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Kinetics of Oxidation of Substituted Benzyl Alcohols by Quinolinium Dichromate

Doyamoy Dey and Mahendra K. Mahanti*

Department of Chemistry, North-Eastern Hill University, Shillong 793 003, India

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Quinolinium dichromate (QDC) oxidizes benzyl alcohol and substituted benzyl alcohols smoothly in dimethyl formamide, in the presence of acid. The reaction has unit dependence on each of the alcohol, QDC, and acid concentrations. Electron-releasing substituents accelerate the reaction, whereas electron-withdrawing groups retard the reaction, and the rate data obey Hammett's relationship. The reaction constant ρ was -1.67 ± 0.08 at 313 K. The kinetic isotope effect, k_H/k_D, was 5.89 at 313 K. The reaction does not induce polymerization of acrylonitrile. The observed experimental data have been rationalized in terms of a hydride ion transfer in the rate-determining step.

Introduction

The kinetics and mechanism of oxidation reactions of chromium(VI) have been fairly well studied. Chromic acid is one of the most versatile of the available oxidizing agents reacting with diverse kinds of organic substrates. The mechanism of oxidation varies with the nature of the chromium(VI) species and the solvent used. The development of newer Cr(VI) reagents[1-7] for the oxidation of organic substrates continues to be a subject of interest. There exists a need for new methods, especially for complex or highly sensitive substances where great selectivity and effectiveness, coupled with mildness of conditions, are prerequisites for success. In addition, many of the existing mild methods become impractical for operations on a scale greater than submolar. New procedures are emerging, involving "nonaqueous" chromium(VI) reagents and the general idea that anhydrous conditions are more conducive to complexation of substrates with Cr(VI) species, and therefore to mild oxidation. The reagent employed in this investigation, quinolinium dichromate (QDC), $(C_9H_7NH^+)_2Cr_2O_7^{2-}$, has emerged as a very useful and versatile oxidant,[8] which is clearly deserving of widespread application.

Experimental Section

(a) Materials. Benzyl alcohol and substituted benzyl alcohols were purified by either recrystallization or distillation, and their purity was checked from physical constants. Quinolinium dichromate (QDC) was prepared by the reported method,[8] and its purity was checked by estimating Cr(VI) iodometrically. Dimethyl formamide (DMF) was a BDH sample and was distilled under reduced pressure before use. Hydrochloric acid (E. Merck) was used as such after a check of its physical constants. α,α-Dideuteriobenzyl alcohol was prepared by the standard method,[9] and its purity was checked by NMR.

(b) Kinetic Measurements. The reactions were performed under pseudo-first-order conditions by keeping a large excess of the alcohols with respect to QDC. The reactions were carried out at constant temperature (±0.1 K). The reactions were followed by monitoring the absorption band at 440 nm, spectrophotometrically. At this wavelength, the maximum absorption due to QDC has been observed, and the absorption due to other reaction species is negligible. The rate constants were evaluated from the linear ($r > 0.992$) plots of log [QDC] against time. The values reported were the mean of at least duplicate runs and were reproducible to within ±3%. The solvent was DMF unless otherwise stated. The reaction mixtures remained homogeneous in the solvent systems used.

Table I. Stoichiometry of the Oxidation of Benzyl Alcohol by QDC. Concentration of Benzyl Alcohol = 0.005 M

[HCl]/M	10^2[QDC]/M	Δ[QDC]/Δ[BA]
0.0	2.50	0.65
0.10	2.60	0.70
0.25	2.70	0.68
0.50	2.80	0.72

Table II. Dependence of the Reaction Rate on Oxidant Concentration ([BA] = 0.01 M; T = 313 K)

10^4[QDC]/M	1.0	5.0	7.5	10.0	15.0	20.0
$10^5k_1/s^{-1}$	4.19	4.03	4.28	4.15	4.56	4.43

Table III. Dependence of the Reaction Rate on Substrate Concentration ([QDC] = 0.001 M; T = 313 K)

10^2[BA]/M	1.0	5.0	7.5	10.0	15.0	20.0
$10^5k_1/s^{-1}$	4.15	20.52	31.05	40.65	62.20	81.30

