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Catalyzed Oxidation Reactions. 4. Picolinic Acid Catalysis of Chromic Acid Oxidations[1,2]

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Abstract: Picolinic acid and several closely related acids are effective catalysts in the chromic acid oxidation of primary and secondary alcohols; the oxidation of other substrates is accelerated only moderately. The reaction is first order in chromium(VI), alcohol, and picolinic acid; it is second order in hydrogen ions at low acidity and approaches acidity independence at high perchloric acid concentrations. A primary deuterium kinetic isotope effect is observed at high but not at low acidities. At low acidity the reaction has a considerably lower activation energy and more negative activation entropy than at higher acidities. The reactive intermediate in the proposed mechanism is a negatively charged termolecular complex formed from chromic acid, picolinic acid, and alcohol. The rate-limiting step of the reaction changes with the acidity of the solution. At higher acidities the intermediate termolecular complex is formed reversibly and the overall reaction rate is determined by the rate of its decomposition into reaction products; at low acidities the formation of the complex is irreversible and hence rate limiting. Picolinic acids with a substituent in the 6 position show a greatly reduced catalytic activity. This observation is interpreted as suggesting a square pyramidal or octahedral structure for the reactive chromium(VI) intermediate. The temperature dependence of the deuterium isotope effect has been determined and the significance of the observed large values for $E_a^D - E_a^H$ and A^D/A^H is discussed.

Oxalic acid[3] and α-hydroxy acids[4] accelerate the oxidation-reduction reaction between alcohols and chromic acid by factors up to 10^4. The rapid reaction taking place under these conditions is a cooxidation process in which both the alcohol and the organic acid are oxidized. We proposed that the rate-limiting step of the cooxidation reaction involves a single-step

three-electron reduction of chromium(VI) to chromium(III).

As we have observed and reported earlier, picolinic acid accelerates the reduction of chromic acid by alcohols to a comparable extent as oxalic acid.[5] However, our preliminary investigation has shown that the nature of the reaction is quite different insofar as picolinic acid acts solely as an oxidation catalyst rather than a coreductant.[1b]

Since the catalytic ability of picolinic acid is quite unique and of considerable interest from both the mechanistic point of view as well as of potential synthetic importance, we undertook a detailed investigation of this reaction.

Experimental Section

Materials. Picolinic acid (Aldrich) was recrystallized four times from methanol, mp 135–136 °C (lit.[6] 136–137 °C); 6-methylpicolinic acid (Aldrich) from hexanes, mp 126–128 °C (lit.[7] 126.5–128 °C); pyrrole-2-carboxylic acid (Aldrich) from water, mp 201–202 °C dec (lit.[6] 208.5 °C dec); quinaldic acid (Aldrich) from water, mp 155–156 °C (lit.[6] 157 °C).

2-Hydroxypyridine (Aldrich), 2-thiophenecarboxylic acid (Aldrich), pipecolinic acid (Aldrich), picolinamide (Aldrich), 2-pyridylacetic acid hydrochloride (Aldrich), 2-pyrazinecarboxylic acid (Aldrich), 2,4-pyridinedicarboxylic acid (Aldrich), 2,6-pyridinedicarboxylic acid (Aldrich), *N*-acetylglycine (Eastman), ethyl picolinate (Aldrich), 2-acetylpyridine (Aldrich), allyl acetate (Eastman), methanol (Spectranalyzed, Fisher), ethanol (200 proof, CSC), 1-propanol (Baker analyzed reagent), isopropyl alcohol (Baker GC-spectrophotometric quality reagent), 1-butanol (Fisher), oxalic acid (Mallinckrodt AR), crotonic acid (Baker analyzed reagent), glycolic acid (Aldrich), perchloric acid (Fisher, 70% reagent), sodium perchlorate (Fisher), ceric ammonium sulfate (Baker), and sodium dichromate (Baker analyzed reagent) were used without further purification. A sample of pyridine-2-sulfonic acid was obtained through the generosity of Dr. Frank Mares, Allied Chemical Co., Morristown, N.J.

The following compounds were fractionally distilled through a 20-cm column packed with Nichrome Heli-pak and their purity was checked by GLC: 2-methyl-1-propanol, 3-methyl-2-butanol, 2,4-dimethyl-3-pentanol, 2,2,4-trimethyl-3-pentanol, butryraldehyde, and cyclohexanone.

Acrylonitrile (Practical Grade) was distilled before using and the fraction boiling between 77 and 79 °C collected.

2-Deuterio-2-propanol was prepared from acetone and lithium aluminum deuteride;[8] GLC analysis on a Carbowax column showed a single peak with the same retention time as isopropyl alcohol. The sample had, by NMR analysis, less than 0.2% proton at C-2. Cyclobutanol was prepared by lithium aluminum hydride reduction of cyclobutanone[9] (Aldrich) followed by isolation through a spinning band column and final purification by GLC. 4-Methylpicolinic acid was synthesized by permanganate oxidation of 2-styryl-4-methylpyridine[10] obtained by refluxing 2,4-lutidine (Aldrich) with freshly distilled benzaldehyde in acetic anhydride. 4-Bromopicolinic acid was prepared from 2-picoline *N*-oxide via 4-nitro-2-picoline *N*-oxide,[11] 4-nitro-2-picoline,[12] and 4-bromo-2-picoline[12] followed by permanganate oxidation.[13] Recrystallization from water gave a pure compound, mp 178–179 °C dec (lit.[12] 177–178 °C dec). 6-Bromopicolinic acid was synthesized from 2,6-dibromopyridine (Aldrich) and *n*-butyllithium[14] (Ventron) followed by carbonation. The pure 4-bromopicolinic acid was recrystallized from a mixture of ether and hexanes, mp 192 °C (lit.[14] 192–194 °C). Di-*tert*-butylcarbinol was prepared by lithium aluminum hydride reduction of the corresponding ketone synthesized from trimethylacetonitrile (Aldrich) and sodium[15] via 2,2,4,4-tetramethyl-3-pentanonimine followed by acid hydrolysis. The pure di-*tert*-butylcarbinol was obtained by sublimation, mp 48–49 °C (lit.[16] 50–51 °C).

Product Analysis. Acetone. In a typical experiment, isopropyl alcohol (2.0 mL, 5.8 M), perchloric acid (1.0 mL, 2.55 M), picolinic acid (5.0 mL, 0.45 M), and sodium dichromate (0.50 mL, 0.45 M) were mixed at room temperature and diluted to 25.0 mL. The solution was kept in the dark until completion of the oxidation. The solution was treated overnight with an excess (92 mL) of a freshly filtered saturated solution of 2,4-dinitrophenylhydrazine in 2 N hydrochloric acid (0.022 mmol/mL). After about 12 h in a refrigerator, the precipitate was filtered, dried, and weighed. The procedure was tested with known concentrations of acetone under the same conditions. The recrystallized (methanol) product was identified by melting point and by comparison of the NMR spectra in $CDCl_3$ with that of an authentic sample.

