Kinetics and Mechanism of the Reaction of α -Phenoxypropanoic Acids with Sodium Salt of N-Chlorobenzenesulphonamide: EDTA Catalysis

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ABSTRACT: EDTA smoothly catalyses the oxidation *cum* chlorination of some 17 α -phenoxypropanoic acids with sodium salt of N-chlorobenzenesulphonamide in acidic solution. A ternary intermediate can be envisaged for describing the enhanced reactivity. Imperfections are observed in the linear Hammett relationship in the case of $-NO_2$ substituents, irrespective of the position. The susceptibility constant, $\rho(\approx +1)$ indicates the development of an electron-rich transition state. © 2001 John Wiley & Sons, Inc. Int J Chem Kinet 34: 27–33, 2002

INTRODUCTION

Perron et al. [1] have synthesized numerous new penicillins by condensing various phenoxypropanoic acids with 6-aminopenicillanic acid (6-APA) and the penicillins obtained are analytically pure. Phenoxy-acetic and α -phenoxypropanoic acids (α -PPA) possess potential biological properties. Substituents of

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these aromatic insulated acids have had widespread application as herbicides and pesticides in recent years, but this has resulted in environmental contamination of soil and ground water. Hence, degradation studies are very much essential. A survey of literature shows that some systematic studies were carried out on the reactions of phenoxyacetic acids by various oxidants such as Mn(VII) [2], Ce(IV) [3], chromic acid [4], bipyridinium chromate [4], phenyliodoso acetate [5], lead tetraacetate [6], PFC [7], pyridiniumhydrobromide perbromide [8], periodate complex of Cu(II) [9], NCP [10], PDC [11], picolinic acid catalyzed Cr(VI) [12], and QFC [13]. The kinetics and

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related studies of the reaction of α -PPA have not been reported so far. In this paper, we present results of the EDTA catalyzed reaction of several α -PPA by *N*-chlorobenzenesulphonamide (CAB) and the substituent effects. The structure–reactivity relationships are ascertained.

EXPERIMENTAL

Pure chlorine gas bubbled through a solution of benzenesulphonamide in 4 M sodium hydroxide over a period of 1 h at 70°C. CAB obtained was dried and recrystallized from water. Sodium salt of EDTA (Merck) was used as such. Acetic acid was purified by a method similar to that of Weissberger [14]. All the α -PPA were prepared by literature methods [1]. The pure acids were obtained by recrystallization from suitable solvents. All the other chemicals used were of AnalaR grade.

The reactions were carried out in 60% (v/v) aqueous acetic acid. Perchloric acid was used as the proton source. The studies were carried out in the temperature range of 303–323 K. All the solutions were kept in a thermostat at constant temperature, which was controlled using Gallenkemp thermostat to an accuracy of $\pm 0.1^{\circ}$. The required volumes of these solutions for each run were mixed and 2 ml aliquots of the reaction mixture were pipetted out at convenient time intervals and quenched in 10 ml 2% KI solution and the liberated iodine was titrated against standard thiosulphate to a starch end point. The pseudo-first-order rate constants were evaluated from log titre vs. time plots. All the rate constants reported are average of two or more determinations.

Stoichiometry and Product Analysis

The stoichiometric runs carried out in the presence of excess of CAB at 40°C reveal that 2 mol of the oxidant are consumed by 1 mol of α -PPA. The reaction mixture was extracted with ether from an actual kinetic run after about 70% completion of the reaction. The solvent was removed by evaporation and the product was methylated with methyl sulphate and alkali. The product was made acidic and extracted with ether. It was found to be chlorophenol as evidenced by its IR spectra.