Table IV. Dependence of the Reaction Rate on Acidity ([BA] = 0.01 M; [QDC] = 0.001 M; T = 313 K)

[HCl]/M	0.05	0.075	0.10	0.25	0.50
$10^5k_1/s^{-1}$	6.13	9.02	12.05	30.15	61.00

(c) Product Analysis. The 2,4-dinitrophenylhydrazone (DNP) of the corresponding benzaldehyde was prepared, recrystallized from ethanol, dried, and weighed. The product, in each case, was identical (mp) with an authentic sample of the DNP of benzaldehyde. The yields of DNP after recrystallization, with all the alcohols, were 85-93%.

Results

The oxidation of benzyl alcohol (BA) by QDC, in dimethyl formamide (DMF), resulted in the formation of benzaldehyde. Under the present experimental conditions, there was no further oxidation of benzaldehyde.

Stoichiometry. The stoichiometric experiments were carried out under nitrogen at 313 K, under the conditions of $[QDC]_0 > [BA]_0$, at varying acid concentrations. The disappearance of Cr(VI) was followed, until the absorbance values became constant. The $[QDC]_\infty$ was estimated. A stoichiometric ratio, Δ[QDC]/Δ[BA], of 0.69 was observed (Table I), which conformed to the overall equation

$$3PhCH_2OH + 2Cr^{VI} \rightarrow 3PhCHO + 2Cr^{III} + 6H^+ \qquad (1)$$

Rate Laws. Since the results for all alcohols studied were similar, with regard to the rate laws and other experimental data, only representative data are reproduced for benzyl alcohol.

Under pseudo-first-order conditions, the individual kinetic runs were first order with respect to QDC. Further, the pseudo-first-order rate constants were independent of

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Table V. Dependence of the Reaction Rate on Solvent Composition ([BA] = 0.01 M; [QDC] = 0.001 M; [HCl] = 0.05 M; T = 313 K)

$DMF:H_2O$ (%, v/v)	100:0	95:5	90:10	85:15	80:20
D	37.6	39.7	41.8	43.9	46.1
$10^5k_1/s^{-1}$	6.13	3.63	2.75	2.09	1.58

Table VI. Rate Constants for the Oxidation of Benzyl Alcohols by Quinolinium Dichromate ($10^5k/s^{-1}$) in the Presence of Acid

substituent	303 K	308 K	313 K	318 K	323 K
H	3.44	4.62	6.13	8.00	11.00
m-Me	4.47	5.75	7.92	11.00	13.80
p-Me	6.61	8.71	12.02	15.85	20.00
p-OMe	9.55	12.60	18.20	25.12	28.84
p-Cl	1.38	1.91	2.29	3.17	4.57
m-Br	0.76	1.01	1.20	1.59	2.63
m-NO_2	0.23	0.30	0.33	0.42	0.79
p-NO_2	0.17	0.23	0.25	0.32	0.63

Table VII. Activation Parameters for the Oxidation of Benzyl Alcohols by Quinolinium Dichromate in the Presence of Acid[a]

substituent	ΔH^{*} (kJ mol^{-1})	ΔS^{*} (J mol^{-1} k^{-1})	ΔG^{*} (kJ mol^{-1})
H	45.3	-181	102.0
m-Me	43.0	-185	101.0
p-Me	41.2	-190	100.7
p-OMe	36.0	-202	99.2
p-Cl	49.5	-170	102.7
m-Br	52.5	-162	103.2
m-NO_2	55.8	-153	103.7
p-NO_2	59.0	-144	104.1

[a] Error limits $\Delta H^{*} \pm 3$ kJ mol^{-1}; $\Delta S^{*} \pm 6$ J mol^{-1} K^{-1}; $\Delta G^{*} \pm 4$ kJ mol^{-1}.

the initial concentration of QDC (Table II). The reaction was of first order with respect to the concentration of alcohol (Table III). The reaction was catalyzed by acid, and the catalyzed reaction showed a first-order dependence on acidity (Table IV).

The rate of oxidation of α,α-dideuteriobenzyl alcohol and benzyl alcohol at 313 K were 10^4k = 1.04 and 6.13 L mol^{-1} s^{-1}, respectively. The kinetic isotope effect, k_H/k_D, was 5.89 at 313 K.

