Kinetics and Mechanism of Chromic Acid Oxidation of Chalcones (Phenyl Styryl Ketones)

By **N. C. Khandual** and **K. K. Satpathy,** Department of Chemistry, G. M. College, Sambalpur, India
P. L. Nayak,* Department of Chemistry, Ravenshaw College, Cuttack 3, Orissa, India

The kinetics of the oxidation by chromic acid of chalcone (phenyl styryl ketone) and several substituted chalcones have been investigated in 95% (v/v) acetic acid. The reaction is overall of the second order, first order in each reactant. The parameters of Arrhenius and transition state theories have been computed. The enthalpies of activation are in the range 12·3—19·4 kcal mol^{-1} and the entropies of activation range from −5 to −22 cal mol^{-1} K^{-1}. The effect of substituents on the rate of oxidation has been evaluated. A Hammett-type correlation with Brown's σ^+ values has been established with ρ^+ −1·2. The data are consistent with a mechanism which involves electrophilic attack of chromic acid at the carbon–carbon double bond resulting in the formation of an epoxide.

CHROMIC ACID is one of the most versatile of oxidising agents.[1] Although numerous studies have been devoted to the oxidation of alkenes by chromic acid and chromyl chloride,[2-9] no kinetic study of the chromic acid oxidation of αβ-unsaturated ketones has appeared.

This investigation was undertaken to gain a clearer understanding of the mechanism of the chromic acid oxidation of chalcone (phenyl styryl ketone) and some of its derivatives. An epoxide was isolated as the product of oxidation. Awasthy and Rocek [6] have presented kinetic evidence suggesting epoxide formation as the rate-limiting step in the chromic acid oxidation of olefins in aqueous acetic acid. Rocek and Drozd [10] have recently reported the first successful trapping and isolation of an epoxide formed in a chromic acid oxidation of a simple olefin. Epoxides have previously been isolated in the chromyl acetate oxidation of some olefins by Hickinbottom and his co-workers.[11-14]

EXPERIMENTAL

Materials.—Pure acetic acid, free from oxidisable impurities was obtained by warming acetic acid (AnalaR; 2 l) with chromium chloride (AnalaR; 40 g) and acetic anhydride (AnalaR; 160 ml) slowly to just below the reflux temperature for 0·5 h; the mixture was then heated under reflux for 0·5 h and then distilled through a fractionating column containing glass helices, b.p. 118°. Perchloric acid (AnalaR) and sodium perchlorate (AnalaR; BDH) were used. Chalcones were prepared and purified by our previous method.[15]

Rate Measurements.—Rate measurements were carried out at constant temperature (±0·1°) in 95% aqueous acetic acid (v/v) containing 0·025M-perchloric acid. The ionic strength was kept constant by the use of sodium perchlorate (1M). The concentrations of chalcone and chromic acid were generally $1{\cdot}5 \times 10^{-2}$ and $3{\cdot}0 \times 10^{-2}$M respectively. The reactions were followed by withdrawing aliquot portions of the reaction mixture at known intervals and quenching the reaction by adding a slight excess of ferrous ammonium sulphate and titrating the residual Fe^{II} against standard potassium dichromate using barium diphenylamine sulphonate as indicator.[16]

The second-order rate constants were computed by least-squares using Tobey's method.[17] The standard deviation of the individual plot was usually within 1% and agreement between duplicates was within 1—2%. Activation parameters were calculated in the usual way from the Arrhenius plots.[18] The estimated precision is *ca.* ±0·5 kcal mol^{-1} in $\Delta H^\ddagger$ and *ca.* ±0·8 cal mol^{-1} K^{-1} in $\Delta S^\ddagger$.

