392. *The Base-catalysed Decomposition of Mononitrochalcones in Aqueous Alcohol.*

By E. A. Walker and J. R. Young.

The velocity constants and activation energies for the hydrolytic decomposition of chalcone and its six ring-substituted mononitro-derivatives in constant-boiling ethanol have been measured. The rate is proportional to the concentration of added base; no acid-catalysis is observed.

All substituents (with the exception of *p*-NO_2) reduce the activation energy and this, with the kinetics, suggests that the rate-determining step is attack by hydroxyl ion. A probable mechanism is suggested.

The anomalous behaviour of the *p*-nitro-group, which has a parallel in the spectra of these compounds, is discussed.

Chalcones (benzylideneacetophenones) offered a suitable system with which to extend the work of Lucas *et al.*[1] on the addition of water to a double bond conjugated with a carbonyl group. In addition, the effect of substituents may be compared under conditions of direct and crossed conjugation between the nucleus and the reaction centre.

Chalcone and the six mononitrochalcones were decomposed in *ca.* 5×10^{-4}M-solution in constant-boiling ethyl alcohol containing sodium hydroxide as catalyst. The reactions were followed by removing samples and measuring the optical density (K) at the long-wavelength maximum of the chalcone after suitable dilution. The observed values of K were corrected for product absorption where necessary, and plots of log $K_{\text{corr.}}$ against time established the reaction order and enabled velocity constants to be calculated.

In all cases the log K plots were linear up to at least 20% of total reaction. Beyond this a curvature appeared which was consistent with an approach to equilibrium. Attempts to follow the equilibrium gave unsatisfactory results which were attributed to

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[1] Lucas, Stewart, and Pressman, *J. Amer. Chem. Soc.*, 1944, **66**, 1818.

various side-reactions involving the initial products. On the other hand, spectrographic analysis of the final reaction mixtures using additional wavelengths gave satisfactory agreement with the expected concentrations of free aldehyde and ketone.

The velocity constant k' calculated from the slope of the linear plots was shown to be proportional to the concentration of sodium hydroxide present (0·05—0·2M). Thus the reaction was of second order and the law, Rate = k'[Chalcone] = k[Chalcone][NaOH], was obeyed. Within the temperature range 25—55° the plots of log k against 1/Temperature (°K) were linear to the expected accuracy and gave the activation energies. The full results are in the Table.

Kinetic data for the decomposition of chalcones in constant-boiling ethanol catalysed by sodium hydroxide.

Compound Subst. Ph·CH:CH·COPh′	Velocity constants 10^2k (mole^{-1} l. min.$^{-1}$) 25°	35°	45°	55°	E_a(kcal.)	log PZ
Nil	—	0·45	1·2	3·4	20·0	10·9
o-NO_2	5·9	12·0	23·0	—	12·6	6·3
m-NO_2	1·6	4·6	12·0	—	19·1	10·5
p-NO_2	1·1	3·5	9·9	—	20·3	11·3
o'-NO_2	0·62	1·8	4·3	—	18·1	9·4
m'-NO_2	1·9	6·0	17·0	—	20·0	11·2
p'-NO_2	2·9	8·1	21·0	—	18·4	10·2

The effect of catalysis by 0·1M-hydrochloric acid was investigated for each compound, without detectable results. Unsuccessful attempts were made in some cases to follow the condensation from the aldehyde and ketone to the chalcone, the presence of the nitro-group in either of the simple compounds leading to an early equilibrium. More success attended measurements upon the system benzaldehyde–acetophenone where a velocity constant of approximately 14 mole^{-1} l. hr.$^{-1}$ was found at 55° (Coombes and Evans's data[2] give 15·0 for this constant), but even here an equilibrium was being approached.

