JOURNAL OF PHYSICAL ORGANIC CHEMISTRY, VOL. 9, 105–110 (1996)

KINETICS OF OXIDATION OF PHENOXYACETIC ACIDS BY PYRIDINIUM HYDROBROMIDE PERBROMIDE

K. KARUNAKARAN
Department of Chemistry, Adhiyamaan College of Engineering, Hosur – 635 109, India

AND

K. P. ELANGO*
Department of Chemistry, Gandhigram Rural Institute, Gandhigram – 624 302, India

The oxidation of several monosubstituted phenoxyacetic acids by pyridinium hydrobromide perbromide (PHPB) was studied in aqueous acetic acid. The reaction is first order with respect to PHPB. Michaelis–Menten-type kinetics are observed with respect to phenoxyacetic acids. The oxidation of [2,2-$^2H_2$]phenoxyacetic acid exhibits a substantial kinetic isotopic effect. The effect of solvent composition indicates that the transition state is more polar than the reactants. The formation constants of the intermediate phenoxyacetic acid–PHPB complexes and the rates of their decomposition were determined at different temperatures. The rates of oxidation of *para*- and *meta*-substituted phenoxyacetic acids were correlated with Hammett's substituent constants. The ρ value is $-2{\cdot}59$ at 35 °C. The rates of oxidation of *ortho*-substituted compounds are correlated with Charton's triparametric equation. A mechanism involving transfer of a hydride ion from the substrate to the oxidant is proposed.

INTRODUCTION

Pyridinium hydrobromide perbromide (PHPB) has been extensively used in synthetic organic chemistry as a brominating agent and as an oxidant.[1,2] However, there are not many reports on the mechanistic aspects of reactions of PHPB.[3–5] The use of an insulated acid substrate (containing groups or atoms between the reaction site and the bulk of the molecule) in a similar study is rare. In continuation of our previous study of the oxidation of (arylthio)acetic acids by PHPB,[6] highlighting the polar and steric effects of *ortho* substituents on the rate of the reaction, without which the correlation analysis of the compounds studied by Lee and Chen[7] is of doubtful significance, we now report the oxidation of phenoxyacetic acids by PHPB. Mechanistic aspects are also discussed.

EXPERIMENTAL

Reagents. Phenoxyacetic acids were prepared by the methods of Koelsch.[8] PHPB was prepared by the reported method[9] and its purity was checked by an iodometric method. Acetic acid was refluxed with chromic oxide and acetic anhydride for 3 h and then fractionated. All other chemicals used were of AR grade.

Kinetic measurements. Reactions were carried out under pseudo-first-order conditions by keeping an excess (×10 or greater) of the substrate over PHPB. The solvent was 9:1 (v/v) acetic acid–water, unless stated otherwise. The reactions were followed to 70% reaction by monitoring the decrease in PHPB concentration at 358 nm. In the case of nitro-substituted compounds the reaction was followed by estimating the unchanged PHPB by standard iodometric procedures. The pseudo-first-order rate constant, k_{obs}, was calculated from the linear least-squares plot of log[PHPB] versus time. Duplicate runs showed that the rate constants were reproducible to within ±3%.

Stoichiometry. The stoichiometry of the reaction was determined by allowing the known excess of PHPB to react with phenoxyacetic acid under the reaction conditions. Iodometric estimation of unreacted PHPB after the completion of the reaction revealed that the stoichiometry was 1:1.

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* Author for correspondence.

CCC 0894-3230/96/020105-06

Received 24 July 1995
Revised 29 September 1995

Product analysis. The organic product of the reaction, phenol, was analysed as follows. Phenoxyacetic acid (0·01 mol) and PHPB (0·01 mol) were made up to 50 ml in 9:1 (v/v) acetic acid–water and kept in the dark for 15 h to ensure completion of the reaction. The solvent was removed under reduced pressure. The residue was treated with diethyl ether (50 ml × 2) and filtered. The ether filtrate was treated with dilute NaOH (50 ml × 2) and shaken well. The aqueous part was separated and treated with benzoyl chloride (1·5 ml). The benzoyl derivative was separated and dried (1·4 g, 71%) and was identified as phenyl benzoate (m.p. 70 °C).

RESULTS AND DISCUSSION

The rate data and other experimental data were obtained for all the phenoxyacetic acids. Since the results are similar, only representative data are reproduced here.