Picolinic Acid–Cr(III) Complexes. In a typical experiment, isopropyl alcohol (2.0 mL, 1.30 M, 2.60 mmol), perchloric acid (0.54 mL, 9.28 M, 5.01 mmol), and picolinic acid (4.0 mL, 0.59 M, 2.36 mmol) were mixed and diluted with water to 25 mL. Sodium dichromate (0.20 mL, 0.287 M, 0.0574 mmol) was added and the reaction allowed to proceed in the dark. After 2 h, the solution was diluted to 500 mL. The Cr(III) species were separated on Dowex 50 W-X8 cation exchange resin in H^+ form, 50–100 mesh; $Cr(PA)_3$, $[Cr(PA)_2(OH_2)_2^+]^+$, and $[Cr(PA)(OH_2)_4]^{2+}$ were eluted with 0.01, 0.15, and 1.0 M $HClO_4$, respectively. No $Cr(H_2O)_6^{3+}$ could be found by elution with 3.0 M $HClO_4$. The total chromium content of the eluted fractions was determined by spectrophotometric analysis of CrO_4^{2-} (ϵ_{372} 4.81×10^{-3} M^{-1} cm^{-1})[17] after oxidation of aliquots with alkaline hydrogen peroxide.[18]

Cyclobutanone and 4-Hydroxybutyraldehyde. Sodium dichromate (0.50 mL, 1.0 M, 0.50 mmol) was added to a solution of cyclobutanol (5.0 mL, 0.722 M, 3.61 mmol) and picolinic acid (2.0 mL, 0.59 M, 1.18 mmol) in 1.18 M aqueous perchloric acid (total volume 59 mL) and the reaction left in the dark until completion. The solution was treated overnight with an excess (100 mL) of a freshly prepared saturated solution of 2,4-dinitrophenylhydrazine in 2 N hydrochloric acid and the precipitate filtered, washed with distilled water, and dried in a vacuum desiccator. The filtrate was continuously extracted with ether. The precipitate dissolved in hot chloroform. The ether solution was neutralized with $NaHCO_3$, washed with water, dried over $MgSO_4$, and combined with the chloroform solution. The dinitrophenylhydrazones were deposited on alumina (3 g, Merck acid washed) in a rotary evaporator, and the coated alumina was dried in a vacuum desiccator, weighed, and charged to a column with alumina (Merck, acid washed, deactivated with 6% water) and eluted with *n*-hexane, cyclobutanone 2,4-dinitrophenylhydrazone, benzene, and chloroform (4-hydroxybutyraldehyde 2-4-dinitrophenylhydrazone). The dinitrophenylhydrazones were identified by comparison of NMR spectra and melting points with authentic samples; yields were determined gravimetrically.

Test for Free-Radical Formation. A series of experiments in which isopropyl alcohol (0.65 M) was oxidized by sodium dichromate (2.5×10^{-3} M, 5×10^{-3} M Cr(VI)) in the presence of picolinic acid (0.024 M) and acrylonitrile (0–0.82 M) or acrylamide (0–0.44 M) in 0.118 and 0.0059 M perchloric acid was carried out at room temperature in the dark. Experiments containing acrylamide were diluted with methanol (45 mL of methanol to 25 mL of reaction mixture) to observe the formation of the polymer.

Kinetic Measurements. In a typical experiment, 2 mL of a solution containing the appropriate amounts of alcohol, picolinic acid, and perchloric acid was placed in a 1-cm glass-stoppered quartz cell and thermally equilibrated in a thermostated cell compartment of a Cary 15 or Zeiss PMQ II spectrophotometer for about 20 min. The reaction was initiated by the addition of a sodium dichromate solution (5 μL) with a microsyringe and monitored by recording the absorbance at 350 nm. Pseudo-first-order rate constants were calculated from slopes of log (absorbance) vs. time plots. Initial slopes were used in measurements with low picolinic acid concentrations. Comparable concentrations of the reactants were used in the study of the stoichiometry with respect to Cr(VI) and picolinic acid. A linear least-square computer program was used to calculate activation parameters log A and E_a; $\Delta S^{\ddagger}$ was calculated from the relationship $\Delta S^{\ddagger} = 2.303R(\log A - \log T - 10.753) = 4.575(\log A - 13.227)$.

Since picolinic acid is a weak base ($K_a = 0.098$)[19] which is partially protonated in the presence of mineral acid, the concentration of free picolinic acid and that of hydrogen ions depends on the amounts of both picolinic acid and of perchloric acid used.

The "total" picolinic acid concentration is

$$[PA_T] = [PA] + [PAH^+] \quad (1)$$

where PA_T, PA, and PAH^+ represent the total, free, and protonated picolinic acid, while the total amount of perchloric acid is given by

$$[ClO_4^-] = [H^+] + [PAH^+] \quad (2)$$

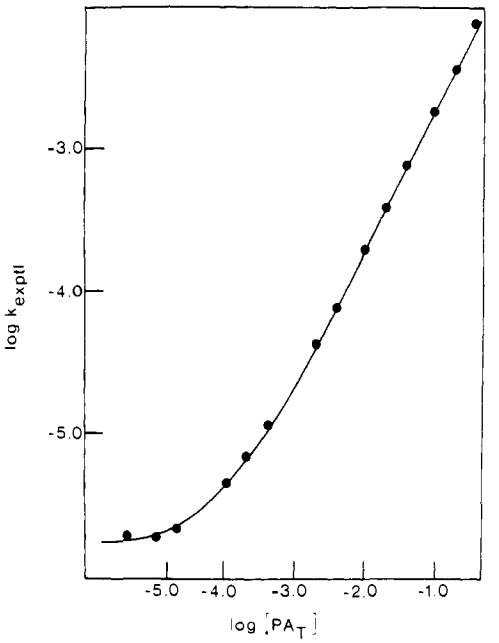


Figure 1. Picolinic acid catalysis at 25 °C at constant ionic strength: $[Cr(VI)]_0 = 4.50 \times 10^{-4}$ M, $[(CH_3)_2CHOH] = 0.0186$ M, $[H^+] = 0.10$ M, ionic strength = 0.596 M.

Table I. Dependence of Pseudo-First-Order Rate Constants on Initial Concentration of Chromium(VI)[a]

Cr(VI), 10^4 M	$10^3 k_{exptl}$, s^{-1}
5.0[b]	7.8
1.0[c]	8.2
0.50[d]	8.0

[a] [*i*-PrOH] = 0.131 M; $[PA_T] = 0.0502$ M; $[HClO_4] = 0.117$ M. [b] 1-cm cell. [c] 5-cm cell. [d] 10-cm cell.

Substituting eq 1 and 2 into

$$K_a = [H^+][PA]/[PAH^+]$$

one obtains

$$[H^+] = \frac{-b + (b^2 + 4K_a[ClO_4^-])^{1/2}}{2} \quad (3)$$

where $b = [PA]_T + K_a - [ClO_4^-]$. Equation 3 was used to calculate $[H^+]$ and pH values in Tables IV and XIII.

Results and Discussion

Rate Studies. Excellent pseudo-first-order plots with respect to chromium(VI) were obtained in all experiments in which an excess of both isopropyl alcohol and picolinic acid was used; the first-order rate constants are independent of the initial chromium(VI) concentration (Table I).

Table II gives the dependence of reaction rates on the concentration of isopropyl alcohol over almost three orders of magnitude and shows that the reaction is first order in alcohol.

Table III gives the results for a series of oxidations with a picolinic acid concentration ranging from zero to 0.44 M. The log-log plot (Figure 1) gives a good straight line with a slope of 0.99 at higher picolinic acid concentrations indicating a first-order dependence on picolinic acid. The catalytic activity of picolinic acid becomes observable at concentration as low as 1.10×10^{-4} M. In 0.44 M picolinic acid, the reaction is 4000 times faster than with no picolinic acid present.

Table IV and Figure 2 show that the acidity dependence is second order in hydrogen ions at low acidities and approaches a zero-order acidity dependence at high acid concentrations.

Table II. Effect of Concentration of Isopropyl Alcohol on Oxidation Rates at 25 °C[a]

$[HClO_4]$, M	[ROH], M	$[PA_T]$, M	k_{exptl}, s^{-1}	$k_{exptl}/[ROH]$, $s^{-1}\ M^{-1}$
1.85	0.117	0.0220	0.016	0.14
1.85	0.0466	0.0220	0.0062	0.13
1.85	0.0230	0.0220	0.0033	0.14
1.85	0.00930	0.0220	0.0013	0.13
1.85	0.00465	0.0220	0.00058	0.12
0.102	0.371	0.0712	0.055	0.15
0.102	0.148	0.0712	0.019	0.14
0.102	0.0742	0.0712	0.010	0.14
0.102	0.0371	0.0712	0.0042	0.11
0.102	0.00371	0.0712	0.00043	0.11
0.102	0.00182	0.0712	0.00020	0.11
0.102	0.00091	0.0712	0.00012	0.13
0.102	0.000456	0.0712	0.0000568	0.13
0.0118	0.131	0.118	0.00342	0.026
0.0118	0.0131	0.118	0.000330	0.025
0.0118	0.00652	0.118	0.000156	0.024

[a] $[Cr(VI)]_0 = 6.24 \times 10^{-4}$ M.

