.64
45:55	34.9	2.56	2.23	2.40
40:60	31.8	3.82	3.58	3.75
35:65	28.6	5.56	5.30	5.45
30:70	25.4	10.6	9.93	10.1

$c(\text{Substrate}) = 0.01 \text{ mol dm}^{-3}$ ;  $c(\text{QDC}) = 0.001 \text{ mol dm}^{-3}$ ;  $c(\text{H}_2\text{SO}_4) = 3.0 \text{ mol dm}^{-3}$ .

**Table 5.** Solvent isotope effect for oxidation of heteroaldehydes at 313 K

Substrate	$k_{\text{H}_2\text{O}}$	$k_{\text{D}_2\text{O}}$	$k_{\text{D}_2\text{O}}/k_{\text{H}_2\text{O}}$
	$10^4 k_{\text{ex}} / \text{s}^{-1}$		
2-Furaldehyde	1.25	2.03	1.62
2-Pyrrole-carbaldehyde	1.18	1.86	1.58
2-Thiophene-carbaldehyde	1.14	1.75	1.54

$c(\text{Substrate}) = 0.01 \text{ mol dm}^{-3}$ ;  $c(\text{QDC}) = 0.001 \text{ mol dm}^{-3}$ ;  
 $c(\text{H}_2\text{SO}_4) = 0.5 \text{ mol dm}^{-3}$ .

**Table 6.** Solvent isotope effect for oxidation of heteroacids at 323 K

Substrate	$k_{\text{H}_2\text{O}}$	$k_{\text{D}_2\text{O}}$	$k_{\text{D}_2\text{O}}/k_{\text{H}_2\text{O}}$
	$10^4 k_{\text{ex}} / \text{s}^{-1}$		
Pyridine-2-carboxylic acid	1.72	2.80	1.63
Pyridine-3-carboxylic acid	1.48	2.31	1.56
Pyridine-4-carboxylic acid	1.64	2.61	1.59

$c(\text{Substrate}) = 0.01 \text{ mol dm}^{-3}$ ;  $c(\text{QDC}) = 0.001 \text{ mol dm}^{-3}$ ;  
 $c(\text{H}_2\text{SO}_4) = 3.0 \text{ mol dm}^{-3}$ .

The effect of a change in the solvent (from  $\text{H}_2\text{O}$  to  $\text{D}_2\text{O}$ ) was studied in order to ascertain the extent of the

solvent isotope effect. The rates of oxidation were increased in  $\text{D}_2\text{O}$  medium (Tables 5 and 6), in agreement with earlier reported observations.<sup>10</sup> Since  $\text{D}_3\text{O}^+$  is about three times stronger than  $\text{H}_3\text{O}^+$  (Ref. 10,11), the solvent isotope effect being greater than unity suggested a proton-catalyzed reaction. This supported the protonation of the oxidant (QDC), an observation reflected in the acid dependence on the rates of the reactions (Tables 1 and 2).

The oxidation reactions were studied in the temperature range 303–333K (Tables 7 and 8). The negative values of  $\Delta S^*$  suggested the formation of a transition state containing both the oxidant and the reducing species.

The induced polymerization of acrylonitrile or the reduction of mercury(II) chloride<sup>12</sup> was not observed, showing that a one-electron oxidation was unlikely. Control experiments, performed in the absence of the substrate, did not show any appreciable change in [QDC].

