34. Base-catalysed Bromination of Substituted-benzyl Phenyl Ketones.

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For the acetate-catalysed bromination of substituted-benzyl phenyl ketones in aqueous acetic acid, rate data have been obtained at 25°, 40°, and 55°. The results are discussed and compared with data on acid-catalysed bromination of the same ketones and with relevant kinetic data on related ketone series.

WE recently reported rates of perchloric acid-catalysed enolisation (bromination) of substituted-benzyl phenyl ketones.[1] These data are now supplemented by the results of similar work on bromination of the same ketones in 87% (by weight) acetic acid catalysed by sodium acetate as base.

EXPERIMENTAL

Reagents.—The ketones used were benzyl phenyl ketone and 3-chloro-, 4-chloro-, 3-fluoro-, 4-fluoro-, 3-methyl-, 4-methyl-, 3-nitro-, and 4-nitro-benzyl phenyl ketone. The purification of acetic acid has been described.[1] Sodium acetate was made from "AnalaR" sodium hydroxide pellets (200 g.) and a solution of the purified acetic acid (500 ml.) in water (250 ml.). Water and excess of acetic acid were removed by heating at 130° for 48 hr., then for 18 hr. at 2 mm. pressure. The stock solution for kinetic measurements was a solution of sodium acetate (0·631 m) in 87% of acetic acid (by weight).

Rate Measurements.—The method of following the kinetics was similar to that used for acid-catalysed bromination. The initial concentration of ketone was within the range M/100—M/30, that of sodium acetate was M/1·5 and of bromine M/100. 4-Nitrobenzyl phenyl ketone (above 25°) and 3-nitrobenzyl phenyl ketone (above 40°) reacted too rapidly for convenient measurement. The solvent reacted slowly with bromine, and all rates were corrected for this. The methyl-substituted ketones reacted with bromine in the absence of added catalyst. For these two ketones, the base-catalysed reactions are slower than the previously studied acid-catalysed reactions, and the blank reaction (attributed to nuclear bromination) is correspondingly more serious. In fact, the blank reaction was so large for 3-methylbenzyl phenyl ketone that accurate measurement of the deprotonation rate was precluded. For the 4-methyl ketone, however, an appropriate correction (of the order of 10%) could be made.

Under the chosen reaction conditions, the base is always present in large excess and the deprotonation should be of pseudo-first order:

$$\log (a - x) = -kt + \text{Constant},$$

where a is the initial concentration of ketone, and x, its decrease in time t, is taken as equal to the decrease in bromine concentration. For 4-nitrobenzyl phenyl ketone at 25° and for all ketones above this temperature, plots of log $(a - x)$ against t were curved in the direction of increasing "rate constant" with increasing extent of reaction. This we attribute to dibromination, a complication not arising in acid-catalysed enolisation where the effect of the α-bromo-substituent ($-I$) should be rate-retarding. This complication was not generally observed in runs at 25° because, except in the case of 4-nitrobenzyl phenyl ketone, the ketone concentration was high (M/30) and at the completion of the run the ratio of concentrations (ketone : monobromo-ketone) was never less than 2·5 : 1. The rate constants for the successive reactions, *i.e.*, k_1 for bromination of the ketone and k_2 for bromination of the α-bromo-ketone were evaluated by Swain's method.[2] Tables and two-cycle log–log plots of k_2/k_1 (0·01—1·00) against k_1t were constructed for values of x/a = 0·04, 0·08, 0·10, 0·12, 0·16, 0·20, 0·24, 0·28, 0·30, 0·32, 0·36, 0·40, 0·44, 0·48, 0·50, 0·52, 0·56, 0·60, 0·65, 0·70, 0·75, and 0·80. To evaluate the rate constants for a particular run, a plot of log $(a - x)$ against t was made and a smooth curve drawn through the points. Interpolation in this curve gave t at each of twelve values of log $(a - x)$, corresponding to values of x/a for which the k_2/k_1 against k_1t plots had been set

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[1] Fischer, Packer, and Vaughan, *J.*, 1962, 3318.
[2] Swain, *J. Amer. Chem. Soc.*, 1944, **66**, 1696.

up. Values of x/a were chosen to correspond as nearly as possible to the measured values. The curves were then grouped in pairs (1st and 7th, 2nd and 8th, etc.) and the values of k_2/k_1 and k_1t read off at the intersection obtained by superposing the two graphs of a pair with the abscissæ displaced in the ratio of the t values. A typical run is given below.

Bromination of m-*Chlorobenzyl Phenyl Ketone at* 55°.—Initial ketone concentration, a, was 12·79 mmoles l.$^{-1}$. Aliquot parts (2·03 ml.) of the mixture were titrated with sodium thiosulphate (0·00865N). In the left-hand part of Table 1 the observed values of t and log $(a - x)$ are recorded. In the right hand section values of t at the listed x/a values are recorded; these were read from the log $(a - x)$ against t plot.