Table III. Effect of Concentration of Picolinic Acid on Oxidation Rates at Constant Ionic Strength at 25 °C[a]

$[PA_T]$, M	$10^3 k_{exptl}$, s^{-1}	$[PA_T]$, M	$10^3 k_{exptl}$, s^{-1}
0.440	7.69	0.000440	0.0115
0.220	3.62	0.000220	0.00689
0.110	1.80	0.000110	0.00461
0.0440	0.750	0.0000220	0.00226
0.0220	0.399	0.0000110	0.00189
0.0110	0.201	0.0000044	0.00195
0.00440	0.0781	0.000	0.00190
0.00220	0.0440		

[a] [*i*-PrOH] = 0.0186 M; $[H^+] = 0.10$ M; $[Cr(VI)]_0 = 4.50 \times 10^{-4}$ M; ionic strength = 0.596 M ($NaClO_4$).

Table IV. Acidity Dependence at 25 °C[a]

$[HClO_4]$, M	pH[b]	k_{exptl}, s^{-1}
1.18	−0.32[c]	4.90×10^{-3}
0.590	0.26	3.21×10^{-3}
0.354	0.50	2.61×10^{-3}
0.236	0.69	2.01×10^{-3}
0.118	1.0	1.05×10^{-3}
0.0590	1.4	3.98×10^{-4}
0.0236	1.8	8.71×10^{-5}
0.0118	2.1	2.67×10^{-5}

[a] [*i*-PrOH] = 0.0261 M; $[PA_T] = 0.0472$ M; $[Cr(VI)]_0 = 4.50 \times 10^{-4}$ M; ionic strength = 1.18 M ($NaClO_4$). [b] pH values calculated from eq 3. [c] H_0; cf. ref 20.

The data fit the empirical rate law

$$k_{exptl} = \frac{[H^+]^2[i\text{-PrOH}][PA_T]}{a[H^+]^2 + b[H^+] + c} \quad (4)$$

The values of a, b, and c were determined graphically from the slopes and intercepts of the straight-line portions of $[H^+]$ $[i\text{-PrOH}][PA_T]/k_{exptl}$ vs. $[H^+]$ and vs. $1/[H^+]$ plots, respectively. These values, $a = 0.277$, $b = 0567$, and $c = 0.00272$, were used to calculate the curve in Figure 2 which gives an excellent fit with the experimental points.

Table V shows the effect of picolinic acid on the chromium(VI) oxidation rates of a series of primary and secondary alcohols. Because of the solubility limitation, these measurements were carried out in 50% dioxane solution. The catalytic effect of picolinic acid is strongest for low molecular weight

Table V. Oxidation Rates of Different Alcohols by Chromium(VI) in the Presence (k_{PA}) and Absence (k) of Picolinic Acid in 50% Aqueous Dioxane[a]

Alcohol	$10^3 k_{PA}$, s^{-1}	$10^6 k$, s^{-1}	k_{PA}/k
CH_3OH	1.76	1.77	990
C_2H_5OH	3.75	3.36	1120
$CH_3CH_2CH_2OH$	4.48	3.76	1280
$CH_3CH_2CH_2CH_2OH$	5.31	6.45	820
$(CH_3)_2CHCH_2OH$	5.06	6.90	730
$CH_3CHOHCH_3$	1.86	5.44	342
	4.90[b]	26.3[b]	186
$(CH_3)_2CHCHOHCH_3$	2.28	12.4	184
$(CH_3)_2CHCHOHCH(CH_3)_2$	0.788	11.3	69
$(CH_3)_3CCHOHCH(CH_3)_2$	1.10	43.5	25
$(CH_3)_3CCHOHC(CH_3)_3$	1.24[c]	9.48[c]	130
	3.25[b]	45.8[b]	70

[a] $[HClO_4]$ = 0.0118 M; $[PA_T]$ = 0.0472 M; [alcohol] = 0.0986 M; 25 °C. [b] 40 °C. [c] Estimated value at 25 °C by applying the $k_{25°C}/k_{40°C}$ factors determined for isopropyl alcohol.

Table VI. Rates of Chromium(VI) Oxidation of Different Substrates in the Presence (k_{PA}) and Absence (k) of Picolinic Acid[a]

Substrate, M		$10^4 k_{PA}$, s^{-1}	$10^4 k$, s^{-1}	$\frac{k_{PA}-k}{k}$
$(CH_3)_2CHOH$	0.522	634	2.98	211
$CH_3CH_2CH_2CHO$	0.0735	43.1	4.41	8.77
$CH_3CH{=}CHCOOH$	0.433	1.26	0.212	3.72
$(COOH)_2$	0.114	239	16.6	13.4
$CH_2(COOH)_2$	1.020	0.703	0.395	0.780
$CH_3COOCH_2CH{=}CH_2$	0.0674	11.3	1.38	7.19
$HOCH_2COOH$	0.30	11.7	3.57	2.28
Cyclohexanone	0.0678	1.73	0.454	2.81

[a] $[HClO_4]$ = 0.0236 M; $[PA_T]$ = 0.0588 M; 25 °C.

primary alcohols and weaker for secondary alcohols. Branching, particularly in secondary alcohols, reduces the ratio k_{PA}/k considerably implying a fairly strong steric inhibition to the catalyzed reaction. Surprisingly, the catalytic effect appears to be larger for di-*tert*-butylcarbinol than for the less branched isopropyl-*tert*-butylcarbinol. This apparent anomaly seems to be due more to a low value of the rate for the uncatalyzed reaction rather then to a high rate for the catalyzed oxidation.

The acidity dependence of several of these alcohols was investigated further. We found that ethanol, 1-propanol, and 2,2,4-trimethyl-3-pentanol exhibit the same acidity dependence as isopropyl alcohol, changing from second to zero order in hydrogen ions (Figure 3). Methanol, on the other hand, is only first order in hydrogen ions at low acidities and becomes zero order at higher hydrogen ion concentrations.

Picolinic acid accelerates the oxidation by chromic acid of a number of other types of compounds (Table VI). However, the rate accelerations are between one and two orders of magnitude smaller than those observed for alcohols. The picolinic acid catalysis is thus quite selective toward primary and secondary alcoholic functions, a finding which may be of considerable usefulness in synthetic applications.

The modest rate acceleration found for glycolic acid is probably due to the fact that glycolic acid forms a stronger complex with chromic acid than does picolinic acid.[21,22]

Table VII summarizes the results of our search for other related oxidation catalysts. It shows that the ability to significantly catalyze chromic acid oxidations of alcohols is narrowly restricted to pyridine-2-carboxylic acid. The only active compound not containing a pyridine ring is the closely related

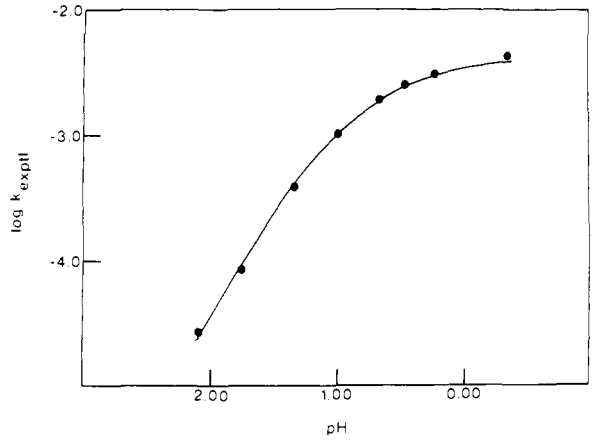


Figure 2. Acidity dependence of the catalyzed oxidation of isopropyl alcohol at 25 °C (curve calculated from eq 4): $[Cr(VI)]_0 = 4.50 \times 10^{-4}$ M, $[(CH_3)_2CHOH]$ = 0.0261 M, $[PA_T]$ = 0.0472 M, ionic strength = 1.18 M.