Effect of Solvent Composition. The acid-catalyzed oxidation of benzyl alcohol was studied in solutions containing varying proportions of DMF and water (Table V). It was observed that an increase in the dielectric constant of the medium reduced the rate of the reaction.

Induced Polymerization. Since all the reactions were performed under nitrogen, the possibility of induced polymerization was tested. It was seen that there was no induced polymerization of acrylonitrile or the reduction of mercuric chloride.[10] This indicated that a one-electron oxidation was quite unlikely. Control experiments were performed in the absence of benzyl alcohol. The concentration of QDC did not show any appreciable change.

Effect of Temperature. The catalyzed oxidation of benzyl alcohols was studied at different temperatures (Table VI). The activation parameters (303–323 K) (Table VII), were evaluated by the standard procedure.[11]

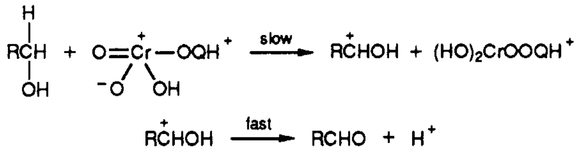
Discussion

The values for the free energy of activation were nearly constant, indicating that the same mechanism operates for all the alcohols.

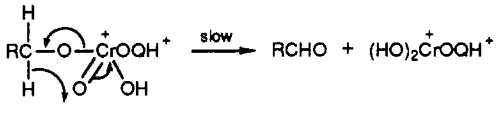
Table VIII. Temperature Dependence of the Reaction Constant for the Oxidation of Benzyl Alcohols by Quinolinium Dichromate in the Presence of Acid

T/K	ρ
303	-1.71 ± 0.04
308	-1.70 ± 0.06
313	-1.67 ± 0.08
318	-1.60 ± 0.05
323	-1.50 ± 0.06

Scheme I



Scheme II



The linear increase in the oxidation rate with acidity suggests the involvement of a protonated Cr(VI) species in the rate-determining step. There have been earlier reports of the involvement of such Cr(VI) species in chromic acid oxidation.[12] Protonated Cr(VI) species have been observed in the presence of *p*-toluenesulfonic acid in nitrobenzene–dichloromethane mixtures.[13]

The kinetic isotope effect (k_H/k_D = 5.89) indicates the cleavage of the C–H bond from the alcohol carbon atom.[14]

The activation enthalpies and entropies for the oxidation reaction are linearly related (r = 0.985). The correlation was tested and found valid by applying Exner's criterion.[15] The isokinetic temperature computed from the plot between ΔH^{*} and ΔS^{*} was 375 K. Without attaching much physical significance to isokinetic temperatures it can be stated that a linear correlation is usually a necessary condition for the validity of the Hammett equation.

The dielectric constants for dimethylformamide–water mixtures have been estimated approximately from the dielectric constants of the pure solvents and have been recorded in Table V. A plot of log k_1 against the inverse of dielectric constant is linear (r = 0.985) with a positive slope. This suggests an interaction between a positive ion and a dipole[16] and is in consonance with the observation that in the presence of an acid, the rate-determining step involves a protonated Cr(VI) species.

Inspection of Table VI brings to light that electron-releasing substituents accelerate the oxidation process and electron-withdrawing groups retard the process. Hence, one should expect a linear free energy relationship of the Hammett equation type to correlate the reactivity with the substituent constant.[17a] A plot of log k_1 versus σ values of substituents was linear (0.995), and the values of ρ are shown in Table VIII.

The manner of electron transfer has to be considered. A hydrogen abstraction mechanism is unlikely, in view of

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the failure to induce polymerization of acrylonitrile and the reduction of mercuric chloride. In most hydrogen abstraction reactions, the reaction constants have small magnitude.[17b] In the present investigation, the large negative value of the reaction constant, together with the substantial kinetic isotope effect, would suggest considerable carbonium ion character in the transition state. The experimental results would point to a hydride ion transfer in the rate-determining step. The hydride ion transfer can occur directly (Scheme I) or may involve the prior formation of a chromate ester (Scheme II). The similarity in rate laws with chromic acid oxidations[12] would suggest the formation of a chromate ester.