TABLE 1.

t_{obs} (min.)	T * (ml.)	$a - x$ (mmoles l.$^{-1}$)	log $(a - x)_{\text{obs}}$	x/a	log $(a - x)$	t (min.)
0·0	4·07	12·79	1·107	0·08	1·071	5·8
5·6	3·60	11·79	1·072	0·12	1·052	8·5
10·5	3·18	10·90	1·037	0·16	1·031	11·6
15·3	2·83	10·15	1·007	0·20	1·010	14·7
20·2	2·44	9·32	0·969	0·24	0·988	17·8
24·7	2·11	8·62	0·936	0·28	0·964	20·9
31·3	1·64	7·61	0·881	0·32	0·940	24·1
35·4	1·36	7·02	0·846	0·36	0·913	27·5
40·4	1·04	6·34	0·802	0·40	0·885	30·9
44·8	0·76	5·74	0·759	0·44	0·855	34·3
				0·48	0·823	38·0
				0·52	0·788	41·8

* Titration figures corrected for solvent blank. Thus $T^* = T + 0{\cdot}06 + 3{\cdot}0 \times 10^{-3}t$ for $t < 20$ min.; $T^* = T + 0{\cdot}12 + 1{\cdot}5 \times 10^{-3}t$ for $t > 20$ min.

From the appropriate pairs of k_2/k_1 against k_1t plots, with abscissæ displaced in the ratios of the corresponding t values, the values of k_2/k_1 and k_1t given in Table 2 were obtained.

TABLE 2.

t ratio	0·241	0·309	0·375	0·429	0·468	0·500
k_2/k_1	0·80	0·48	0·54	0·57	0·55	0·51
k_1t	0·081	0·123	0·167	0·209	0·255	0·300
10^3k (min.$^{-1}$)	13·9	14·5	14·4	14·2	14·3	14·4

Hence k_1 (mean) = 14·3 min.$^{-1}$; k_2/k_1 = 0·53.

Mean (two runs) apparent bimolecular rate constants (k_1/[acetate]) are listed in Table 3 together with the derived Arrhenius parameters.

TABLE 3.

Bromination of X-benzyl phenyl ketones in 87% acetic acid containing 0·631 m sodium acetate.

Values of 10^5k (*l. mole*$^{-1}$ *sec.*$^{-1}$).

X =	4-Me	H	4-F	4-Cl	3-F	3-Cl	3-NO$_2$	4-NO$_2$
At 25°	0·39	0·51	0·88	1·53	1·95	2·14	8·40	37·6
At 40°	2·03	2·76	3·73	7·37	8·63	9·83	36·2	—
At 55°	8·1	11·3	15·8	26·4	33·2	38·2	—	—
Arrhenius parameters.								
E	19·6	20·0	18·7	18·4	18·3	18·7	18·1	—
log A	8·9	9·4	8·7	8·7	8·7	9·0	9·2	—

In general, the rate constants (k_1) are estimated to be accurate to ±5%. Because all reactions were followed over low x/a values, the rate constants for bromination of the α-bromoketones (k_2) are much less accurate (±30%). Within the noted limits of accuracy k_2/k_1 was constant for all compounds at a given temperature. At 25°, k_2/k_1 (4-nitrobenzyl phenyl ketone) was 0·1. At 40°, k_2/k_1 (mean) was 0·3, and at 55° 0·5.

DISCUSSION

A regression line was fitted to the log k against σ^0 data for the *meta*-substituted and unsubstituted compounds at each temperature. The reaction constant (ρ), correlation coefficient (r), and intercept with the ordinate (log k_0) are listed in Table 4.

TABLE 4.

Temp.	ρ	r	$-\log k_0$
25°	+1·733	0·999	5·301
40	+1·592	0·997	4·582
55	+1·390	0·998	3·948

Although the ρ-value obtained at 55° is based on data for three compounds only, ρ appears to vary oppositely to temperature. In agreement with this conclusion, the Arrhenius parameters indicate that the reaction series is isoentropic.[3]