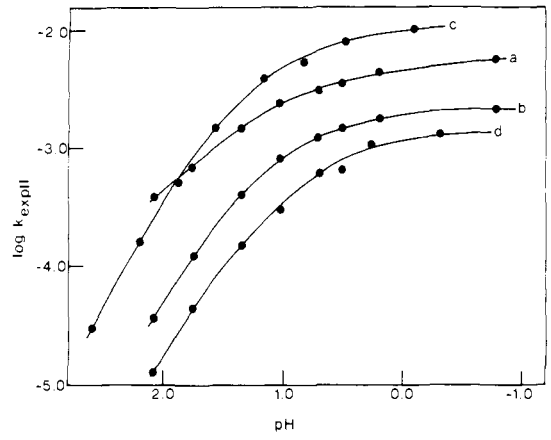


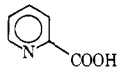
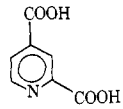
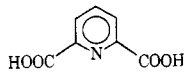
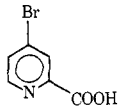
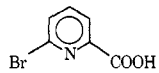
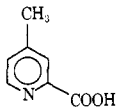
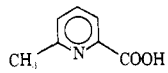
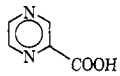
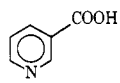
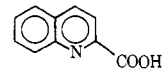
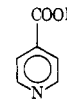
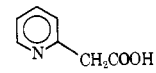
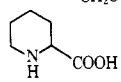
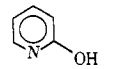
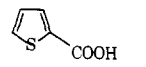
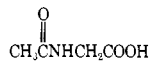
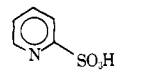
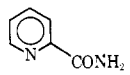
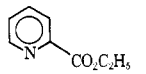
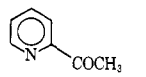
Figure 3. Acidity dependence of the catalyzed oxidation of methanol, ethanol, 1-propanol, and 2,2,4-trimethyl-3-butanol at 25 °C: $[PA_T]$ = 0.0472 M; $[Cr(VI)]_0 = 5.0 \times 10^{-4}$ M. (a) $[CH_3OH]$ = 1.23 M; ionic strength = 1.18 M. (b) $[C_2H_5OH]$ = 0.0197 M; ionic strength = 1.18 M. (c) [*n*-PrOH] = 0.0394 M; ionic strength = 0.928 M. (d) [(*t*-Bu)CHOH(*i*-Pr)] = 0.0129 M; 10% dioxane solutions were used; catalyzed reaction rate constants were corrected by subtracting those of uncatalyzed oxidations.

1,4-pyrazine-2-carboxylic acid. A negative substituent in the 4 position of the pyridine ring further enhances catalytic effectiveness, but 6 substitution strongly reduces it. Table VIII shows the catalytic effect of 4-substituted 2-pyridinecarboxylic acids at three different acidities.

Reaction Products. The organic oxidation products formed in the chromic acid oxidation of alcohols are generally unaffected by the presence of picolinic acid. The oxidation of isopropyl alcohol gives acetone in a quantitative yield in the absence as well as in the presence of picolinic acid (Table IX).

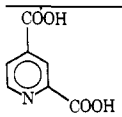
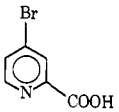
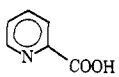
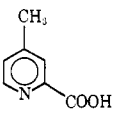
Similarly, cyclobutanol yields a mixture of cyclobutanone and of 4-hydroxybutyraldehyde regardless of whether the oxidation is carried out in the presence or in the absence of picolinic acid (Table X). The last result is particularly significant from the mechanistic point of view since it is known that the formation of 4-hydroxybutyraldehyde is due exclusively to the one-electron oxidation by chromium(IV).[23,24] The formation of 4-hydroxybutyraldehyde during the picolinic acid catalyzed oxidation of cyclobutanol therefore indicates that chromium(IV) is formed in the course of the reaction in the presence of picolinic acid and that it participates to an extent similar to the uncatalyzed reaction. Picolinic acid catalysis differs in this respect fundamentally from the oxalic acid co-

Table VII. Oxidation Rates of Isopropyl Alcohol in the Presence of Pyridinecarboxylic Acids and Related Compounds[a]

Compd	M	$10^4 k_{exptl}$, s^{-1}	$\frac{k_{exptl} - k_0}{k_0[C]}$
None		4.25 ($=k_0$)	
	0.0154	306	4 610
	0.0154	1210	18 400
	0.0132	24.2	356
	0.00106	395[b]	86 700
	0.00326	7.85[b]	260
	0.0154	123	1 810
	0.0154	5.44	18
	0.0154	246	3 690
	0.0147	3.06	
	0.0156	9.55	80
	0.0146	3.43	
	0.0154	3.79	
	0.0162	5.22	14
	0.0154	5.27	16
	0.0136	3.33	
	0.0201	6.38	25
	0.0154	3.19	
	0.0165	3.99	
	0.0154	2.95	
	0.0154	6.33	32

[a] [*i*-PrOH] = 0.928 M, $[Cr(VI)]_0 = 5.0 \times 10^{-4}$ M, $[HClO_4]$ = 0.185 M, 25 °C. [b] $[Cr(VI)]_0 = 5.0 \times 10^{-5}$ M. Rate constants were obtained from the initial rates of reactions. Under these conditions, good pseudo-first-order plots could not be obtained.

Table VIII. Relative Rates of Chromic Acid Oxidation of Isopropyl Alcohol in Presence of Catalysts at 25 °C[a]

Catalyst	M	$HClO_4$, M	*i*-PrOH, M	$10^2 k_{exptl}$, s^{-1}
	0.0117	1.18	0.0653	1.60
	0.0117	0.590	0.0653	1.19
	0.0154	0.185	0.928	12.10
	0.0117	1.18	0.0653	1.15
	0.0117	0.590	0.0653	0.833
	0.00106[b]	0.185	0.928	3.95
	0.0117	1.18	0.0653	0.403
	0.0117	0.590	0.0653	0.257
	0.0154	0.185	0.928	3.06
	0.0117	1.18	0.0653	0.204
	0.0117	0.590	0.0653	0.105
	0.0154	0.185	0.928	1.23

[a] $[Cr(VI)]_0 = 5.0 \times 10^{-4}$ M. [b] $[Cr(VI)]_0 = 5.0 \times 10^{-5}$ M.

Table IX. Yield of Acetone in Chromic Acid Oxidation Catalyzed by Picolinic Acid at 25 °C[a]

Isopropyl alcohol, M	Perchloric acid, M	Acetone, yield, mmol	Acetone, mmol/ Cr(VI), mmol
0.46	0.10	0.67	1.49
0.46	0.010	0.672	1.49
0.052	0.10	0.666	1.48

[a] 0.45 mmol of Cr(VI); $[PA_T] = 0.090$ M.

Table X. Products of the Chromic Acid Oxidation of Cyclobutanol in the Presence and Absence of Picolinic Acid[a]

Picolinic acid, M	Products, yield, %	
	Cyclobutanone	4-Hydroxybutyraldehyde
0.0	49	31
0.0486	46	33

[a] Cyclobutanol, 3.62 mmol (0.0724 M); sodium dichromate, 0.541 mmol (0.0108 M); $HClO_4$, 1.1 M.

oxidation reaction, in which the formation of chromium(IV) is suppressed and, consequently, cyclobutanol is oxidized exclusively to cyclobutanone.[3b]

Stoichiometry. The stoichiometry of the reaction with respect to picolinic acid was determined kinetically in an experiment in which picolinic acid and chromic acid were used in comparable concentrations, while isopropyl alcohol was present in large excess.