RESULTS AND DISCUSSION

First-order dependence on [CAB] was evidenced by the linear semilogarithmic plots of titre vs. time. A perfect linearity is observed (r > 0.996; s < 0.024) in the first-order plots and the pseudo-first-order rate coefficients are almost constant. The order dependence on the concentration of substrate is <1. Tendency for curvature is noticed in k_{obs} vs. [α -PPA] plot as shown in Fig. 1 (r = 0.982; s = 0.222). The inverse–inverse plot (Fig. 2) reaches a limiting value. The catalytic activity of EDTA is depicted in Fig. 3. EDTA enhances the conversion of the insulated acids and the system can be characterized as,

$$k_{\rm obs} = a + b$$
 [EDTA]

where *a* and *b* are rate constants for catalyzed and uncatalyzed reactions respectively. The rate of conversion is proportional to the acidity. No leveling off rate



Figure 1 Plot of k_{obs} vs. [α -PPA] in the EDTA catalyzed reaction of [α -PPA] with CAB.



Figure 2 Michaelis–Menten plot in the EDTA catalyzed reaction of α -PPA with CAB.

constants takes place at higher acidities. The kinetic data are summarized in Table I.

The catalyzed reaction is accelerated in the presence of Cl⁻. The reactivity of the insulated acids increases as the amount of acetic acid in the solvent is increased as shown in Table II. The insensitivity on rates of added acrylonitrile rules out a free radical process. Ionic strength has a significant effect on the reactivity (Table III).

The Hammett correlations are primarily used for reactions occurring in homogeneous solutions. Effect of substituents on the reactivity has been examined by employing 17 meta-, para-, and ortho-substituents at three different temperatures and the results are listed in Table IV. It appears that the substituent effects are small in this reactivity as expected since the order dependence on the concentration of substrate is very low. A scan of Table IV reveals quite interesting results. Exceptional behavior is observed in the case of $-NO_2$ substituents, irrespective of the position. Although the Hammett plot of log k vs. σ shows a very poor correlation (r = 0.275; s = 0.525) when considering all the substituents, when the $-NO_2$ groups and the other substituents are evaluated separately, good correlations are



Figure 3 Catalytic activity of EDTA on the reaction rate. (a) 10^2 [EDTA] = 1.00 mol dm⁻³, 10^3 [CAB] = 1.20 mol dm⁻³; (b) 10^2 [S] = 2.00 mol dm⁻³, 10^3 [CAB] = 1.20 mol dm⁻³; (c) 10^2 [S] = 2.00 mol dm⁻³, 10^2 [EDTA] = 1.00 mol dm⁻³, 10^3 [CAB] = 1.20 mol dm⁻³, 10^2 [EDTA] = 4.00 mol dm⁻³, 10^3 [CAB] = 1.20 mol dm⁻³.

10^{3} [CAB] (mol dm ⁻³)	$10^{2}[\alpha\text{-PPA}]$ (mol dm ⁻³)	$10[\text{HClO}_4] \\ (\text{mol dm}^{-3})$	$\frac{10^4 k_{\rm obs}}{({\rm s}^{-1})}$
0.80	2.00	6.00	5.03
1.20	2.00	6.00	4.99
1.80	2.00	6.00	4.98
2.30	2.00	6.00	4.87
1.20	1.00	6.00	4.38
1.20	2.00	6.00	4.99
1.20	4.00	6.00	5.43
1.20	6.00	6.00	5.99
1.20	10.00	6.00	6.51
1.20	14.00	6.00	7.30
1.20	2.00	3.00	2.25
1.20	2.00	4.50	3.53
1.20	2.00	6.00	4.99
1.20	2.00	7.50	6.53
1.20	2.00	9.00	7.89

Table IEffect of Reactants on the Reaction Rate in theEDTA Catalyzed Reaction of α -PPA by CAB at 313 K

 $[EDTA] = 1.00 \times 10^{-2} \text{ mol } dm^{-3}; AcOH : H_2O = 60 : 40 (v/v).$

observed (Fig. 4) (r = 0.947; s = 0.111). Few orthosubstituents are not included in the correlation since the corresponding σ_0 values are not available in literature. The Brown–Okamoto $\rho\sigma^+$ correlations are inferior (r = 0.889; s = 0.158). The σ^- values (correlation for p-substituents only) describe the reactivity

