656. *The Acid-catalysed Bromination of Substituted Benzyl Phenyl Ketones.*

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Rate data, obtained at 25° and 55°, are reported for the perchloric acid-catalysed bromination, in 87% acetic acid, of a series of substituted-benzyl phenyl ketones. In the case of *p*-nitrobenzyl phenyl ketone there is evidence of resonance stabilisation of the enolisation transition state, which involves the nitro-group and the developing enol double bond.

Hughes *et al.*[1] suggested that, by analogy with eliminations, prototropic reactions may be influenced by both inductive and conjugative interactions of suitably sited substituents. In acid-catalysed enolisation, the transition state carries a positive charge and it is well established that the reaction is aided by electron-donation to the reaction site. Thus the Hammett ρ value for acid-catalysed bromination of *meta*- and *para*-substituted acetophenones [2] is negative,[3] reflecting the inductive influence of the substituted phenyl groups on the reaction. Similarly, bromoacetone is brominated, under acid conditions, more slowly than acetone,[4] a result which may be ascribed to the unfavourable

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[1] Hughes, *Nature*, 1941, **147**, 813.

[2] Nathan and Watson, *J.*, 1933, 217; Evans, Morgan, and Watson, *J.*, 1935, 1167.

[3] Jaffé, *Chem. Rev.*, 1953, **53**, 191.

[4] Hughes, Watson, and Yates, *J.*, 1931, 3318.

—*I* effect of the bromine atom. Information on the influence of substituents conjugated with the developing enol double bond is less plentiful and more ambiguous. From quantitative analyses of the proportions in which α- and α'-substitution occurs in preparative bromination of alkyl ketones, Cardwell and Kilner [5] concluded that enolisation gave the most hyperconjugatively stabilised enol, but some of their results are in conflict with earlier kinetic evidence [6] which leads to the opposite conclusion.

A reaction of particular interest, in this connection, would be the enolisation of substituted benzyl phenyl ketones, because resonance interaction between *para*-substituents and the developing enol double bond should be indicated by an exalted σ-value and by the magnitude of the *para*-resonance interaction energy.[7] We therefore measured the rates of perchloric acid-catalysed bromination, in 87% (by weight) acetic acid, of this series of ketones.

EXPERIMENTAL

Substituted Benzyl Phenyl Ketones.—These were prepared by Friedel–Crafts reaction of the appropriately substituted phenylacetyl chloride with benzene and aluminium chloride.[8] The following phenyl ketones were prepared: 3-chlorobenzyl, m. p. 43°; 4-chlorobenzyl, m. p. 136·5°; 3-fluorobenzyl, m. p. 47°; 4-fluorobenzyl, m. p. 111°; 3-methylbenzyl, b. p. 126°/0·5 mm., n_D^{25} 1·5865; 4-methylbenzyl, m. p. 95·5°; 3-nitrobenzyl, m. p. 82°; 4-nitrobenzyl, m. p. 144°; benzyl, m. p. 56°.

Acetic Acid.—The commercial acid was heated under reflux with chromium trioxide (20 g. $l.^{-1}$). After distillation and a further refluxing with more chromium trioxide (2·5 g. $l.^{-1}$), the acid was fractionated; it had b. p. 117—118°/760 mm., m. p. 16·55°.

Perchloric Acid Solutions.—60% " AnalaR " perchloric acid was diluted to 46% and then standardised. To a weighed amount of the solution a quantity of sodium hydroxide pellets, slightly less than the equivalent amount, was added and the solution restandardised. A solution 0·838m in sodium perchlorate and 0·050m in perchloric acid in 87·0% (w/w) acetic acid was then prepared, as was a solution 0·889m in perchloric acid in 87% (w/w) acetic acid. Solutions of constant ionic strength but of variable acid concentration were obtained by mixing the two standard solutions.

Rate Measurements.—Reactions were followed both at 25° and at 55°. The reaction was initiated by adding 2 ml. of a 0·1M-solution of bromine to a 0·01—0·05M-solution (20 ml.) of the ketone, both in perchloric acid–perchlorate–acetic acid. At measured times, aliquot parts (2 ml.) of the mixture were quenched in an ice-cold solution (2 ml.) of potassium iodide (M/25) and sodium hydroxide (M), and the liberated iodine was titrated (starch indicator) with thiosulphate (N/125). Chloroform (0·25 ml.) was added to dissolve the precipitated ketone which otherwise obscured the end-point. Rates were evaluated graphically by using either the integrated second-order rate equation

$$k = [2{\cdot}3/(a + b)t]\,[\log (b + x) - \log (a - x)] + \text{Constant},$$

or, more commonly, the pseudo first-order equation

$$k = [2{\cdot}3/(b + d)t] \log (a - x) + \text{Constant},$$

where a is the initial concentration of ketone, b that of perchloric acid, x the decrease in concentration of bromine after time t, and $d = x_{\text{final}}/2$. For all ketones, with the exception of 3-methylbenzyl phenyl ketone, kinetic runs followed to 80% ketone consumption and to complete bromine consumption gave excellent linear plots. There was therefore no rate dependence on bromine concentration, *i.e.*, the measured rates are indeed rates of enolisation. Further, when some runs on benzyl phenol ketone were carried past 100% monobromination, the rate of bromination of the α-bromo-ketone was found to be less than 1% of that of the unbrominated ketone. Thus dibromination is negligible. For 3-methylbenzyl phenyl ketone, runs carried out in 87%

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[5] Cardwell and Kilner, *J.*, 1951, 2430.