Since the reaction is first order in both chromium(VI) and in picolinic acid, the course of the reaction under these conditions will reflect the number of picolinic acid molecules removed by complexation with chromium(III). Neglecting the components present in large excess (alcohol and hydrogen

Table XI. Ion Exchange Analysis of Chromium(III)-Picolinic Acid Complexes Formed in the Picolinic Acid Catalyzed Oxidation of Isopropyl Alcohol[a]

Eluent[c] $HClO_4$, M	Cr(III) complex	Yield, %[b] Expt A	Expt B	Expt C
0.01	$Cr(PA)_3$	0.0	43.0	10.2
0.15	$[Cr(PA)_2(OH_2)_2]^+$	5.5	3.2	1.5
1.0	$[Cr(PA)(OH_2)_4]^{2+}$	95.7	50.4	85.3
3.5	$Cr(OH_2)_6^{3+}$	0.0	0.0	0.0

[a] Concentrations: $HClO_4$, 0.20 M; *i*-PrOH, 0.10 M; Cr(VI), 4.6×10^{-3} M. [b] Picolinic acid: A, 0.094 M; B, 0.92 M; C, 0.094 M initially, but additional picolinic acid was added after the reduction of chromium(VI) was completed to bring the final concentration to 0.92 M. [c] The concentrations are the same as those used in the separation of chromium(III)-thiocyanate complexes by E. L. King and E. B. Dismukes, *J. Am. Chem. Soc.*, **74**, 1674 (1952).

ions), the stoichiometry of the reaction can be written in general terms as

$$Cr(VI) + nPA \rightarrow (PA)_nCr(III) \quad (5)$$

where n is the number of molecules of picolinic acid forming a stable complex with chromium(III). The concentration of picolinic acid available to accelerate the oxidation at any time of the reaction thus will be

$$[PA_T] = [PA_T]_0 - nx \quad (6)$$

where x is the concentration of chromium(III). The rate equation thus is

$$\frac{dx}{dt} = k'[Cr(VI)][PA_T]$$
$$= k'[Cr(VI)]([PA_T]_0 - nx)$$
$$= k'([Cr(VI)_0] - x)([PA_T]_0 - nx) \quad (7)$$

On integration eq 7 gives

$$\frac{1}{n[Cr(VI)]_0 - [PA_T]_0} \ln \frac{[PA_T]_0[Cr(VI)]}{[Cr(VI)]_0([PA_T]_0 - nx)} = k't \quad (8)$$

If $n = 0$, i.e., if no picolinic acid is lost during the reaction due to complexation with chromium(III), eq 8 simplifies to

$$-\frac{1}{[PA]_0} \ln \frac{[Cr(VI)]}{[Cr(VI)]_0} = k't \quad (9)$$

and a straight line should be obtained when ln [Cr(VI)] or log A_{350} is plotted vs. time. If one or more molecules of picolinic acid form a stable complex with chromium(III), a straight-line plot for log $[Cr(VI)]/([PA_T]_0 - nx)$ should be obtained. As the best straight line is obtained for $n = 1$ (Figure 4) one can conclude that the chromium(III) species formed in the reaction is a 1:1 chromium(III)-picolinic acid complex.

This result is consistent with those obtained by analysis of the chromium(III) species formed in the reaction (Table XI). When the concentration of picolinic acid is low (experiment A) 95.7% of the products is eluted only with rather strong acid (1.0 M $HClO_4$) and we therefore assume that the complex is the doubly charged 1:1 chromium(III)-picolinic acid ion, $[Cr(PA)(OH_2)_4]^{2+}$.

When a fairly large excess of picolinic acid is used (experiment B) a high fraction of chromium is converted to the uncharged 1:3 complex, $Cr(PA)_3$. Experiment C shows that the amount of $Cr(PA)_3$ is much lower when the same excess of picolinic acid is added after the reduction of chromium(VI) has been completed. Thus, although $[Cr(PA)(OH_2)_4]^{2+}$ can react with an excess of picolinic acid to yield higher picolinic acid-chromium(III) complexes, this ligand exchange reaction is too slow to account for the results obtained in experiment B. As the strictly first-order kinetic dependence in picolinic acid excludes the presence of more than one molecule of picolinic acid in the activated complex of the reaction, the incorporation of the second and third molecule of picolinic acid must occur primarily through its reaction with an unstable intermediate like a chromium(IV) or chromium(V) species.

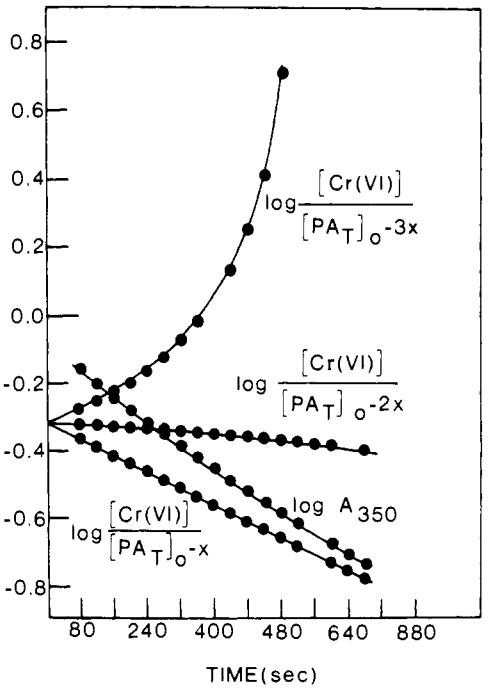


Figure 4. Kinetic test for complex formation between chromium(III) and picolinic acid. Conditions: $[(CH_3)_2CHOH] = 0.261$ M, $[PA_T]_0 = 0.0110$ M, $[HClO_4] = 0.0928$ M, $[Cr(VI)]_0 = 0.00502$ M, 25 °C.

Even at low picolinic acid concentrations all chromium(III) is found to be complexed with picolinic acid; the observation that no $[Cr(OH_2)_6]^{3+}$ is formed strongly suggests that the actual oxidant in the picolinic acid catalyzed chromium(VI) oxidation is a picolinic acid-chromium(VI) complex.

Free Radical Formation. The formation of free-radical intermediates is indicated by the formation of a polymer when the reaction was carried out in the presence of acrylamide (0.30 M) at very low acidity (0.0059 M $HClO_4$). At higher acidity (0.118 M $HClO_4$) no polymer formation could be observed with either acrylamide or acrylonitrile. This behavior is consistent with our earlier observation that the formation of free radicals in the uncatalyzed oxidation of isopropyl alcohol can be observed only at low acidities, obviously because at higher acidities the oxidation of free radicals becomes faster than their ability to react with vinylic compounds and initiate polymerization reactions.[25,26] The observation that in the picolinic acid catalyzed reaction polymer formation becomes noticeable only at extremely low acid concentrations suggests that picolinic acid is capable of accelerating the oxidation of free radicals as well as of alcohols. As the free radical formed in the oxidation of isopropyl alcohol, $(CH_3)_2\dot{C}OH$, has retained its hydroxyl group, this is consistent with picolinic acid's ability to accelerate specifically the oxidation of alcohols (Table VI).

Reaction in the Presence of Cerium(IV). The presence of cerium(IV) reduces the reaction rate (Table XII). A quite noticeable effect can be observed at cerium(IV) concentrations as low as 1×10^{-6} M; at higher concentrations the oxidation rate is reduced by almost 50%.

A similar effect of cerium(IV) on chromic acid oxidation of isopropyl alcohol was observed earlier[27] and interpreted by

Table XII. Effect of Cerium(IV) on Rates of Chromium(VI) Oxidation of Isopropyl Alcohol in the Presence of Picolinic Acid at 25 °C[a]

Ce(IV), M	$10^3 k_{expt}$, s^{-1}	Ce(IV), M	$10^3 k_{expt}$, s^{-1}
0.0	4.14	1.16×10^{-5}	3.29
5.82×10^{-8}	3.97	2.91×10^{-5}	3.22
1.16×10^{-7}	4.16	1.16×10^{-4}	2.81
2.91×10^{-7}	4.10	2.91×10^{-4}	2.34
1.16×10^{-6}	3.53	1.16×10^{-3}	2.40
2.91×10^{-6}	3.49	2.91×10^{-3}	2.26

[a] $[PA_T] = 4.43 \times 10^{-2}$ M; [*i*-PrOH] = 0.0783 M; $[Cr(VI)]_0 = 2.13 \times 10^{-3}$ M.