Table IIDependence of [EDTA], Solvent Composition,and [NaCl] on the Reaction Rate at 313 K

10^{2} [EDTA] (mol dm ⁻³)	D^a	10^4 [NaCl] (mol dm ⁻³)	$\frac{10^4 k_{\rm obs}}{({\rm s}^{-1})}$
0.50	35.14	_	3.38
1.00	35.14	_	4.99
2.00	35.14	_	7.96
3.00	35.14	_	9.34
4.00	35.14	_	12.23
6.00	35.14	-	16.05
1.00	49.60	-	2.51
1.00	42.37	-	3.22
1.00	35.14	-	4.99
1.00	27.90	-	7.56
1.00	20.67	-	17.98
1.00	35.14	2.00	7.15
1.00	35.14	3.50	8.89
1.00	35.14	5.00	10.40
1.00	35.14	7.50	12.22
1.00	35.14	10.00	13.75

 $[CAB] = 1.20 \times 10^{-3} \text{ mol } dm^{-3}; [\alpha-PPA] = 2.00 \times 10^{-2} \text{ mol } dm^{-3}; [H^+] = 6.00 \times 10^{-1} \text{ mol } dm^{-3}.$

^{*a*} Dielectric constant values are calculated from the values of pure solvents.

Table III	Dependence of the Reaction Rate at 313 K
on Ionic St	rength and Acrylonitrile

10^2 [NaClO ₄] (mol dm ⁻³)	$10^{3}[Acry]$ (mol dm ⁻³)	$10^4 k_{\rm obs}$ (s ⁻¹)	
_	_	4.99	
1.00	-	6.09	
2.00	-	7.91	
3.00	_	9.85	
4.00	_	11.59	
_	_	4.99	
_	1.00	4.93	
_	2.00	5.06	
_	4.00	4.89	
_	7.00	5.10	

$$\label{eq:cAB} \begin{split} & [CAB] = 1.20 \times 10^{-3} \mbox{ mol } dm^{-3}; \mbox{ [EDTA]} = 1.00 \times 10^{-2} \mbox{ mol } dm^{-3} \mbox{ [α-PPA]} = 2.00 \times 10^{-2} \mbox{ mol } dm^{-3}; \mbox{ [H^+]} = 6.00 \times 10^{-1} \mbox{ mol } dm^{-3}. \end{split}$$

exceptionally well with a correlation coefficient, r = 0.985 and standard deviation, s = 0.075. The susceptibility constant (ρ) values are listed in Table V.

The behavior of $-NO_2$ substituents is puzzling. The general nonadherence to the Hammett equation suggests that the nitro and other substituents exhibit different reaction mechanisms. Similar type of imperfections are observed in the Os(VIII)- catalyzed oxidation of sulfides [15] by CAB. Also, it has been reported [16] that for an electrically charged group Hammett's equation would be in error because of the direct effect in addition to inductive and resonance effects.

The susceptibility constant, ρ is a measure of the reaction to polar substitution. A positive ρ value (\approx +1) in this system means that the rate is increased by electron-attracting substituents. Low ρ values indicate that there is only a moderate degree of charge separation in the transition state. A transition state similar to the one shown below can be envisaged which can explain the positive ρ values.

Charge separation in the transition state is supported by the marked increase in the rate of conversion with decrease in dielectric constant of the medium (Table III).