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*Product.**—Chalcone (1 mol. equiv.) reacted overnight with chromic acid (1 mol. equiv.) under the conditions of rate measurement. The mixture was neutralised with sodium hydrogen carbonate solution and extracted with ether. The ether was evaporated and the residue (75%), m.p. 87°, crystallised several times from aqueous ethanol and identified as chalcone epoxide [19] (mixed m.p.) (Found C, 80·3; H, 5·30. Calc. for $C_{15}H_{12}O_2$: C, 80·35; H, 3·35%).

TABLE 1

Dependence of rate on the concentration of chromic acid and chalcone. Solvent: 95% acetic acid (v/v); $[H^+] = 0{\cdot}025\,\mathrm{M}$; temp. 30°

$10^2[CrO_3]/\mathrm{M}$	3·5	3·0	2·8	2·5	2·0	1·5
10^2[Chalcone]/M	1·75	1·5	1·4	1·25	1·0	0·75
10^3k/l mol^{-1} s^{-1}	6·13	6·14	6·15	6·13	6·14	6·14

TABLE 2

Values of specific reaction rate, energy of activation, and entropy of activation for the Cr^{VI} oxidation of chalcones

	10^3k/l mol^{-1} s^{-1}						
Substituent[a]	25°	30°	35°	40°	E_a/kcal mol^{-1}	$-\Delta S^{\ddagger}$/cal mol^{-1} K^{-1}	$\Delta H^{\ddagger}$/kcal mol^{-1}
4-OMe	61·0	122·8	168·8		12·90	22·0	12·30
2-OMe	53·73	80·6	124·9		14·30	17·20	13·70
4-Cl	23·03	42·9	73·0		15·30	15·90	14·7
3-Cl	11·3	21·3	37·3		16·40	13·7	15·8
2-Cl		9·21	13·80	21·50	17·70	10·7	17·0
H		6·14	18·28	30·36	18·40	7·30	17·8
$3-NO_2$		4·6	7·68	12·30	19·70	6·40	19·1
$4-NO_2$		3·83	6·52	9·96	20·0	5·60	19·4

[a] Substituents on phenyl ring.

TABLE 3

Effect of added acid on rate. [Chalcone] = 0·01M; $[CrO_3]$ = 0·02M; temp. 30°

$[H^+]$/M	0·025	0·035	0·04	0·045	0·06
10^3k/l mol^{-1} s^{-1}	6·14	8·44	11·52	17·66	29·10

RESULTS

Kinetic Data.—The kinetic data are summarised in Table 1. The reaction obeys the second-order rate law, being first order in the organic substrate and in the oxidant.

Isokinetic Relationship.—A linear relationship between the entropy of activation ($\Delta S^{\ddagger}$) and the enthalpy of activation ($\Delta H^{\ddagger}$) has been observed for the oxidation.[20] The data can be fitted in the equation $\Delta H^{\ddagger} = \Delta H_0^{\ddagger} + \beta\Delta S^{\ddagger}$. $\Delta H^{\ddagger}_0$ Has the value 22·80 kcal mol^{-1} and β, the isokinetic temperature, is 540 K for the reaction. The linear relationship shown by the majority of the substituted chalcones indicates that the same mechanism prevails in all cases.[21]

Acidity.—A plot of log k *versus* the acidity function, H_0, is linear showing the applicability of the Zucker–Hammett treatment.[22]

Linear Free Energy Relationships.—Correlation of the rate constants with σ^+ [23] gave a ρ^+ −1·2. The correlation coefficient (r) was 0·986 and the standard deviation (s) from the regression line was 0·0476. A similar correlation between log k and σ^+ has been noted for bromination,[24] methoxymercuriation,[15] Tl^{III} oxidation,[25] and epoxidation [19] of chalcones. The values of reaction constants are in Table 5.

Freeman and Yamachika [9] have computed the reaction constant (ρ^+ −1·99) for the chromyl chloride oxidation of styrenes. Ouellette *et al.*[26] have computed the reaction constant (ρ^+ −2·2) for Tl^{III} oxidation of styrenes. A ρ^+ value of −1·3 has been computed for the epoxidation of styrenes.[27] These values of reaction constants are similar to ours computed for the oxidation of chalcones by various reagents.