The reactions are of first order with respect to PHPB, as proved by the linearity of log[PHPB] against time plots over 70% of the reaction. Further, the values of k_{obs} are independent of the initial concentration of PHPB. The reaction rate increases with increase in the concentration of the phenoxyacetic acid but not linearly (Table 1). A plot of $1/k_{obs}$ against 1/[phenoxyacetic acid] is linear (correlation coefficient $r = 0{\cdot}999$) with an intercept on the rate ordinate. Thus, Michaelis–Menten-type kinetics are observed with respect to the phenoxyacetic acid. This leads to the postulation of the following overall mechanism [equations (1) and (2)] and rate law [equation (3)].

$$\text{phenoxyacetic acid} + \text{PHPB} \overset{K}{\rightleftharpoons} [\text{complex}] \qquad (1)$$

$$\text{complex} \xrightarrow[\text{slow}]{k_2} \text{products} \qquad (2)$$

$$\text{rate} = \frac{k_2K[\text{phenoxyacetic acid}]\,[\text{PHPB}]}{1 + K[\text{phenoxyacetic acid}]} \qquad (3)$$

Table 1. Rate constants for the oxidation of phenoxyacetic acid by PHPB in 95% (v/v) aqueous acetic acid at 308 K

10^3 [PHPB] (mol dm^{-3})	10[PAA] (mol dm^{-3})	10^4 k_{obs} (s^{-1})
1·0	0·10	5·39
1·0	0·20	8·42
1·0	0·30	10·9
1·0	0·40	12·8
1·0	0·50	14·4
1·0	0·75	16·2
1·0	1·00	17·2
1·5	0·30	11·1
2·0	0·30	10·8
3·0	0·30	11·0
4·0	0·30	10·9
1·0	0·30[a]	11·0
1·0	0·30[b]	10·9
1·0	0·30[c]	3·41

[a,b] Contained 0·02 and 0·50 mol dm^{-3} pyridinium bromide, respectively.
[c] Contained [2,2-$^2H_2$]phenoxyacetic acid.

Solvent effect

The rates of oxidation of phenoxyacetic acids were determined in solvents containing different amounts of water and acetic acid. The value of k_{obs} increases as the water content of the solvent increases.

To determine whether the changes in solvent composition affect the formation constant, K, and/or the rate of decomposition, k_2, the dependence on phenoxyacetic acid concentration was studied in solvents of different composition. The results showed that the effect of solvent is primarily on the rate constant for decomposition of the complex, k_2. The formation constant, K, is virtually independent of solvent composition (Table 2). The increase in k_2 with increase in polarity of the medium suggests that, in the rate-determining step, the transition state is more polar than the reactant. A plot of log k_2 against the inverse of relative permittivity is non-

Table 2. Dependence of k_{obs} on phenoxyacetic acid concentration in solvents of different composition[a]

	10^4 k_{obs} s^{-1}			
10[PAA] (mol dm^{-3})	90·0% (v/v) AcOH	92·5% (v/v) AcOH	95·0% (v/v) AcOH	97·5% (v/v) (v/v) AcOH
0·10	22·5	12·7	5·52	1·83
0·30	44·8	25·5	10·9	3·49
0·50	59·3	33·6	14·5	4·62
0·75	66·5	37·6	16·3	5·23
1·00	70·5	40·0	17·2	5·48
K (mol dm^{-3})	31·2	30·9	31·1	31·2
10^4 k_2 (mol^{-1} dm^{-3} s^{-1})	94·5	53·8	23·1	7·42

[a] [PHPB] = 0·001 mol dm^{-3}; $T = 308$ K; solvent = AcOH–H_2O.

linear. The solvent effect was analysed using the Grunwald–Winstein equation:[10]

$$\log k_2 = \log k_0 + mY \qquad (4)$$

where Y is an empirical parameter characteristic of the given solvent which will provide some measure of the ability of the solvent to separate ions. The plot of $\log k_2$ against Y was linear ($r = 0{\cdot}999$) with $m = 1{\cdot}20$. The positive value of m indicates a transition state which is more polar than the reactant. Thus, charge separation takes place in the transition state of the decomposition of the PHPB–substrate complex.

Kinetic isotope effect

To ascertain the importance of the rate-determining step, the oxidation of [2,2-$^2H_2$]phenoxyacetic acid was studied. The results shows a considerable primary kinetic isotope effect ($k_H/k_D = 3{\cdot}2$ at 308 K) (Table 1).