Mechanism

The probable oxidizing species in acid medium [17] are CAB, RNHCl, RNCl₂, and HOCl. It seems that the experimental observations can be explained by assuming CAB as the effective electrophile. It has been reported

		$10^3 k'^a / (s^{-1})$		A 77#	۸.c#	۸ <i>C</i> #			
No.	Substrate	30°C	$40^{\circ}C$	50°C	$(kJ \text{ mol}^{-1})$	$(J K^{-1} mol^{-1})$	(kJ mol^{-1})	r	S
1	Н	4.99	10.50	21.15	64.5	96.9	94.8	0.997	0.087
2	<i>p</i> -CH ₃	1.92	4.59	7.96	55.6	132.6	97.1	0.993	0.114
3	p-OCH ₃	1.60	3.54	6.20	53.1	142.5	97.7	0.996	0.082
4	<i>p</i> -Cl	5.34	14.16	31.11	69.4	67.7	90.6	0.999	0.053
5	<i>p</i> -Br	4.84	10.90	32.45	74.9	62.0	94.3	0.994	0.136
6	p-NO ₂	0.61	1.16	2.75	58.6	132.8	100.2	0.995	0.099
7	p-COOH	18.64	38.56	92.07	62.3	92.0	91.1	0.997	0.076
8	m-OCH3	5.90	13.49	25.73	57.6	116.9	94.1	0.998	0.061
9	<i>m</i> -Cl	5.64	12.61	27.72	62.4	101.6	94.2	0.999	0.010
10	$m-NO_2$	0.30	0.57	1.18	53.4	155.8	102.2	0.999	0.044
11	o-OCH ₃	1.87	4.28	8.79	60.4	117.3	97.1	0.999	0.027
12	o-Cl	9.12	22.51	46.25	63.7	93.1	92.8	0.999	0.057
13	o-Br	11.69	22.88	50.70	57.0	113.4	92.5	0.997	0.074
14	o-CHO	9.49	22.64	53.53	67.7	79.8	92.6	0.999	0.020
15	o-COOH	1.83	4.09	9.29	63.6	107.1	97.1	0.999	0.027
16	o-COOCH3	1.73	3.79	7.74	58.7	123.4	97.4	0.999	0.015
17	o-NO ₂	1.42	2.34	4.92	47.6	162.2	98.4	0.991	0.108

Table IVRate Constants and Activation Parameters for the EDTA Catalyzed Reaction of α -PPA with CAB

 $[S] = 2.00 \times 10^{-2} \text{ mol } dm^{-3}; [CAB] = 1.20 \times 10^{-3} \text{ mol } dm^{-3} [H^+] = 6.00 \times 10^{-1} \text{ mol } dm^{-3} \text{ AcOH}: H_2O = 60:40 \text{ (v/v)}; [EDTA] = 1.00 \times 10^{-2} \text{ mol } dm^{-3}.$

(1)

 ${}^{a}k' = k_{obs}/[S]^{n}$ where *n* is the order with respect to substrate.

[18] that an electrophilic attack by the positive halogen of the oxidant at the neutral nitrogen of EDTA gives the intermediate C_1 . Structure of C_1 is given as, The observed 1:2 stoichiometry between the substrate and oxidant very much supports the proposed mechanism.

Rate Law

$$-\frac{d[CAB]}{dt} = \frac{k_3 K_1 K_2[S][H^+][EDTA][OX]_t}{1 + K_1[EDTA] + K_1 K_2[S][EDTA]}$$
(5)

$$k_{\rm obs} = \frac{k_3 K_1 K_2 [S] [H^+] [EDTA]}{1 + K_1 [EDTA] + K_1 K_2 [S] [EDTA]}$$
(6)

Table V The Reaction Constant Values for $\rho\sigma$, $\rho\sigma^+$, and $\rho\sigma^-$ Correlations

Correlation	$\operatorname{Temp}(C)$	ρ^+	r	\$	n
ρσ	30	1.19 ^a	0.918	0.140	
	40	1.16 ^a	0.919	0.136	8
	50	1.34 ^a	0.938	0.138	
$\rho\sigma^+$	30	0.73 ^a	0.872	0.172	
	40	0.72^{a}	0.889	0.158	8
	50	0.85^{a}	0.902	0.171	
$\rho\sigma^{-}$	30	0.98^{b}	0.984	0.075	
	40	1.02^{b}	0.972	0.096	6
	50	1.13 ^b	0.970	0.118	

 ${}^{a}m$ -NO₂ and p-NO₂ excluded in the correlation.