## Mechanism

### (i) Oxidation of heteroaldehydes

It has been shown that aldehyde oxidation reactions proceeded *via* the hydrated form.<sup>13–18</sup> Table 9 lists the experimental rate constants ( $k_{\text{ex}}$ ) for the oxidation of the aldehydes by QDC, and the aldehyde hydrate dehydra-

**Table 7.** Effect of temperature and activation parameters for oxidation of heteroaldehydes

$T (\pm 0.1 \text{ K})$	$10^4 k_{\text{ex}} / \text{s}^{-1}$		
	2-Furaldehyde	2-Pyrrolecarbaldehyde	2-Thiophenecarbaldehyde
303	0.62	0.59	0.56
308	0.94	0.89	0.84
313	1.25	1.18	1.14
318	1.78	1.74	1.71
323	2.54	2.41	2.35
$\Delta H^* / \text{kJ mol}^{-1}$	$51 \pm 2.2$	$54 \pm 2.3$	$56 \pm 2.1$
$\Delta S^* / \text{J mol}^{-1} \text{ K}^{-1}$	$-152 \pm 3.5$	$-145 \pm 3.7$	$-142 \pm 4.1$

$c(\text{Substrate}) = 0.01 \text{ mol dm}^{-3}$ ;  $c(\text{QDC}) = 0.001 \text{ mol dm}^{-3}$ ;  $c(\text{H}_2\text{SO}_4) = 0.5 \text{ mol dm}^{-3}$ .

**Table 8.** Effect of temperature and activation parameters for oxidation of heteroacids

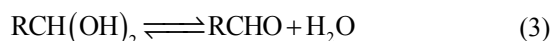
$T (\pm 0.1 \text{ K})$	$10^4 k_{\text{ex}} / \text{s}^{-1}$		
	Pyridine-2-carboxylic acid	Pyridine-3-carboxylic acid	Pyridine-4-carboxylic acid
313	0.87	0.75	0.82
318	1.30	1.12	1.20
323	1.72	1.48	1.64
328	2.62	2.25	2.41
333	3.50	2.95	3.26
$\Delta H^* / \text{kJ mol}^{-1}$	$54 \pm 2.2$	$55.7 \pm 2.4$	$54.8 \pm 2.3$
$\Delta S^* / \text{J mol}^{-1} \text{ K}^{-1}$	$-145 \pm 4.1$	$-135 \pm 3.6$	$-141 \pm 3.5$

$c(\text{Substrate}) = 0.01 \text{ mol dm}^{-3}$ ;  $c(\text{QDC}) = 0.001 \text{ mol dm}^{-3}$ ;  $c(\text{H}_2\text{SO}_4) = 0.5 \text{ mol dm}^{-3}$ .

**Table 9.** QDC oxidation of heteroaldehydes at 313 K

Aldehydes	$K_{\text{deh}}$	$10^4 k_{\text{ex}} / \text{s}^{-1}$	$k_{\text{Hy}} / \text{mol}^{-2} \text{dm}^6 \text{s}^{-1}$	$k_{\text{A}} / \text{mol}^{-2} \text{dm}^6 \text{s}^{-1}$
2-Furaldehyde	1.29	1.25	$2.38 \pm 0.22$	$57.7 \pm 1.32$
2-Pyrrolicarbaldehyde	0.92	1.18	$1.88 \pm 0.18$	$54.5 \pm 1.25$
2-Thiophenecarbaldehyde	0.84	1.14	$1.59 \pm 0.16$	$52.1 \pm 1.20$

tion constants ( $K_{\text{deh}}$ ) for the reaction:



From  $k_{\text{ex}}$  and  $K_{\text{deh}}$ , it was possible to compute two sets of rate constants for the oxidation of the aldehyde:

(a) the values of  $k_{\text{Hy}}$  were obtained by assuming that only the hydrate form appears in the rate law:

$$v = k_{\text{Hy}} [\text{QDC}] [\text{RCH}(\text{OH})_2] [\text{H}^+] \quad (4)$$