[6] Bartlett and Stauffer, *J. Amer. Chem. Soc.*, 1935, **57**, 2580.

[7] van Bekkum, Verkade, and Wepster, *Rec. Trav. chim.*, 1959, **78**, 815.

[8] Fischer, Grigor, Packer, and Vaughan, *J. Amer. Chem. Soc.*, 1961, **83**, 4208.

acetic acid without added catalyst showed an appreciable blank of *ca.* 7% of the rate in 0·91M-perchloric acid. Linear rate plots were obtained with this ketone when the catalyst concentration was 0·91M. As the catalyst concentration was reduced, the plots became progressively more curved and the mean slope indicated an increasingly higher rate than expected. We attribute these kinetic complications to concurrent nuclear substitution for this, the most activated of the ketones. In general, runs with all ketones were followed to 40% ketone consumption at 25°, and to 70% consumption at 55°. Individual rate constants are estimated to be accurate to ±4%, and mean rate constants (3 runs) are listed in Table 1.

TABLE 1.

Bromination of benzyl phenyl ketones in 87% acetic acid: $10^5 k$ (l. mole^{-1} sec.$^{-1}$).

(i) At 25°, [$HClO_4$] = 0·91M.

X =	*p*-Me	*m*-Me	H	*p*-F	*p*-Cl	*m*-F	*m*-Cl	*m*-NO_2	*p*-NO_2
	5·12	5·00	4·46	4·07	4·08	3·93	3·78	3·23	4·31

(ii) At 25°, I = 0·91M with added sodium perchlorate.

$HClO_4$ =	0·05	0·14	0·33	0·66	0·91	0·45 *
X = H:	3·17	3·09	3·34	3·94	4·46	2·74
X = *m*-NO_2:	—	2·37	—	—	3·23	—
X = *p*-NO_2:	—	3·25	—	—	4·31	—

(iii) At 55°, [$HClO_4$] = 0·32M, [$NaClO_4$] = 0·56M.

X =	*p*-Me	*m*-Me	H	*p*-F	*p*-Cl	*m*-F	*m*-Cl	*m*-NO_2	*p*-NO
	94	90	77	66	72	63	64	55	71

(iv) At 55°, I = 0·88M with sodium perchlorate.

$HClO_4$ =	0·05	0·14	0·26	0·32
X = H:	72	71	75	77
X = *m*-NO_2:	55	—	—	56
X = *p*-NO_2:	79	—	—	71

* No added perchlorate, I = 0·45.

DISCUSSION

In order that bimolecular rate constants could be derived, salt effects were minimised; sodium perchlorate was used to maintain constant the ionic strength. Examination of Table 1 reveals that this device was partially successful. The bimolecular rate constants do decrease with decreasing perchloric acid concentration, but the variation is substantially less than that found in the absence of added perchlorate. Further, on the reasonable assumption that the variation of rate with perchloric acid concentration should be the same for each ketone, the results indicate that there can be no significant contribution (<1%) of a solvent(base)-catalysed process to enolisation, even of the most acidic ketone (4-nitrobenzyl phenyl ketone) in 0·91M-perchloric acid. The fact that the rate constant found at 55° with this ketone in 0·05M-acid is slightly higher than that for 0·32M-acid suggests a slight incursion of a solvent-catalysed reaction at the higher temperature.

The Hammett reaction constant (ρ) for the enolisation was evaluated by using rate and σ^0 data [9] for the *m*-substituted-phenyl substituents; the *m*-tolyl substituent was omitted from this calculation because of the larger uncertainty in its rate constant. The derived figures are: $\rho = -0{\cdot}202$; correlation coefficient (r) = 0·995; intercept of the regression line with the ordinate ($\log k_0$) = $-4{\cdot}346$. Effective σ values [9] [$\bar{\sigma} = (\log k - \log k^0)/\rho$] and interaction-energy differences [7] [$\Delta\Delta F_p = -2{\cdot}3\boldsymbol{RT}\rho(\bar{\sigma} - \sigma^0)$] are listed for *para*-substituents in Table 2.