The net reaction studied is:

$$\text{Ph·CH:CH·COPh}' + H_2O \longrightarrow \text{Ph·CHO} + \text{Ph}'\text{·COMe}$$

Since water was in excess in the solvent used, its concentration did not enter the rate equation. The observed proportionality to the sodium hydroxide concentration is consistent with the attack of the reactant anion on the β-carbon atom of the double-bond conjugated to the carbonyl group, *e.g.*:

$$(1)\quad (H_2O + EtO^- \rightleftharpoons EtOH + OH^-)$$

$$(2)\quad \text{Ph·CH:CH·COPh}' + OH^- \rightleftharpoons \text{Ph·CH(OH)·}\bar{\text{C}}\text{H·COPh}' \quad (A)$$

This conclusion is analogous to the proposal made by Ingold[3] on general grounds for the rate-determining stage of typical Michael reactions and supported by the results of Kamlet and Glover[4] in such an instance.

The interest of the reaction concerns the fate of the ion (A). Thus we may consider that it accepts a proton from a solvent molecule to form the ketol, which then breaks down by the accepted mechanism.[5] This possibility leads to the scheme:

$$(3)\quad \text{Ph·CH(OH)·}\bar{\text{C}}\text{H·COPh}' + ROH \rightleftharpoons \text{Ph·CH(OH)·}CH_2\text{·COPh}' + OR^-$$

(4)


$$\text{Ph·CH(OH)·}CH_2\text{·COPh}' + OR^- \rightleftharpoons \text{Ph·}\underset{O^-}{\text{CH}}\text{·}CH_2\text{·COPh}' + ROH \quad (B)$$

$$(5)\quad (B) \rightleftharpoons \text{Ph·CHO} + {}^-CH_2\text{·COPh}'$$

$$(6)\quad {}^-CH_2\text{·CO·Ph} + ROH \rightleftharpoons CH_3\text{·COPh}' + OR^-$$

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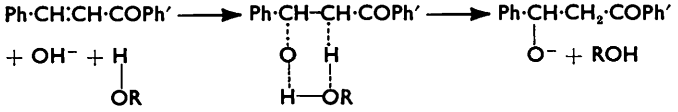
[2] Coombes and Evans, *J.*, 1942, 1295.

[3] Ingold, "Structure and Mechanism in Organic Chemistry," Bell, London, 1953, p. 693.

[4] Kamlet and Glover, *J. Amer. Chem. Soc.*, 1956, **78**, 4556.

[5] Ingold, *op. cit.*, p. 682.

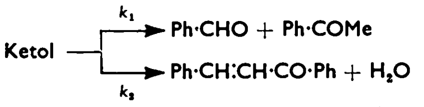
Alternatively we may consider that, since the intermediate ions (*A*) and (*B*) differ only in the position of a single hydrogen atom, there is a direct route from (*A*) to (*B*) not involving the ketol. Such a route might be provided if the transition state for reaction (2) involves a solvent molecule, *e.g.* :



$$\mathrm{Ph{\cdot}CH{:}CH{\cdot}COPh' + OH^- + H{-}OR \longrightarrow Ph{\cdot}CH(O\cdots H{-}OR\cdots H){\cdot}CH{\cdot}COPh' \longrightarrow Ph{\cdot}CH(O^-){\cdot}CH_2{\cdot}COPh' + ROH}$$

This suggestion is taken from Laidler and Landskroener [6] who find theoretical support for the occurrence of such forms in, for example, base-catalysed ester hydrolysis.

Against the attractiveness of the proposal must be placed Noyce and Pryor's results,[7] which, in addition to providing kinetic evidence for the occurrence of the ketol in the acid-catalysed condensation of benzaldehyde and acetophenone, include a synthesis of this compound (by an indirect route) and measurement of its acid- and base-catalysed dehydration and decomposition. Their values for the base-catalysed reactions are :



$$\mathrm{Ketol} \xrightarrow{k_1} \mathrm{Ph{\cdot}CHO + Ph{\cdot}COMe}$$

$$\mathrm{Ketol} \xrightarrow{k_2} \mathrm{Ph{\cdot}CH{:}CH{\cdot}CO{\cdot}Ph + H_2O}$$

Rate = $(k_1 + k_2)$[NaOH][Ketol]

At 26° in 90% ethyl alcohol $k_1 = 11{\cdot}5$ mole^{-1} l. min.$^{-1}$.
$k_2 = 3{\cdot}1$ „