(b) the values of  $k_{\text{A}}$  were calculated using the concentration of free aldehyde according to the rate law:

$$v = k_{\text{A}} [\text{QDC}] [\text{RCHO}] [\text{H}^+] \quad (5)$$

The values of  $k_{\text{Hy}}$  and  $k_{\text{A}}$  are given (Table 9). Using the  $\sigma^+$  values derived from a consideration of the electrophilic substitution for the five-membered hetero systems,<sup>19</sup> a plot of  $\log k_{\text{Hy}}$  against  $\sigma^+$  was linear ( $r = 0.990$ ), with a slope of  $\rho = +2.0$ . On the other hand, the correlation of  $\sigma^+$  with  $k_{\text{A}}$  gave a value of  $\rho = +0.64$  ( $r = 0.992$ ). The positive value of  $\rho$  could be interpreted as being due to a superimposed effect of the ring substituents on the hydration equilibrium, wherein it had been shown that all the aldehydes oxidized by chromic acid were completely hydrated in aqueous solution.<sup>20</sup> The chromic acid oxidation of benzaldehyde had yielded a value of  $\rho = +1.06$ , which was in consonance with a pathway proceeding by way of an intermediate chromic acid ester of hydrated benzaldehyde.<sup>21</sup> In the range of acid concentrations used (present study), the hydrated forms of the substrates would remain as undissociated molecules (since  $[\text{H}^+]$  would be much greater than the dehydration constants of the substrates). In the present investigation, the correlation with  $k_{\text{Hy}}$  supported the mechanistic pathway for the oxidation reactions as proceeding *via* the hydrated form of the aldehydes. Hence, a mechanism involving a direct hydrogen-transfer reaction between a free aldehyde and QDC was very unlikely.

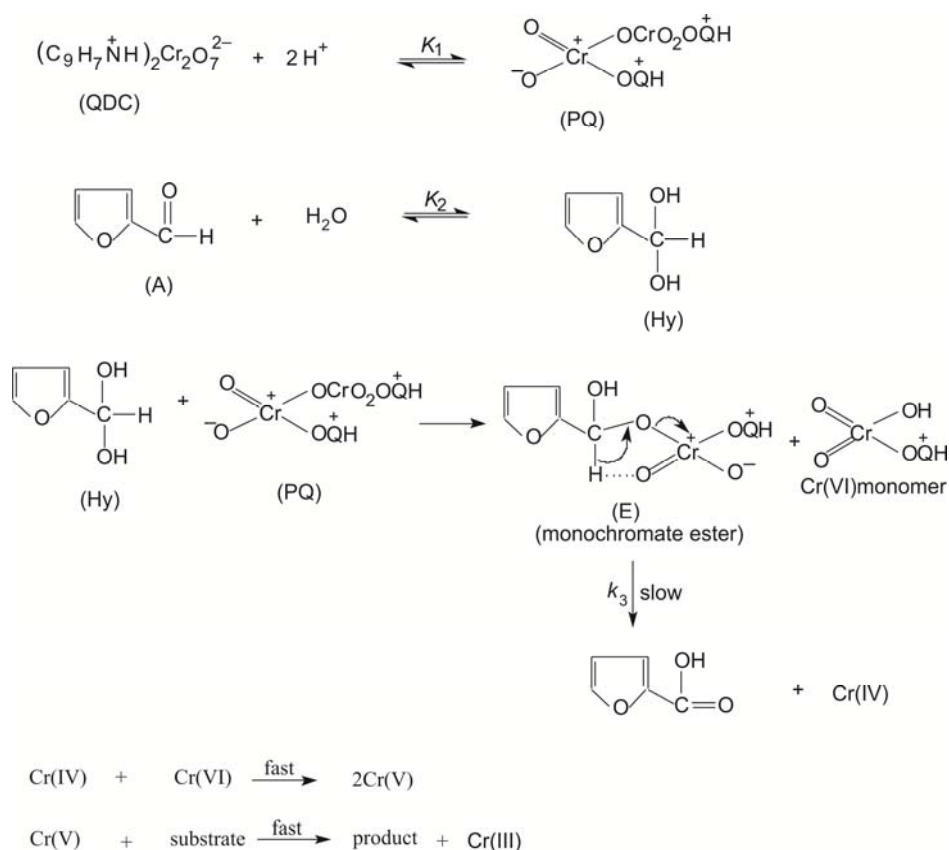
In the case of heteroaldehydes, the heteroatoms are strong resonance donors in these five-membered ring systems, an effect which completely overrides their inductive withdrawal. By treating these rings as transmitting systems, one could look for a correlation between the structure and the reactivity of these heterocyclic

