Kinetic evidence for steric enhancement of resonance: Oxidation of phenylmethylcarbinols with Cr(VI) and reduction of substituted acetophenones with sodium borohydride

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Abstract. The rates of oxidation of 3-substituted-4-methoxyphenylmethylcarbinols with Cr(VI) have been measured. The results show that the mesomeric effect of the methoxy group in 3-substituted-4-methoxyphenylmethylcarbinols is greater than that in 4-methoxyphenylmethylcarbinol even after taking the polar effect of the 3-substituent into consideration, indicating that the adjacent 3-substituent sterically enhances the resonance of the 4-methoxy group. The expected steric inhibition of resonance is observed in 3,5-disubstituted-4-methoxyphenylmethylcarbinols. The rates of reduction of some substituted acetophenones with sodium borohybride furnish additional evidence for steric enhancement of resonance.

Keywords. Steric enhancement of resonance; steric inhibition of resonance; Cr(VI) oxidation of 4-methoxyphenylmethycarbinols; reduction of substituted acetophenones with $NaBH_4$.

1. Introduction

The discovery of steric enhancement of resonance (Baliah and Uma 1960) led to further studies (Baliah and Kanagasabapathy 1978; Baliah *et al* 1988; Baliah and Diana Jeyanthy 1988) to obtain additional evidence for this phenomenon. The present investigation, which deals with the kinetics of oxidation of substituted phenylmethylcarbinols by Cr(VI) and the kinetics of reduction of substituted acetophenones with sodium borohydride, provides further data in support of steric enhancement of resonance.

2. Experimental

2.1 *Materials*

The substituted acetophenones were prepared by standard methods. The phenylmethylcarbinols were prepared by the reduction of the corresponding acetophenones with lithium aluminium hydride. The purity of the compounds was checked by g.l.c.

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2.2 *Solvents*

Acetic acid (Wiberg and Mill 1958) and propan-2-ol (Bowden and Hardy 1966) were purified by known procedures.

2.3 *Rate measurements*

The kinetics of oxidation of phenylmethylcarbinols with Cr(VI) in 75% (v/v) acetic acid–water was studied by the titrimetric method of Wiberg and Mill (1958). The kinetic procedure for the reduction of substituted acetophenones with sodium borohydride in propan-2-ol was essentially that of Wheeler and Mateos (1958). The thermostat was accurate to $\pm 0.05°C$.

3. Results and discussion

The chromic acid oxidation of alcohols has been shown (Wiberg 1965) to proceed through two consecutive steps: (1) a rapid reversible formation of the chromate ester of the alcohol, and (2) a rate-determining cyclic decomposition of the ester. In the transition state for the cyclic decomposition of the chromate ester, the reaction centre has been shown to possess sufficient carbonyl character (Stewart and Lee 1964). An electron-releasing substituent stabilizes the developing carbonyl group thereby increasing the rate of the reaction (Kwart and Francis 1955). The rate constants for the oxidation of substituted phenylmethylcarbinols are given in table 1. The rate constants calculated on the basis of additivity of group effects (Crocker and Jones 1959) are also given in table 1. Electron-releasing groups like methyl and methoxyl accelerate the rate of oxidation whereas electron-withdrawing substituents like chloro and bromo retard the reaction. For the 3-substituted-4-methoxyphenylmethylcarbinols the observed rate constants are significantly higher than the calculated values, indicating that the

Table 1. Second-order rate constants for the Cr(VI) oxidation of substituted phenylmethylcarbinols in 75% (v/v) in acetic acid–water at 31°C.

Substituent(s)	$10^3 k_2 (dm^3 eq^{-1} s^{-1})$	
	Obs.	Calc.
H	2·97	
4-OCH$_3$	5·38	
3-CH$_3$	3·33	
3-Cl	2·80	
3-Br	2·78	
3-I	2·90	
3-CH$_3$, 4-OCH$_3$	6·90	6·03
3-Cl, 4-OCH$_3$	6·51	5·07
3-Br, 4-OCH$_3$	7·13	5·04
3-I, 4-OCH$_3$	8·32	5·25
3-CH$_3$, 4-OCH$_3$, 5-CH$_3$	4·40	6·76
3-Cl, 4-OCH$_3$, 5-Cl	3·66	4·78
3-Br, 4-OCH$_3$, 5-Br	3·63	4·72

3-substituent in 3-substituted-4-methoxyphenylmethycarbinols exerts an accelerating influence on the rate. The 3-substituent, which is ortho to the methoxy group, sterically enhances the resonance interaction of the methoxy group with the aromatic ring, resulting in greater electron-release to the carbinol carbon. It is interesting to note that the steric enhancement of resonance increases with the bulk of the substituent indicating the importance of the steric effect. In the case of halogeno substituents it may be seen to increase in the order $Cl < Br < I$. In 3,5-disubstituted-4-methoxyphenylmethylcarbinols the expected steric inhibition of resonance of the methoxy group is evident from the fact that the observed oxidation rates are lower than the calculated values.