As would be expected for a deprotonation, the reaction is aided by a reduction in electron density at the reaction site (ρ is positive). Watson and Morgan [4] showed that acetate-catalysed bromination of substituted acetophenones is aided by electron-withdrawing substituents and Hughes, Watson, and Yates [5] found that the rate of solvent-(base-)catalysed bromination of bromoacetones increases with the number of bromo-substituents ($-I$). It might therefore have been expected that the introduction of an α-bromo-substituent would increase the rate of enolisation of a benzyl phenyl ketone, *i.e.*, $k_2 > k_1$. The opposite is true, and presumably the bromine substituent also introduces some additional, rate-retarding steric strain into the transition state (one canonical form of such an enolate ion would be a tetra-substituted olefin). The deprotonation of the ketones by acetate ion is very much more sensitive to the polar effect of the substituted aryl groups ($\rho = +1{\cdot}73$) than is the similar reaction of the conjugate acid and solvent molecules [1] ($\rho = +0{\cdot}39$). In the deprotonation of the conjugate acid there is competition between the protonated carbonyl group and the aryl group for the electrons of the key C–H bond. In the deprotonation of the ketone there is similar competition between the carbonyl group and the aryl group. The electron affinity of the protonated carbonyl group is much higher than that of the unprotonated group, and with the second group there is a much greater demand on the aryl group to aid in the dispersal of the electronic charge. Hence ρ is greater in this case. Acid-catalysed enolisation of substituted-benzyl phenyl ketones is less sensitive to the electronic effects of substituents ($\rho = -0{\cdot}20$) than is the similar reaction of substituted acetophenones [6] ($\rho = -0{\cdot}60$). In contrast, base-catalysed enolisation of the benzyl phenyl ketones ($\rho = +1{\cdot}73$) is more sensitive to substituent effects than is base-catalysed enolisation of acetophenones ($\rho = +0{\cdot}31$; calculated from the data of Morgan and Watson [4]). Now the transition state for acid-catalysed enolisation will be intermediate between ketone conjugate acid and enol. To some extent, therefore, the carbonyl carbon atom will be electron-deficient, and positive. This atom is adjacent to the aryl group in the acetophenones but isolated from it in the benzyl phenyl ketones. On the other hand, the transition state for base-catalysed enolisation is intermediate between ketone and enolate ion. The negative charge of the latter is divided mainly between the oxygen and the carbon at which dissociation occurs. This carbon is adjacent to the aryl group in the benzyl phenyl ketones but, like the oxygen atom, it is isolated from the aryl group in the acetophenones. The different sensitivities to acid- and base-catalysis are therefore understandable.

With the relation [7] $\bar{\sigma} = (1/\rho)\log(k/k_0)$, effective values for *para*-substituted aryl groups and the corresponding resonance-energy differences,[6] $[\Delta\Delta F_{\mathrm{p}} = -2{\cdot}3\boldsymbol{R}T\rho(\bar{\sigma} - \sigma^0)]$, are given in Table 5.

Since rate constants are accurate to ±5%, σ values should be accurate to ±0·02. The difference between $\bar{\sigma}$ and σ° for the 4-tolyl group is probably without significance, however, because of the greater uncertainty in the rate constants for the 4-methyl benzyl phenyl ketone. For the 4-chlorophenyl and 4-fluorophenyl groups there is good agreement

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[3] Fischer and Vaughan, *J. Chem. Phys.*, 1957, **27**, 976.
[4] Morgan and Watson, *J.*, 1934, 1173.
[5] Hughes, Watson, and Yates, *J.*, 1931, 3318.
[6] van Beekum, Verkade, and Wepster, *Rec. Trav. chim.*, 1959, **78**, 815.
[7] Taft, *J. Phys. Chem.*, 1960, **64**, 1805.

TABLE 5.

Effective σ values and resonance interaction-energy differences at 25°.

X	4-Me	4-Cl	4-F	4-NO$_2$
$\bar{\sigma}$	$-0{\cdot}06$	$+0{\cdot}28$	$+0{\cdot}14$	$+1{\cdot}08$
$\bar{\sigma} - \sigma^0$	$+0{\cdot}09$	$-0{\cdot}01$	$-0{\cdot}03$	$+0{\cdot}26$
$\Delta\Delta F_p$	$-0{\cdot}22$	$+0{\cdot}02$	$+0{\cdot}07$	$-0{\cdot}62$

between $\bar{\sigma}$ and σ^0 within the precision of the latter ($\pm 0{\cdot}03$). Thus there appears to be no stabilisation of the transition state through the operation of $+M$ effects. This result is in agreement with the earlier observation by Hughes[8] that, in the base-catalysed enolisation of alkyl phenyl ketones, Ph·CO·CHRR′, the inductive (rather than the hyperconjugative) effect of the alkyl groups is dominant. The effective σ value, and the magnitude of the resonance interaction-energy, for the 4-nitrophenyl group demonstrated that there is important and substantial resonance interaction between the substituent and reaction centre in the transition state. This is in accord with the expected transition state for deprotonation, in which there will be substantial accumulation of negative charge on the carbon atom adjacent to the aryl group. Such charge is therefore ideally situated for conjugative dispersal by the 4-nitrophenyl substituent.

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