aldehydes. The observed order of reactivity was: 2-furaldehyde > 2-pyrrolicarbaldehyde > 2-thiophenecarbaldehyde (Table 1), which was in conformity with the decreasing electronegativities of O, N and S atoms (electronegativities were: O, 3.50; N, 3.07; S, 2.44).<sup>22</sup> The inference was that electronegative substituents increased the oxidation rates by increasing the equilibrium concentrations of the intermediate chromate ester of the aldehyde hydrate. Thus, the rate-accelerating effect of the electronegative substituents could be interpreted in terms of greatly increased hydration (Table 1).

The close resemblance in the structures of aldehyde hydrates and alcohols would favor similar pathways in their oxidation processes. The oxidation of alcohols had demonstrated the rate-determining decomposition of the protonated acid chromate ester.<sup>23</sup> In an analogous manner, the oxidation of aldehydes could be visualized as proceeding *via* the formation of a similar intermediate (an ester of the aldehyde hydrate). If the chromium was coordinated through the  $-\text{OH}$  group (of the aldehyde hydrate) in the cyclic transition state,<sup>24,25</sup> this would facilitate the formation of the chromate ester and enhance the ease of its oxidation to the corresponding carboxylic acid. Such a transition state envisaged the transfer of electrons towards the chromium, occurring by the formation of the carbon-hydrogen-oxygen bonds, as well as by the carbon-oxygen-chromium bonds.

The slow step of the reaction involved the participation of the aldehyde hydrate, protonated QDC, and two electrons in a cyclic system. Removal of the hydrogen (on the carbon) was part of this step, as evidenced by the kinetic isotope effect for the oxidation of 2-furaldehyde- $d_1$  ( $k_{\text{H}}/k_{\text{D}} = 5.8$ ). Since the five-membered heterocyclic ring system was a planar pentagon with  $\text{sp}^2$  hybridized carbon atoms, and possessed considerable aromatic character arising from delocalization of the two paired electrons, it would undergo a reaction via an electrocyclic mechanism involving six electrons; being a Hückel-type system ( $4n + 2$ ), this was an allowed process.<sup>26</sup>

The sequence of reactions for the oxidation of heteroaldehydes by QDC, in acid medium (Scheme 1) showed that QDC was converted to the protonated dimetallic  $\text{Cr}^{\text{VI}}$  species (**PQ**) (in the acid range used for the present investigation, the protonated QDC would have the  $\text{Cr}^{\text{VI}}$  existing mainly as  $\text{Cr}_2\text{O}_7^{2-}$  (Ref. 27)). The substrate (**A**) was converted to the hydrated form (**Hy**),



Scheme 1.

which reacted with **PQ**, giving the monochromate ester intermediate (**E**) and a  $\text{Cr}^{\text{VI}}$  monomer. The monochromate ester (**E**) underwent decomposition, in the rate-determining step, to give the product (the corresponding acid), along with the  $\text{Cr}^{\text{IV}}$  species. The rate law has been derived as follows:

$$-d[\text{QDC}]/dt = k_3[\text{E}] = k_3[\text{Hy}][\text{PQ}] \quad (6)$$

where  $[\text{PQ}] = K_1[\text{QDC}][\text{H}^+]$ , and  $[\text{Hy}] = K_2[\text{A}][\text{H}_2\text{O}]$ .

Substituting the values of  $[\text{PQ}]$  and  $[\text{Hy}]$  in Eq. 6 (taking the activity of water to be unity), we obtain

$$-d[\text{QDC}]/dt = K_1K_2k_3[\text{A}][\text{QDC}][\text{H}^+] \quad (7)$$

indicating that the reaction exhibited first-order dependence on the concentrations of each reactant (substrate, oxidant and acid).