The rates of oxidation of substituted phenylmethylcarbinols were correlated with the dissociation constants of the cyanohydrins of the corresponding acetophenones (Sundari 1977) by plotting log (k/k_0) of the alcohols against log (K/K_0) of the cyanohydrins where k and k_0 are the rate constants of oxidation of the substituted phenylmethylcarbinol and phenylmethylcarbinol, and K and K_0 are the dissociation constants of the cyanohydrins of substituted acetophenone and acetophenone, respectively. The substituents which are used for the plot are (i) 4-OCH_3, (ii) 3-CH_3 (iii) 3-CH_3, 4-OCH_3 and (iv) 3-CH_3, 4-OCH_3, 5-CH_3. The plot obtained by the least squares method was found to be linear with a correlation coefficient of 0·98. The slope of the plot, which is less than 1·0, indicates that the chromic acid oxidation of alcohols is less susceptible to electronic factors than the dissociation of cyanohydrins, and also suggests that the carbonyl character is less fully developed in the transition state for the Cr(VI) oxidation of secondary alcohols than in that for the dissociation of cyanohydrins of the corresponding ketones.

The reaction of a carbonyl compound with sodium borohydride is considered to proceed with a rate-determining transfer of the first hydrogen atom of the borohydride ion to the carbonyl carbon. Hammett treatment of the data (Bowdern and Hardy 1966) using σ_m constants yields a ρ value of $+3·06$, indicating that the borohydride ion is a moderately strong nucleophile and that a fairly polar complex, involving the formation of a C–H bond with some likely loss of conjugation, may be obtained. With aromatic ketones possessing similar steric environments for the carbonyl groups, the rate of attack by the hydride ion is dependent on the electrophilicity of the carbonyl carbon. In the initial state, resonance interaction between the phenyl and carbonyl groups should favour coplanarity of the carbonyl group with the benzene ring. On the other hand, in the transition state, the partial transfer of a hydride ion from the borohydride ion to the carbonyl carbon should reduce the possibilities for such resonance interaction and greatly modify the geometry of the organic moiety. Thus substituents which increase the electron density at the carbonyl carbon stabilize the ketone in the ground state and reduce the sensitivity of the carbonyl group to attack by the nucleophile.

The rate of constants for the reduction of substituted acetophenones are given in table 2. 4-Methoxyacetophenone undergoes reduction about ten times slower than acetophenone. This rate decrease is due to the resonance interaction of the carbonyl group with the para methoxy substituent. 3-Methylacetophenone undergoes reduction about two and a half times slower than acetophenone. The rate constant for the reduction of 4-methoxy-3-methylacetophenone is remarkably low compared with that of acetophenone. Considering the influence of the methoxy and methyl substituents, the rate was expected to be retarded about twenty-five times but it is actually about forty-five times slower. This large decrease in the rate indicates that the ability of the

Table 2. Second-order rate constants for the reduction of substituted acetophenones with sodium borohydride in propan-2-ol at 31°C.

Substituent(s)	$10^4 k_2 \,(\mathrm{dm^3\,mol^{-1}\,s^{-1}})$
H	23·40
4-OCH$_3$	2·43
3-CH$_3$	8·70
3-CH$_3$, 4-OCH$_3$	0·52
3-CH$_3$, 4-OCH$_3$, 5-CH$_3$	5·18

4-methoxy group to interact conjugatively with the carbonyl group is significantly higher in 4-methoxy-3-methylacetophenone than in 4-methoxyacetophenone. This may be explained as follow. The 3-methyl group makes the adjacent O-Me adopt a preferred orientation *trans* to it. Consequently the probability of the methoxy group becoming coplanar with the benzene ring increases, and its resonance interaction with the carbonyl group through the benzene ring also increases. In this connection it is of interest to note that while 4-methoxy-3-methylacetophenone reacts at a slower rate than 4-methoxyacetophenone, 3,5-dimethyl-4-methoxyacetophenone reacts at a higher rate indicating steric inhibition of resonance in the latter.

The rate constants for the reduction of 3-halogeno and 3,5-dihalogeno 4-methoxyacetophenones could not be determined by the present method due to the reactions being very fast.

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