Effect of pyridinium bromide

Addition of pyridinium bromide has no effect on the rate of oxidation (Table 1). In solution, PHPB may undergo the following reactions:

$$P_yH^+Br_3^- \rightleftharpoons Br_2 + P_yH^+Br^- \qquad (5)$$

$$P_yH^+Br_3^- \rightleftharpoons Br_3^- + P_yH^+ \qquad (6)$$

The possible oxidizing species in a solution of PHPB are therefore PHPB itself, tribromide ion and molecular bromine. However, a strict first-order dependence on PHPB and the absence of any effect of pyridinium bromide rule out both bromine and tribromide ion as the reactive oxidizing species in this reaction.

Correlation analysis and reactivity

The dependence of k_{obs} on the phenoxyacetic acid concentration was studied at different temperatures and the values of K and k_2 were evaluated from the double reciprocal plots. The thermodynamic parameters of the complex formation and activation parameters of the decomposition of the complexes were calculated from the values of K and k_2, respectively, at different temperatures (Tables 3 and 4).

The data in Table 3 revealed that the formation constants of the substrate–PHPB complexes are not very sensitive to the nature of the substituent in the phenoxyacetic acid molecule. Similar observations have been recorded previously in the oxidation of benzyl alcohols[11] and mandelic acids[12] by ammonium cerium(IV) nitrate and of aliphatic alcohols by PHPB[5] and pyridinium fluorochromate.[13] The rates of decomposition of the complexes (Table 4), however, showed considerable variation.

Examination of the rates of decomposition of the complexes reveals that the electron-releasing substituents increase the rate of the reaction whereas electron-

Table 3. Formation constants and thermodynamic parameters for oxidation of phenyoxyacetic acids by PHPB[a]

	K (dm^3 mol^{-1})					
Substituent	293 K	303 K	308 K	318 K	$-\Delta H$ (kJ mol^{-1})	$-\Delta S$ (J K^{-1} mol^{-1})
H	46·5	36·3	31·2	23·7	23·5	293·0
p-OMe	46·2	34·8	30·1	21·6	25·9	301·4
p-C(Me)$_3$	44·9	35·2	30·2	21·5	25·6	300·3
p-Me	46·6	36·0	30·8	23·2	24·2	295·4
p-Et	47·6	36·2	31·2	24·0	23·4	292·6
p-Cl	48·2	37·1	32·1	24·8	23·1	291·6
p-Br	47·6	37·2	31·8	23·6	24·2	295·3
p-I	45·7	35·6	30·3	22·2	24·9	298·1
p-NO$_2$	49·0	39·3	34·2	25·7	22·5	289·1
m-OMe	44·8	35·7	29·7	21·2	25·7	300·8
m-Me	45·3	35·7	30·9	22·9	23·6	293·7
m-Et	45·0	35·2	30·9	22·8	23·5	293·2
m-Cl	47·2	36·8	31·5	24·0	23·4	292·8
m-Br	47·4	36·7	31·5	23·9	23·8	294·0
m-NO$_2$	49·2	39·0	34·6	25·8	22·4	289·0
o-OMe	43·3	34·2	29·0	20·6	25·5	300·5
o-Me	44·7	34·8	30·2	21·7	24·9	298·0
o-Et	44·6	35·0	30·4	21·6	25·2	298·7
o-Cl	46·8	36·5	31·1	23·8	23·4	292·8
o-Br	47·0	37·2	32·4	24·5	22·7	290·4
o-NO$_2$	48·8	39·4	34·0	26·0	22·0	287·7

[a] [PHPB] = 0·001 mol dm^{-3}; solvent = 97·5% (v/v) aqueous AcOH.

Table 4. Second-order rate constants for the oxidation of phenoxyacetic acids by PHPB[a]