Table XIII. Isotope Effect in the Oxidation of 2-Deuterio-2-propanol at Different Acidities[a]

	k_H/k_D	
$[H^+]$, M[b]	Exptl	Calcd from eq 34
0.00822	1.5	1.4
0.0168	1.9	1.8
0.0445	2.9	2.6
0.0950	3.6	3.6
0.204	4.3	4.6
0.318	5.1	5.0
0.550	5.5	5.5

[a] $[PA]_T = 0.0472$ M; [*i*-PrOH] = 0.0261 M. [b] From eq 3.

the following mechanism, in which cerium(IV) in effect acts as a catalyst for the disproportionation of chromium(IV) to chromium(VI) and chromium(III):

$$Cr(IV) + Ce(IV) \rightarrow Cr(V) + Ce(III) \quad (10)$$

$$Cr(V) + Ce(IV) \rightarrow Cr(VI) + Ce(III) \quad (11)$$

$$2Cr(IV) + 2Ce(III) \rightarrow 2Cr(III) + 2Ce(IV) \quad (12)$$

The observation that cerium(IV) has a similar effect on oxidation rates in the presence of picolinic acid indicates that the reaction mechanisms of the catalyzed and uncatalyzed reactions are closely related and that chromium(IV) is an intermediate in both reactions. This result thus confirms the conclusion reached on the basis of the cleavage reaction observed in the oxidation of cyclobutanol.

Isotope Effect. 2-Deuterio-2-propanol reacts with chromic acid in the presence of picolinic acid at a substantially lower rate than isopropyl alcohol. The isotope effect (Table XIII), however, shows an unusual acidity dependence. At high acidities the values of k_H/k_D approach those expected for a typical primary kinetic deuterium isotope effect of a reaction in which a carbon–hydrogen bond is broken in the rate-limiting step; at low hydrogen ion concentrations the isotope effect seems to disappear and k_H/k_D approaches the value of 1.0.

This acidity dependence of the kinetic isotope effect suggests that the reaction proceeds by a multistep mechanism and undergoes a change in the rate-limiting step when the acidity is changed. At high acidity the rate-limiting step obviously involves the oxidative cleavage of the carbon–hydrogen bond, while at low acidities it is an earlier step in the reaction sequence, most likely the formation of an ester from the alcohol and the chromic acid–picolinic acid complex, which must become rate limiting.

Activation Parameters. Table XIV shows the temperature dependence of the picolinic acid catalyzed oxidation of 2-propanol and 2-deuterio-2-propanol at four acidities; the activation parameters obtained from these data are given in Table XV.

At low acidity (0.00472 M $HClO_4$) the reaction has a considerably lower activation energy (by about 3–5 kcal/mol) and a more negative entropy of activation (by over 20 eu) than at higher temperatures. This observation is consistent with the conclusion reached from isotope effect measurements at a single temperature (Table XIII) that the reaction has different rate-limiting steps at low and high acidities. The lower activation energy and more negative activation entropy at low acidity support the view that the rate-limiting step under these conditions consists in the formation of an intermediate complex and does not involve the breaking of a bond. The increase in activation energy and entropy at higher acidities is consistent with a rate-limiting step in which a carbon–hydrogen bond is broken and the intermediate complex is fragmented into two parts.

Table XIV. Temperature Dependence of Second-Order Oxidation Rates for 2-Propanol (k_2^H) and 2-Deuterio-2-propanol (k_2^D)

$[HClO_4]$, M	Temp, K	k_2^H, $s^{-1}\,M^{-1}$	k_2^D, $s^{-1}\,M^{-1}$	k_2^H/k_2^D
4.65	353	32.8	8.92	3.68
4.65	333	11.6	2.71	4.30
4.65	313	4.82	0.877	5.50
4.65	298	2.11	0.313	6.74
1.86	353	3.19	1.05	3.05
1.86	333	1.28	0.356	3.58
1.86	313	0.561	0.108	5.21
1.86	298	0.261	0.0367	7.11
0.59	353	1.38	0.533	2.58
0.59	333	0.655	0.179	2.74
0.59	313	0.257	0.0517	4.97
0.59	295	0.103	0.0159	6.48
0.00472	353	0.00337	0.00237	1.42
0.00472	333	0.00171	0.00118	1.45
0.00472	313	0.000962	0.000649	1.49
0.00472	298	0.000563	0.000340	1.66

[a] $[PA_T] = 0.0472$ M; $[Cr(VI)]_0 = 5.00 \times 10^{-4}$ M.

Mechanism. Any mechanism for the reaction must explain the following findings:

(a) The reaction results in a quantitative oxidation of an alcohol to a carbonyl compound (Table IX), with no oxidation of picolinic acid taking place.

(b) Cyclobutanol gives both one- and two-electron oxidation products (Table X).

(c) Picolinic acid is a highly specific catalyst; the only catalytically active compounds are some substituted 2-pyridinecarboxylic acids and 2-pyrazinecarboxylic acid (Table VII).

(d) The reaction is first order in the oxidant, the substrate, and the catalyst (Tables I–III).

(e) The order with respect to hydrogen ions changes from second order to zero order except for methanol, where the order changes from first to zero (Figures 1 and 3).

(f) The isotope effect is acidity dependent; the value of k_H/k_D is 5.5 at higher acidities but approaches 1.0 at low acid concentrations (Table XIII).

(g) The activation energy at low acidity is considerably lower and the activation entropy more negative than at higher acidities (Table XV).

(h) The presence of cerium salts reduces the reaction rate to about one-half of its original value (Table XII).

(i) At low concentrations, picolinic acid–chromium(III) is formed predominantly as the 1:1 picolinic acid–chromium(III) complex. At higher picolinic acid concentrations, the 2:1 and 3:1 complexes are also formed. No formation of $[Cr(OH_2)_6]^{3+}$ is observed (Table XI).

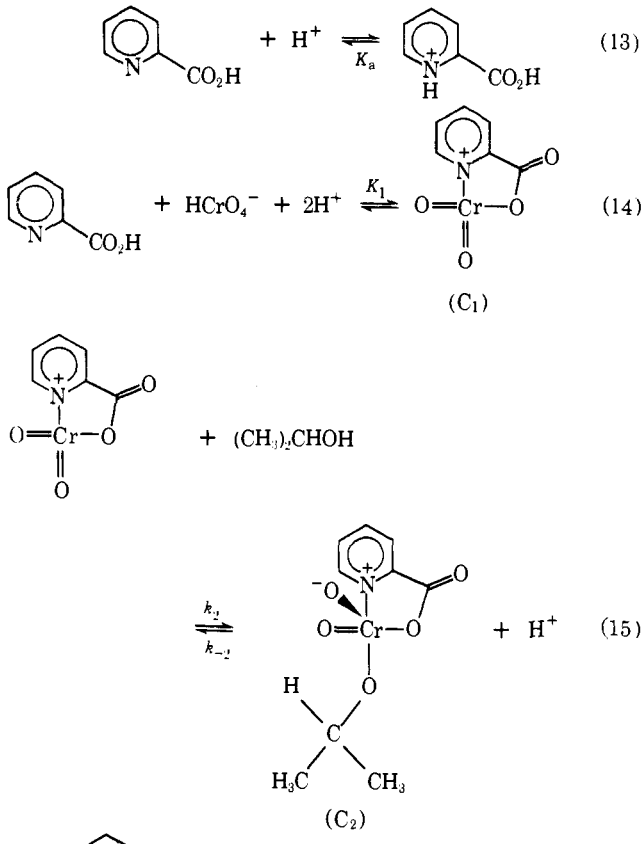
(j) Polymer formation was observed in the presence of acrylamide at low acidity.