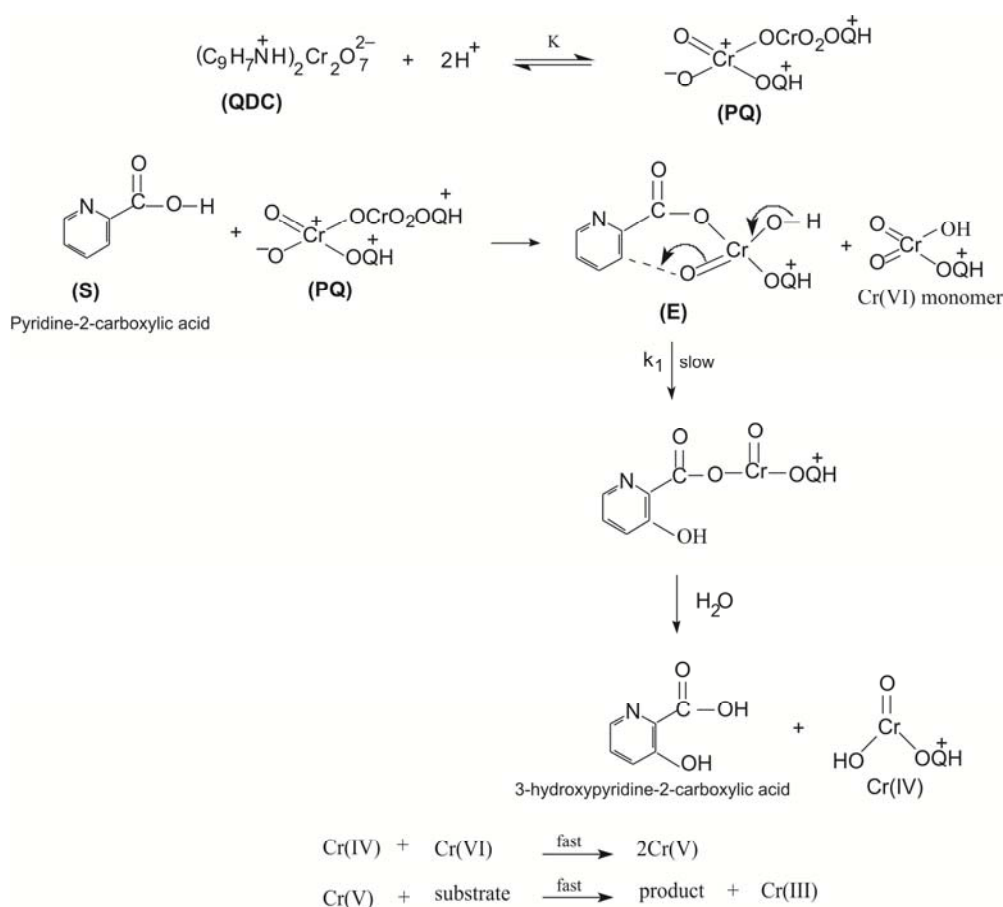
#### (ii) Oxidation of heteroacids

The oxidation of heteroacids by QDC was performed in solvent mixtures containing water-acetic acid (50:50, v/v). The data in Table 4 showed that with increasing proportions of acetic acid (decrease in  $\epsilon_r$  of the medium), there was an increase in the value of the pseudo-first-order rate constant, suggesting the absence of de-

carboxylation. This experimental observation was significant in view of the fact that a reduction in the pseudo-first-order rate constant with decreasing  $\epsilon_r$  had earlier been used as evidence to support the process of decarboxylation.<sup>28</sup> Hence, a change in  $\epsilon_r$  of the solvent medium (Table 4) affected the rate by decreasing the concentration of available protons required for decarboxylation.

In the case of heteroacids, the observed order of reactivity was: pyridine-2-carboxylic acid > pyridine-4-carboxylic acid > pyridine-3-carboxylic acid (Table 2). 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 the carboxylic group in the 3-position or the 4-position. Steric considerations would favor 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.