TABLE 4

Relative rates of reactions of chalcone at 30°

	Methoxymercuriation	Tl^{III} oxidation	Epoxidation	Cr^{VI} oxidation	Bromination
k/l mol^{-1} s^{-1}	$1{\cdot}25 \times 10^3$	$1{\cdot}72 \times 10^{-3}$	$3{\cdot}60 \times 10^3$	$6{\cdot}4 \times 10^{-3}$	$3{\cdot}57 \times 10^{-3}$

Effect of Substituents.—It is clear from the data in Table 2 that the reaction is enhanced by electron-releasing substituents on the phenyl nucleus directly attached to the olefin and retarded by electron-attracting groups. The observed rates conform to the following order of reactivity: 4-OMe > 3-OMe > 2-OMe > 4-Cl > 3-Cl > 2-Cl > H > $3-NO_2$ > $4-NO_2$.

DISCUSSION

Our kinetic data reveal that the oxidation of chalcone by Cr^{VI} is first order both in olefin and metal, acid catalysed, and solvent dependent. Although more studies on solvent effects are required, the preliminary

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[*] Since chalcone epoxides are very stable, most probably they do not undergo solvolysis under the reaction conditions. An investigation of the minor products by g.l.c. is in hand.

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TABLE 5

Hammett reaction constants for some reactions of chalcones

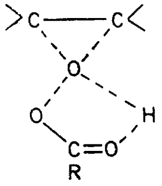
Reaction	ρ^+	Reference
Methoxymercuriation	$-1{\cdot}50$	15
Thallium(III) oxidation	$-1{\cdot}35$	25
Perbenzoic acid oxidation	$-1{\cdot}1$	19
Bromination	$-1{\cdot}0$	24
Chromic acid oxidation	$-1{\cdot}2$	Present work

results show that the rate of oxidation increases with an increase of solvent polarity. The ρ^+ value is negative indicating that electron-releasing groups enhance the reaction rate and electron-withdrawing groups retard it.

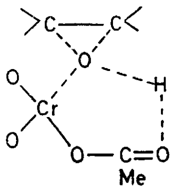
Scrutiny of our results indicates that the behaviour of chalcones closely parallels that of other olefins upon treatment with chromyl chloride [9] and can be similarly interpreted. The rate-limiting step in the chromic acid oxidation of an olefin is a symmetric electrophilic attack of chromium(VI) on the double bond leading to an epoxide. Although there are various possibilities, it seems attractive to regard the reaction as similar to the epoxidation of olefins by peracids for which the transition state (I) has been suggested.[19,28]

In acetic acid solution, chromic acid is known to exist predominantly in the form of its monoacetate [29] and the reaction may proceed through the transition state (II).

The close mechanistic parallel between the chromic acid oxidation and bromine addition,[24] methoxymercuriation,[15] Tl^{III} oxidation,[25] and perbenzoic acid [19] oxidation of chalcones is shown by the relative rates in Table 4 and the ρ^+ values in Table 5. The effect of substituents in all these reactions is similar, *i.e.* electron-releasing groups enhance and electron-withdrawing groups retard the rate. The present data and comparison with the relative rates are compatible with a three-membered ring activated complex. A similar complex has been suggested by Freeman and Yamachika [9] for the chromyl chloride oxidation of olefins by comparing the rate with those for epoxidation, bromine addition, dibromocarbene addition, picryl azide addition, and benzonitrile oxide addition to styrene and some other olefins. Such a complex can support an increasing positive charge as electron accession to the reaction centre increases due to the presence of electron-donating groups in the phenyl nucleus of the chalcone molecule.



(I)



(II)

This picture of the transition state is further confirmed by the negative *para*-resonance interaction energy value[30] ($\Delta\Delta F_p$) for the methyl group ($-$**247** cal mol^{-1}) which means that it stabilises the transition state by electron donation.

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