Substituent	$10^4 k_2$ (s^{-1}) 293 K	303 K	308 K	318 K	$+\Delta H^*$ (kJ mol^{-1})	$-\Delta S^*$ (J K^{-1} mol^{-1})
H	2·7	5·5	7·3	14·6	48·9	145·9
p-OMe	32·0	51·0	61·2	97·6	31·7	184·3
*p*C(Me)$_3$	27·6	47·3	58·6	93·8	35·2	173·6
p-Me	18·9	33·6	41·7	72·2	39·6	161·8
p-Et	17·3	31·2	39·0	70·3	40·4	159·8
p-Cl	0·8	1·7	2·4	5·4	53·5	137·5
p-Br	0·7	1·6	2·2	5·0	55·9	132·9
p-I	0·6	1·4	2·0	4·4	55·7	134·6
p-NO$_2$	0·0	0·0	0·1	0·3	72·6	102·7
m-OMe	2·3	4·8	6·4	12·8	49·5	145·3
m-Me	6·6	12·6	16·3	31·1	45·0	151·9
m-Et	7·0	13·3	17·2	32·8	43·9	152·5
m-Cl	0·3	0·8	1·1	2·7	60·8	122·5
m-Br	0·3	0·7	1·0	2·5	61·1	122·3
m-NO$_2$	0·0	0·1	0·2	0·5	68·0	112·7
o-OMe	29·5	48·0	58·4	92·9	32·7	181·5
o-Me	15·8	29·5	37·4	67·0	38·9	166·2
o-Et	15·4	29·4	37·5	66·9	39·4	162·5
o-Cl	0·7	1·6	2·3	5·3	56·7	129·9
o-Br	0·7	1·5	2·4	5·2	57·2	128·5
o-NO$_2$	0·0	0·0	0·1	0·3	74·8	95·4

[a] [PHPB] = 0·001 -91-mol dm^{-3}; solvent = 97·5% (v/v) aqueous AcOH.

withdrawing substituents decrease it. A linear correlation (r = 0·998) was observed between log k_2 values at 20 and 45 °C for the oxidation of 21 phenoxyacetic acids. This suggests that all the phenoxyacetic acids are oxidized by same mechanism.[14] The value of the isokinetic temperature is 513 K.

Correlation analysis were carried out on *para-* and *meta*-substituted phenoxyacetic acids. They correlate well with the Hammett substituent constants, yielding negative reaction constants (Table 5). A negative reaction constant indicates an electron-deficient centre in the transition state of the rate-determining step, similar to the oxidation of these acids with potassium permanganate,[15] ammonium cerium(IV) nitrate,[16] chromic acid[7] and phenyliodoso acetate,[6] which gave ρ values of −3·05, −1·62, −1·34 and −2·26, respectively.

Table 5. Temperature dependence of the reaction constants[a]

Temperature (K)	ρ	r	SD
293	−2·91	0·992	0·120
303	−2·70	0·992	0·113
308	−2·59	0·992	0·109
318	−2·40	0·993	0·096

[a] No. of data points = 15, including unsubstituted compound.

The rate constants of the oxidation of *ortho*-substituted phenoxyacetic acids failed to yield any significant correlation with Taft's polar and steric substituent constants.[17] The rates were therefore analysed by Charton's[18] equations (7) and (8):

$$\log k = a\sigma_I + \beta\sigma_R + h \qquad (7)$$

$$\log k = a\sigma_I + \beta\sigma_R + \phi V + h \qquad (8)$$

where σ_I, σ_R and V represent field, resonance and steric substituent constants, respectively; the values used were those compiled by Aslam *et al.*[19] In multiple linear regression using both equations, the coefficient of multiple correlation (R) is excellent and the standard deviation (SD) is low (Table 6).

We also used Exner's statistical parameter[20] and the parameter f as measures of the goodness of fit.[21]

The reaction constants and the statistical data for the *ortho*-substituted phenoxyacetic acids are given in Table 6. The contribution of the resonance effect to the polar effects, P_R, and that of the steric effect to the total effect of the *ortho* groups, P_S, were calculated by Charton's method.[18] The results indicate that as in the case of phenoxyacetic acids, in the oxidation of *ortho*-substituted compounds the field and resonance effects are predominant. Steric effects play a minor role.

Table 6. Reaction constants for the oxidation of *ortho*-substituted phenoxyacetic acid at 308 K[a]

Equation	α	β	ϕ	R	SD	ψ	f	P_S	P_R
(7)	−2·48	−2·27	—	0·995	0·042	0·011	0·04	—	47·8
(8)	−2·35	−2·28	0·28	0·996	0·031	0·008	0·02	5·7	46·4

[a] No. of data points = 7, including unsubstituted compound; $\psi = [n(1-R)^2/(n-m)]^{1/2}$; f = SD/root mean square.