It is clear that the magnitude of resonance interaction in the transition state is quite small by comparison with, for example, the solvolysis of α,α,4-trimethylbenzyl chloride,[10]

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[9] Taft, *J. Phys. Chem.*, 1960, **64**, 1805.

[10] Brown, Brady, Grayson, and Bonner, *J. Amer. Chem. Soc.*, 1957, **79**, 1897.

TABLE 2.

Effective σ values and resonance interaction-energy differences.

X	*p*-Me	*p*-Cl	*p*-F	*p*-NO$_2$
$\bar{\sigma}$	$-0{\cdot}27$	$+0{\cdot}21$	$+0{\cdot}22$	$+0{\cdot}09$
$\bar{\sigma} - \sigma^0$	$-0{\cdot}12$	$-0{\cdot}06$	$+0{\cdot}05$	$-0{\cdot}73$
$\Delta\Delta F_p$	$-0{\cdot}03$	$-0{\cdot}02$	$+0{\cdot}01$	$-0{\cdot}20$

a reaction for which[7] $\Delta\Delta F_p$ is $-1{\cdot}17$ kcal. mole^{-1} and which presumably involves an incipient carbonium ion. However, such comparison can be misleading, because the influence of a resonance interaction in the transition state is to be judged by the magnitude of such interaction compared with that of the polar contribution to the relative free energy of activation, *i.e.*, by the ratio $\Delta\Delta F_p/2{\cdot}3\boldsymbol{R}T\sigma^0 = (\bar{\sigma} - \sigma^0)/\sigma^0$. Within the accuracy ($\pm 0{\cdot}1$) of the effective σ-values for the ketone series, $\bar{\sigma}$ differs from σ^0 only in the case of the *p*-nitrophenyl group. It is true that in view of the relatively large error in the effective σ-values resulting from the small value of ρ, one cannot rule out the possibility of some resonance interaction, in the transition state, between conjugatively electron-donating substituents and developing enol double bond. However, such interaction cannot be of an importance comparable with that accepted for the transition state of carbinyl chloride solvolysis.

A striking feature of the present results is the implication that a positively charged transition state is stabilised by resonance interaction with the electron-withdrawing nitro-group. This is, however, consistent with the structure of the transition state in which one of the methylene-hydrogen atoms is being removed as a proton. As a consequence, in 4-nitrobenzyl phenyl ketone, the benzyl α-carbon bears an excess of electronic charge, part of which is delocalised into the adjacent carbonyl group but which is also available for delocalisation into the attached nitrophenyl system. Support for this interpretation can be found on resolution of the overall enolisation reaction into the consecutive steps of (1) equilibrium protonation of the ketone carbonyl group and (2) rate-determining deprotonation at α-carbon. Then $k_2 = K_1k$, where k_2 is the rate of deprotonation (at α-carbon) of the conjugate acid for which K_1 is the acid dissociation constant (at oxygen); k is the measured rate of enolisation. Hence $\rho_2 = \rho_1 + \rho$. We assume that the reaction constant for dissociation of the ketone conjugate acids in 87% acetic acid is similar to that for dissociation in water[8] ($+0{\cdot}59$). Then $\rho_2 = +0{\cdot}59 -0{\cdot}20 = +0{\cdot}39$. Relative values of k_2 for the ketones were derived from the calculated dissociation constants * and the measured rates of enolisation. From the values of log k_2, and with $\rho_2 = 0{\cdot}39$, effective σ-values could then be derived. Only for the *p*-nitrophenyl group ($\bar{\sigma} = 1{\cdot}17$) does $\bar{\sigma}$ differ significantly from σ^0. This " normally " enhanced value of σ for the *p*-nitrophenyl group confirms the view that resonance interaction in the transition state is greater than in the conjugate acid.

On the basis of the above argument, the extraordinarily small " effective " σ-value ($\bar{\sigma} = 0{\cdot}09$) for the *p*-nitro-group is readily understandable. With subscripts referring to the consecutive steps of the reaction, the effective σ-value may be expressed as $\sigma = (\rho_1\sigma_1 + \rho_2\sigma_2)/(\rho_1 + \rho_2)$. It is only in the case where $\sigma_1 = \sigma_2$, that $\bar{\sigma} = \sigma_1 = \sigma_2$ and the effective σ has the " normal " value. Such a situation is, however, unusual for a *para*-($+M$) substituent because the different steps of a set of consecutive reactions often involve different resonance interactions and require different σ-values. Such reactions are generally found to be inadequately covered by the original Hammett equation (*e.g.*, the correlation coefficient for acid-catalysed methyl-esterification was found[3] to be only $0{\cdot}457$). In the present example the very small value for $\bar{\sigma}$ is simply the result of an unusual balance of conflicting terms in the above expression.

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[*Received, March 12th*, 1962.]

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* By using log $K^0 = 6{\cdot}92$, $\rho = -0{\cdot}202$ (ref. 8), and σ^0 values of Taft (ref. 9).