A mechanism consistent with these facts is given in Scheme I. Picolinic acid is a weak base ($K_a = 0.098$)[19] and is proton-

Table XV. Activation Parameters

$HClO_4$, M	E_a^H	E_a^D	$E_a^D - E_a^H$	Log A^H	Log A^D	$\Delta S_H^{\ddagger}$	$\Delta S_D^{\ddagger}$	A^D/A^H
0.00472	6.64 ± 0.23	7.14 ± 0.18	0.50 ± 0.29	1.62 ± 0.16	1.77 ± 0.10	−53.1 ± 0.7	−52.4 ± 0.5	1.4
0.59	9.24 ± 0.09	12.54 ± 0.14	3.30 ± 0.16	5.87 ± 0.07	7.46 ± 0.10	−33.7 ± 0.3	−26.4 ± 0.5	38.9
1.86	9.29 ± 0.23	12.59 ± 0.06	3.30 ± 0.23	6.24 ± 0.15	7.81 ± 0.01	−32.0 ± 0.7	−24.8 ± 0.1	18.2
4.65	10.20 ± 0.37	12.49 ± 0.23	2.29 ± 0.44	7.78 ± 0.23	8.64 ± 0.16	−24.9 ± 1.1	−21.0 ± 0.7	7.2

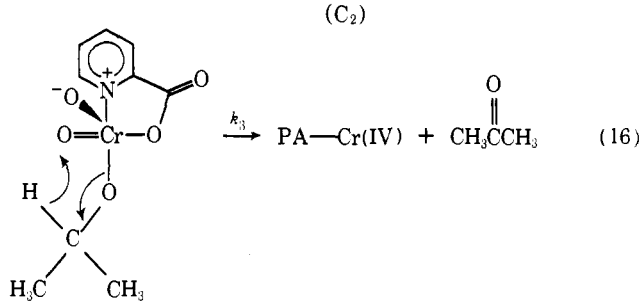
Scheme I



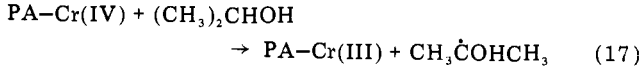
(13)

(14)

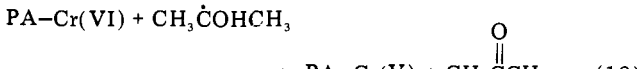
(15)



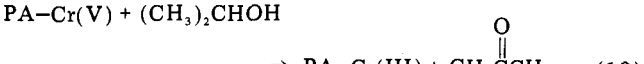
(16)



(17)



(18)



(19)

ated to a varying degree under the conditions employed in our study (eq 13). It reacts with chromic acid to form a complex C_1, which is the reactive chromium(VI) compound (eq 14). The observation that only 2-pyridinecarboxylic acids and the 2-pyrazinecarboxylic acid show a significant catalytic effect strongly suggests that the intermediate complex C_1 has a cyclic structure. Since we were unable to observe any decrease in reaction order with respect to picolinic acid even at the highest picolinic acid concentrations used, we must assume that the equilibrium constant for reaction 14 is quite low, certainly below 0.2 in 1 M perchloric acid. In this respect picolinic acid stands in sharp contrast to oxalic[3,26] and glycolic[21] acids, both of which form similar complexes of considerably higher stability. Because we were unable to determine the equilibrium constant of this reaction, we could not determine the number of protons involved in the equilibrium reaction 14 directly. However, the second-order kinetic dependence in hydrogen ions for the oxidation process at low acidities strongly suggests the participation of two hydrogen ions and thus the formation of a positively charged complex.

In the next step (eq 15) the chromic acid-picolinic acid complex C_1 reacts with a molecule of alcohol to give a zwitterionic complex C_2 and a hydrogen ion. This step, the formation of an esterlike intermediate, is rate limiting at low acidities; since the carbon-hydrogen bond of the alcohol remains unchanged during this step, the reaction exhibits no primary deuterium isotope effect at low acidities. At high acidities and for methanol under all conditions the reverse reaction, the hydrolysis of C_2, becomes fast enough to make reaction 15 reversible. The observation that picolinic acid catalyzes the oxidation of alcohols much more effectively than that of other compounds is entirely consistent with the assumption that the critical intermediate is an ester of the alcohol undergoing oxidation.

The termolecular complex C_2 undergoes oxidative decomposition in the next step of the reaction sequence (eq 16). This reaction resulting in the formation of a carbonyl compound and a chromium(IV)-picolinic acid complex intermediate is fast compared with reaction 15 at low acidities, but is rate limiting for methanol at all acidities and becomes rate limiting for other alcohols at higher acidities. As it involves the breaking of a carbon-hydrogen bond, it results in an appreciable isotope effect.

The chromium(IV)-picolinic acid complex found in reaction 16 reacts rapidly with an alcohol molecule to yield chromium(III) and a free radical (eq 17), which, in turn, will reduce another molecule of the chromic acid-picolinic acid complex to a chromium(V) complex (eq 18). The chromium(V) compound will react with another molecule of alcohol (eq 19).

At higher concentrations of picolinic acid, higher picolinic acid-chromium(III) (2:1 and 3:1) complexes are formed, although the rate law remains strictly first order in picolinic acid. The incorporation of the second or third molecule of picolinic acid therefore cannot occur at the chromium(VI) stage, but must involve one of the intermediate chromium valence states. Because chromium(V) is generally the more stable and therefore longer lived intermediate,[28,29] additional molecules of picolinic acid may be incorporated at this point (Scheme II).

From Scheme I one can derive the rate law

$$-\frac{d[Cr(VI)]}{dt} = k_{exptl}[HCrO_4^-] = k_3[C_2] + k_0[HCrO_4^-] \quad (20)$$

where k_0 refers to the uncatalyzed oxidation reaction. Substituting for $[C_2]$ gives

$$k_{exptl} - k_0 = k_{cat} = \frac{K_1 K_a k_2 k_3 [PA_T][ROH][H^+]^2}{(k_{-2}[H^+] + k_3)([H^+] + K_a)} \quad (21)$$

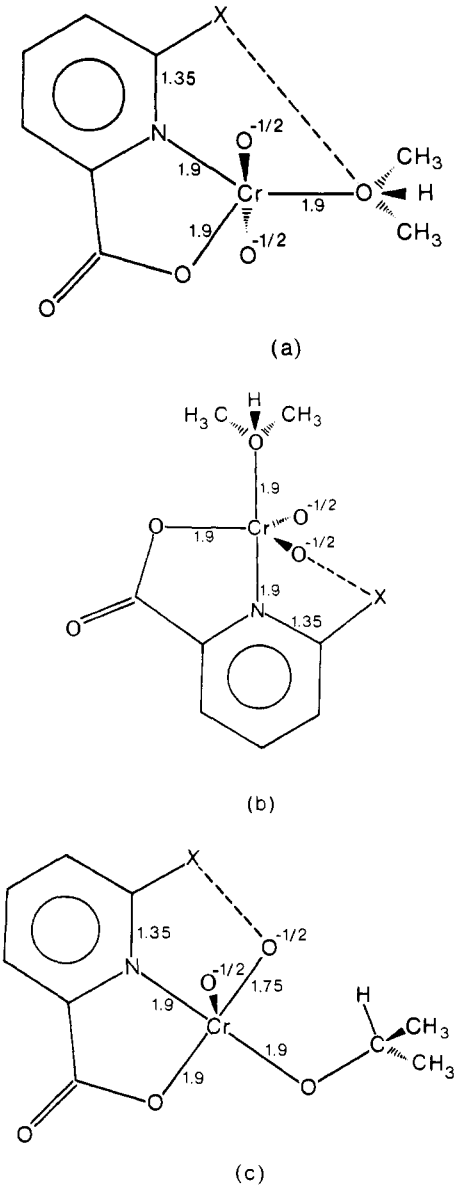


Figure 5. Termolecular complex C_2 as (a) trigonal bipyramid with picolinic acid in basal position, (b) trigonal bipyramid with picolinic acid in apical position, (c) square pyramid.

$$= \frac{K_1K_ak_2k_3[PA_T][ROH][H^+]^2}{k_3K_a + (k_{-2}K_a + k_3)[H^+] + k_{-2}[H^+]^2} \quad (22)$$

Since the uncatalyzed reaction is slow compared with the catalyzed oxidation, k_0 can be neglected and $k_{cal} \approx k_{expll}$ except for very low picolinic acid concentrations.