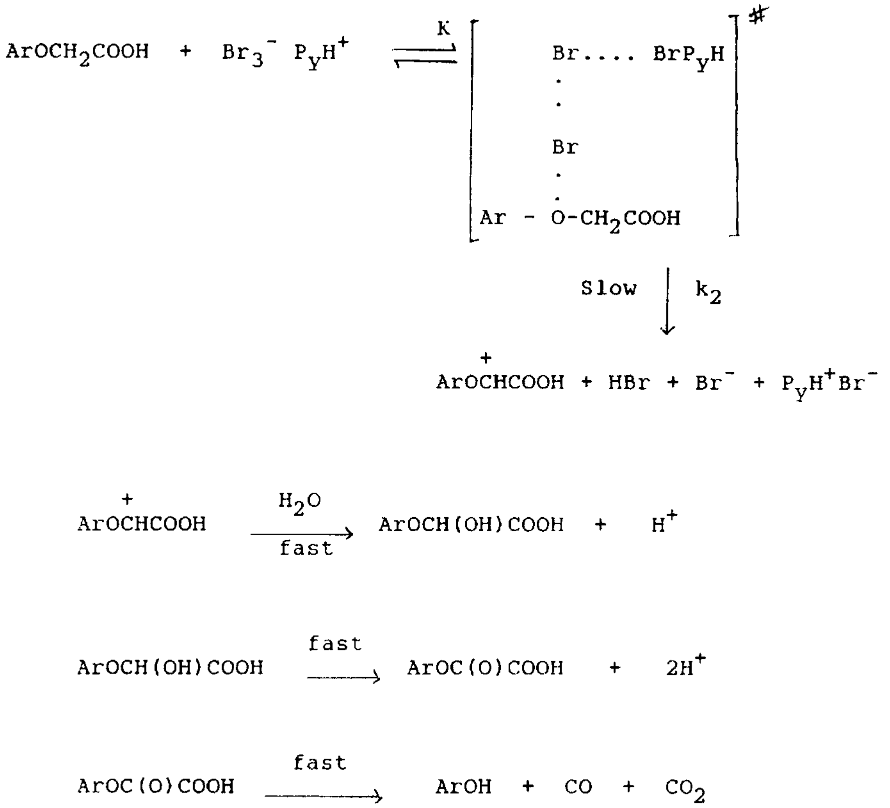
MECHANISM

On the basis of the foregoing kinetic picture, transfer of a hydride ion from the substrate to the oxidant may be proposed for the oxidation of phenoxyacetic acid by PHPB. From the rate law [equation 3], it is apparent that an intermediate complex is formed in a rapid pre-equilibrium step. With the present data, it is not possible to state definitely the nature of the intermediate complex.

Formation of a hypobromite ester [equation (9)] as an intermediate is unlikely in view of the absence of any effect of pyridinium bromide.

$$ArOCH_2COOH + P_yH^+Br_3^- \rightarrow ArOBr + BrCH_2COOH + P_yH^+Br^- \quad (9)$$

Similar intermediate complexes have been postulated in the reaction of alkenes[2] and alcohols[5] with PHPB. The formation of a moderately stable intermediate is supported by the observed values of the thermodynamic parameters (Table 4). The complex formation is favoured by the enthalpy term but there is a loss of entropy, indicating the formation of a rigid structure.



$$ArOCH_2COOH + Br_3^- \; P_yH^+ \overset{K}{\rightleftharpoons} \left[\begin{array}{l} Br....\;BrP_yH \\ \vdots \\ Br \\ \vdots \\ Ar - O\text{-}CH_2COOH \end{array}\right]^{\#} \xrightarrow[k_2]{Slow} Ar\overset{+}{O}CHCOOH + HBr + Br^- + P_yH^+Br^-$$

$$Ar\overset{+}{O}CHCOOH \xrightarrow[fast]{H_2O} ArOCH(OH)COOH + H^+$$

$$ArOCH(OH)COOH \xrightarrow{fast} ArOC(O)COOH + 2H^+$$

$$ArOC(O)COOH \xrightarrow{fast} ArOH + CO + CO_2$$

Scheme 1

The correlation analysis of the substituent effect indicated the presence of highly electron-deficient carbon centre in the transition state. Therefore, a hydride ion transfer in the rate-determining step is postulated, which was confirmed by the observed kinetic isotopic effect. A moderate degree of charge separation in the transition state of the rate-determining step is supported by the observed value of *m*. The observed negative entropy of activation also supports a polar transition state. As the charge separation takes place, the two charged ends become highly solvated. This results in immobilization of a large number of solvent molecules, reflected in the loss of entropy.

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