Registry No. QDC, 56549-24-7; $PhCH_2OH$, 100-51-6; m-$MeC_6H_4CH_2OH$, 587-03-1; p-$MeC_6H_4CH_2OH$, 589-18-4; p-$OMeC_6H_4CH_2OH$, 105-13-5; p-$ClC_6H_4CH_2OH$, 873-76-7; m-$BrC_6H_4CH_2OH$, 15852-73-0; m-$NO_2C_6H_4CH_2OH$, 619-25-0; p-$NO_2C_6H_4CH_2OH$, 619-73-8.

Erythromycin A as a Supramolecular Catalyst: Effect on Rhodamine B Lactonization

Mônica Barra,[†] Juan José Cosa,*[,‡] and Rita H. de Rossi*[,†]

Instituto de Investigaciones en Físico Química de Córdoba (INFIQC), Departamento de Química Orgánica, Facultad de Ciencias Químicas, Universidad Nacional de Córdoba, Suc. 16, C.C. 61, 5016 Córdoba, Argentina, and Departamento de Química y Física, Universidad Nacional de Rio Cuarto, 5800 Rio Cuarto, Córdoba, Argentina

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The intramolecular lactonization reaction of rhodamine B base in chloroform solution is remarkably accelerated by the antibiotic erythromycin A. The rate increases by a factor of ca. 10^{10}, a value significantly higher than typical enzymatic factors. This effect is ascribed to the formation of a host–guest complex between the dye and the antibiotic, a process that induces a conformational change conducive to the rehybridization of the central carbon atom of the dye.

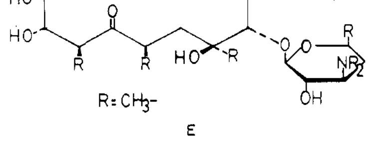
Introduction

The study of reactions that involve noncovalent interactions between two molecules, one acting as a host and the other acting as a guest, is a subject of great current interest in fundamental as well as in applied research.[1,2]

The ability of biochemical compounds to recognize and selectively bind guest species and eventually alter chemical reactivity represents one of the most important properties of these molecules. Thus, certain antibiotics have been characterized as receptors for charged hydrophilic species such as Na^+, K^+, Ca^{2+}, etc., and have been studied as natural ionophores.[2] However, there are few reports in the literature on the complexation of antibiotics with organic molecules,[3,4] and, as far as we know, no kinetic studies have been conducted on such systems.

Erythromycins are widely used antibiotics of the macrolide family whose structures are well defined in both the solid state and in solution.[5] These compounds consist of a polyfunctionalized 14-membered lactone ring bonded to sugar units, a structure that suggests that these macrocycles may be good receptors for organic guests.

We recently initiated studies using erythromycin A (E) as a supramolecular receptor, with the finding that E forms molecular complexes with several organic dyes in nonaqueous solutions.[6] We further found that ring-opened erythromycin A inhibits the alkaline hydrolysis of p-nitrophenyl esters through the formation of a host–guest complex.[7]



E

Table I. Rate and Equilibrium Constants for the Lactonization Reaction of Rhodamine B Base in Chloroform[a]

T, °C	k_1, s^{-1}	K_1, M
50	1.70×10^{-3}	0.211
40	8.33×10^{-5}	0.125
25	6.2×10^{-7} [b]	0.054[b]

[a] Initial concentrations of Z = 1×10^{-5} M. [b] Extrapolated values.

In a previous communication we pointed out the remarkable effect of E on the lactonization reaction of rhodamine B base in aprotic or weakly polar solvents.[8] We wish to report herein the enormous rate enhancement of the intramolecular ring closure reaction of rhodamine B base in chloroform solution in the presence of E.

Results and Discussion

The xanthene dye rhodamine B base exists in solution as an equilibrium mixture of a colored zwitterion Z and a colorless lactone L (Eq 1).

The equilibrium constant for this system was found to depend on both the solvent hydrogen-bond donating ability (favoring the zwitterion) and the solvent dielectric/polarizability properties.[9]

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