^bCorrelation for para-substituents only.

$$RNCl^- + -CH_2 - \ddot{N} < CH_2COOH CH_2COOH$$

$$\begin{array}{c} \text{Cl} \cdots \cdot \text{NR}^{-} \\ \vdots \\ \hline \\ \leftarrow & -\text{CH}_2 - \dot{\text{N}} - \text{CH}_2 - \text{COOH} \\ & | \\ \\ \text{CH}_2 - \text{COOH} \\ & (\text{C}_1) \end{array}$$

$$C_1 + PhOCHCOOH \stackrel{K_2}{\longleftrightarrow} C_2$$

$$| CH_3$$
(2)

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$$C_2 + H^+ \xrightarrow{k_3}_{\text{Slow}} - OH^+ + \text{other products}$$
(3)

$$\xrightarrow{fast} Cl \longrightarrow OH + RNH_2$$
(4)



Figure 4 The Hammett plot in the EDTA catalyzed reaction of phenoxypropanoic acids with CAB (numbered as in Table IV).

This equation predicts a linear relationship between $1/k_{obs}$ and 1/[S] at constant [H⁺] and [EDTA] as per Eq. (7).

$$\frac{1}{k_{\rm obs}} = \frac{1}{k_3 K_2[S][{\rm H}^+]} \left[\frac{1}{K_1[{\rm EDTA}]} + 1 \right] + \frac{1}{k_3[{\rm H}^+]}$$
(7)

Figure 2 shows that there is a linearity at high [α -PPA]. It appears that the linearity is limited to a concentration

region of the substrate. The enhanced catalytic activity is explained by envisaging a ternary complex (C₂). This complex containing EDTA, oxidant, and the substrate offers the reaction a more favorable pathway. EDTA forms an intermediate complex with CAB, which act as a more powerful electrophile than the uncomplexed CAB. This is supported by the observation that a plot of k_{obs} vs. EDTA is a straight line (Fig. 5) (r = 0.995; s = 0.504) with a positive slope and intercept. The graph of k_{obs}^{-1} vs. [α -PPA]⁻¹ (Fig. 2) shows a limiting value which further supports the formation of a



Figure 5 Plot of k_{obs} vs. [EDTA] in the EDTA catalyzed reaction of α -PPA with CAB.



Figure 6 The Hammett plot on the EDTA catalyzed reaction of phenoxypropanoic acids with CAB (numbered as in Table IV).

ternary intermediate. Enhanced reactivity in the EDTA catalyzed hydrazine-Cr(VI) reaction [19] and isopropyl alcohol oxidation by Cr(VI) in the presence of oxalic acid [20] are explained by envisaging the formation of a intermolecular complex. Highly negative activation entropy suggests that there is a highly ordered transition state.

Enhanced reactivity in the presence of Cl⁻ can be explained by the formation of molecular chlorine, an effective electrophile under the experimental conditions maintained. k_{obs} is a composite quantity. Attempts have been made to evaluate the rate coefficients of the slow step (k_3) separately using the intercept of the double reciprocal plot of $1/k_{obs}$ vs. 1/[S] at constant [H⁺] and [EDTA] (Eq. (7)). Deviation of $-NO_2$ substituents in the established Hammett line using k_3 values determined at high substrate concentrations, is again quite clear in Fig. 6 (r = 0.530; s = 0.441). The treatment by the Yukawa-Tsuno equation [21], which can give an idea regarding the extent of involvement of cross conjucation in the transition state also fails to explain the reactivity (100 $R \approx 73$, where R is the correlation coefficient).

Except –COOH substituent, in all the other cases the ratio of rate constants of ortho- and para-substituted α -PPA is >1 and <2. It suggests that in CAB oxidation of these ortho-derivatives the steric inhibition is slightly overcompensated by an effective anchimeric assistance.

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