Equation 22 has the same form as the experimental rate law (eq 4), with

$$a = k_{-2}/K_1K_ak_2k_3 \quad (23)$$

$$b = (k_{-2}K_a + k_3)/K_1K_ak_2k_3 \quad (24)$$

$$c = 1/K_1k_2 \quad (25)$$

Hence,

$$K_1k_2 = 1/c \quad (26)$$

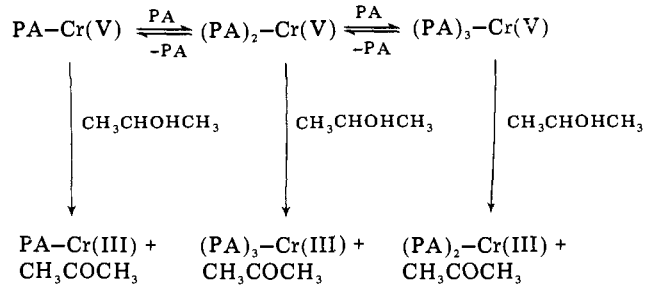
and

$$k_3/k_{-2} = b/a - K_a \quad (27)$$

$$= c/aK_a \quad (28)$$

$$= cK_a/(bK_a - c) \quad (29)$$

Scheme II



For the isopropyl alcohol the experimentally obtained values are $a = 0.277$, $b = 0.0567$, $c = 0.00272$.

Thus from eq 26 $K_1k_2 = 370\ s^{-1}\ M^{-1}$. Since we have concluded that $K_1 < 0.2\ M^{-3}$, $k_2 > 2 \times 10^3\ s^{-1}\ M^{-1}$. The values for k_3/k_{-2} obtained from eq 27, 28, and 29 are 0.107, 0.100, and 0.094 s^{-1} M, respectively and show thus a very good agreement. Since k_{-2} will be of comparable magnitude as k_2, the value of k_3 is probably $< 100\ s^{-1}$.

For 2-deuterio-2-propanol the following values were obtained: $a = 1.81$, $b = 0.203$, $c = 0.00283$. Equation 26 gives $K_1k_2 = 350\ s^{-1}\ M^{-1}$ which is in good agreement with the values obtained for the protio compound.

The values for k_3^D/k_{-2} obtained from eq 27, 28, and 29 are 0.0142, 0.0160, and 0.0163, respectively, and show thus quite a good agreement. Since the values of a and c were determined from slopes rather than intercepts and, further, since eq 28 is a simple fraction, we assume that the best values are obtained from this equation. From them the isotope effect for reaction 16 for isopropyl alcohol can be obtained:

$$\frac{k_3^H}{k_3^D} = \frac{k_3^H/k_{-2}}{k_3^D/k_{-2}} = \frac{0.100}{0.0160} = 6.3$$

This value is in full agreement with those values generally obtained for reactions in which a carbon-hydrogen bond is broken.

Since only k_3 is subject to a significant isotope effect, the rate law for a deuterated alcohol will be

$$k_{cat}^D = \frac{K_1K_ak_2k_3^D[PA_T][ROH][H^+]^2}{(k_{-2}[H^+] + k_3^D)([H^+] + K_a)} \quad (30)$$

The dependence of the observed experimental isotope effect on the acidity can be obtained by dividing eq 21 by eq 30:

$$\frac{k_{cat}^H}{k_{cat}^D} = \frac{k_3^H(k_3^D + k_{-2}[H^+])}{k_3^D(k_3^H + k_{-2}[H^+])} \quad (31)$$

$$= \frac{k_3^H(k_3^D/k_{-2} + [H^+])}{k_3^D(k_3^H/k_{-2} + [H^+])} \quad (32)$$

$$= 6.3\,\frac{0.016 + [H^+]}{0.10 + [H^+]} \quad (33)$$

The values calculated from eq 33 are compared with those obtained experimentally in Table XIII and show a very satisfactory agreement.

The most intriguing question is why picolinic acid should be such an efficient catalyst for the oxidation of alcohols. Since picolinic acid accelerates the Cr(VI) → Cr(IV) step, it probably stabilizes the chromium(IV) state relativity to chromium(VI) and thus increases the Cr(VI)/Cr(IV) oxidation potential. This relative stabilization may well be due to the considerably higher formation constant for the chromium(IV) picolinic acid complex relative to the weak chromium(VI) complex. The stabilization of the chromium(IV) is of course not sufficient to make the chromium(IV) intermediate an isolable or directly detectable intermediate. The step Cr(IV) → Cr(III) is obviously still very fast. As chromium(III) also forms very stable complexes with picolinic acid[30] (log K_1 = 4.76, log

K_2 = 4.38, log K_3 = 4.55), this is hardly surprising since the Cr(IV)/Cr(III) potential is probably increased as well or at least not diminished.

A more detailed understanding of the reaction intermediate C_2 can be gained by a closer examination of the surprising sensitivity of picolinic acid toward substitution in the 6 position (Table VII). While the catalytic activity of picolinic acid is quite strongly enhanced by electronegative substituents (CO_2H, Br) in the 4 position, it is strongly reduced if these substituents are in the 6 position. The ratios of catalytic activities of 4 to 6 substituent picolinic acids are 52 for CO_2H, 100 for CH_3, and 333 for Br. Consistent with this finding, a very low catalytic effectiveness was also found for quinaldic acid where the hydrogen atom in the 8 position blocks the access to the nitrogen atom.

In the cyclic chromic complex C_2 there must be at least five ligands around the central chromium atom. The compound can therefore have the structure of a trigonal bipyramid (Figures 5a, 5b), a square pyramid (Figure 5c), or, if a sixth ligand (solvent molecule) is present, of an octahedron; the spatial relationship between the oxygen atom and 6 substituent on the pyridine ring in the last two structures will be essentially the same. The interatomic distances between O · · · H and O · · · Br calculated from standard bond lengths and angles for these models are given in Table XVI together with the sums of the van der Waals radii. This comparison leads to the conclusion that the termolecular complex C_2 must have a square pyramidal or octahedral structure in order to give the observed steric effects. It is interesting to note that the square pyramidal structure resembles that recently established by x-ray analysis for a chromium(V) complex with two molecules of 2-hydroxy-2-methylbutyric acid.[31]

Temperature Dependence of the Kinetic Isotope Effect. Kwart and Nickle[32] recently investigated the temperature dependence of the deuterium isotope effect in the chromic acid oxidation of several alcohols. They found that for the bulky di-*tert*-butylcarbinol the differences between the activation energies for the deuterio and the protio compound ($E_a^D - E_a^H$) were under some conditions more than three times as high as the differences in the zero-point energies of the C-D and C-H bonds. These high values were accompanied by a compensating increase in the entropy of activation (or the Arrhenius A factor) for the deuterated compound resulting thus in an only moderate increase in the isotope affect at a low acidity and a complete disappearance of the effect under high acidity conditions. Similar results were obtained for trifluoromethylphenylcarbinol. The authors interpreted these results as evidence for proton transfer by a tunneling mechanism and proposed further that the high values of ($E_a^D - E_a^D$) and of A^D/A^H indicate a change in mechanism from a direct transfer of the hydrogen atom to an oxygen ligand of the chromium to a mechanism in which the hydrogen is transferred through a chain of solvent molecules by "proton jump" (Grotthus mechanism).

Our results summarized in Table XV provide evidence that unusually high differences in activation parameters for a deuterated compound may occur as a result of a well-documented change in the rate-limited step within the same mechanism. In a situation of this type, the activation parameters are by no means "pure" values representing a single activated complex but reflect "average" values in a system of reactions where the fraction associated with a given activated complex changes with isotope substitution, medium, and temperature. To consider higher than expected values of $E^D - E^H$ and A^D/A^H in the absence of a very high value of $\Delta F_H^{\ddagger} - \Delta F_D^{\ddagger}$ (k_H/k_D) as evidence for quantum mechanical tunneling seem imprudent; to associate it with a complete change in the mechanism of hydrogen transfer, in the geometry of the activated complex and in the role of the solvent, appears even less justified.

Table XVI. van der Waals Radii and Interatomic Distances (Å)

	Sum of van der Waals radii	Trigonal bipyramid picolinic a. basal (Figure 5a)	Trigonal bipyramid picolinic a. apical (Figure 5b)	Square pyramid (Figure 5c) or octahedron
O . . . H	2.50	3.8	2.8	2.3
O . . . Br	3.35	3.6	3.0	2.1

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