Scheme 2 shows the sequence of reactions for the oxidation of heteroacids by QDC. The first step was the reaction between the protonated QDC (**PQ**) and the substrate (**S**). One could envisage a mechanism involving the formation of the cyclic transition state, in which the carbon (of the substrate) was bonded to the oxygen (of the oxidant), to form the chromate ester (**E**). This



Scheme 2.

would enable the transfer of electrons towards the chromium, facilitating the formation of the chromium–oxygen–carbon bond. Such an electrocyclic mechanism involved six electrons; being a Hückel-type system ( $4n+2$ ), this was an allowed process.<sup>26</sup> The rate of oxidation of the substrates did not increase rapidly by a decrease in the water concentration in water-acetic acid mixtures (Table 4), suggesting that a molecule of water was not involved in a kinetically important stage of the oxidation reaction. This intermediate underwent reaction with a nucleophile (e.g. water), in the reaction mixture, to form the product, along with the formation of the  $\text{Cr}^{\text{IV}}$  species. The conversion of  $\text{Cr}^{\text{IV}}$  to  $\text{Cr}^{\text{III}}$  was *via* the reaction  $\text{Cr}^{\text{IV}} + \text{Cr}^{\text{VI}} \rightarrow 2\text{Cr}^{\text{V}}$ . The standard potential for the  $\text{Cr}^{\text{VI}}\text{--}\text{Cr}^{\text{V}}$  couple was favorable ( $E^\circ = 0.62$  volt), and this reaction proceeded rapidly.<sup>29</sup> The  $\text{Cr}^{\text{V}}\text{--}\text{Cr}^{\text{III}}$  couple has a potential of 1.75 volt, enabling the rapid conversion of  $\text{Cr}^{\text{V}}$  to  $\text{Cr}^{\text{III}}$ , after reaction with the substrate.<sup>29,30</sup> The driving force for this reaction was the electrophilic nature of the oxygen (of the oxidant) and the electron-donor character of the charged oxygen atom of the substrate. The rate law was given by :

$$-d[\text{QDC}]/dt = k_1[\text{E}] = k_1[\text{S}][\text{PQ}] \quad (8)$$

where  $[\text{PQ}] = K [\text{QDC}] [\text{H}^+]$ .

Hence,

$$-d[\text{QDC}]/dt = Kk_1[\text{S}][\text{QDC}][\text{H}^+] \quad (9)$$

indicating that the reaction exhibited first-order dependence on the concentrations of each reactant (substrate, oxidant and acid).

The cyclic mechanism proposed for the oxidation of heterocyclic acids indicated that the hydroxyl group was located *ortho* to the carboxyl group (in 2-hydroxypyridine-3-carboxylic acid). This *ortho* isomer was the only one isolated as a pure compound, from the oxidation of pyridine-3-carboxylic acid. This was in contrast to the Kolbe-Schmitt reaction,<sup>31</sup> wherein reaction conditions favored entry of the carboxyl group at the *para* position.

The experimental protocol in the present investigation has established that in the QDC oxidation of heteroaldehydes, there was an attack of the oxidant on the aldehydic function, leaving the heteroatom site intact. The QDC oxidation of heteroacids offers a unique advantage for the production of hydroxylated heterocarboxylic acids.

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## SAŽETAK

### Kinetika oksidacije heterocikličkih spojeva kinolinijevim dikromatom

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Kinolinijev dikromat je u sumpornoj kiselini oksidirao heterocikličke aldehide (u odgovarajuće kiseline) i heterocikličke karboksilne kiseline (u odgovarajuće hidroksi-supstituirane kiseline) u mediju voda-octena kiselina (volumnog omjera,  $v(\text{voda})/v(\text{octena kiselina}) = 50:50$ ). Kinetički rezultati su podržali mehanistički put koji se od- vija preko dekompozicije kromatnog estera koja određuje brzinu reakcije.