Under the same conditions the condensation of benzaldehyde and acetophenone has a rate constant of $4{\cdot}5 \times 10^{-2}$, whilst our results in constant-boiling alcohol (*ca.* 96%) give a calculated value of $1{\cdot}5 \times 10^{-3}$ for the decomposition of chalcone at this temperature. The rates of the ketol reactions are thus sufficiently large by comparison to ensure that the rate-controlling steps of the base-catalysed condensation and chalcone decomposition do not involve ketol. On the other hand, they establish a degree of stability for the ketol which suggests that it is likely to be formed at least in small quantity. It would be interesting to examine these reactions more closely than we have been able to do, with a view to establishing the route taken or the proportions of molecules following alternative routes between chalcone and products.

Effects of Substituents.—The effects of then itro-substituents are consistent with the suggestion that hydroxyl-ion attack is rate-determining. Thus in most cases the energy of activation is lower than that of the unsubstituted compound.

The mesomeric effect of the nitro-group will not be called into operation from substituents in the ring remote from the carbonyl group and we may expect reductions of activation energy to be produced by the inductive effects alone. E_A for the *meta*-compound is 1 kcal. lower than for the parent, and this value sets the magnitude of the differences to be expected. On this basis the *ortho*-group is exerting an enhanced effect and the *para*-group a reduced electron attraction. The same observation holds when the velocity constants of the *meta*- and *para*-compounds are compared; this is desirable in this case since the estimated accuracy of the E_A is $\pm 0{\cdot}6$ kcal.

We explain the *ortho*-anomaly on steric grounds. Thus in this compound mutual steric hindrance between side-chain and nitro-group force both structures out of the ring-plane. Thus the required polarisation of the carbonyl group and the adjacent double bond (form I) is not reduced by interaction with the ring π-electrons, *i.e.*, the electron density on the β-carbon atom is lower than it would be were the *p*-orbitals of this atom perpendicular to the ring plane as required in the polarised cinnamoyl form (form II).

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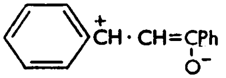
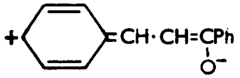
[6] Laidler and Landskroener, *Trans. Faraday Soc.*, 1956, **52**, 200.
[7] Noyce and Pryor, *J. Amer. Chem. Soc.*, 1955, **77**, 1397.

Moreover, the inductive effect of the nitro-group is here acting from the nearest position to the side-chain. Thus the apparent energy of activation has the very low value of 12·6 kcals. whilst the simultaneously low steric factor reflects the difficulty of approach to the β-carbon atom.

(I)

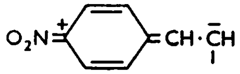


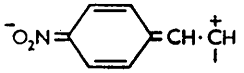


(II)

The behaviour of the *p*-nitro-group in showing either no effect or possibly a very small $+I$ effect was also evident in the spectrum of this compound, where it exerted a slight bathochromic influence upon the 300 mμ band (see ref. 8). Such anomalies in the effect of the nitro-group are not unknown and have been recently discussed by Braude and Waight.[9] These workers suggest that in the *p*-nitrostyryl system the styryl polarisation may make a greater contribution to the ground state than the nitro-polarised form, *i.e.*, (III) contributes more than (IV), leading to smaller effects from the *p*-nitro-group than

(III)





(IV)

were expected. However, we consider that in the present system the contribution from form (IV) depresses the polarisation of the carbonyl group to give (I), leading to the slightly higher activation energy of the *para*- than of the *meta*-compound. The spectrographic anomaly (see ref. 8) is explicable if the 300 mμ band for the *para*-compound arises from superimposed cinnamoyl and *p*-nitrostyryl absorption; this complexity is rendered more likely if form (IV) makes a relatively large contribution to the ground state, as assumed above.

In the *o*′-, *m*′-, and *p*′-compounds the substituent effects are more regular. The absence of measurable effect from the *m*′-group and the approximately equal diminutions of E_A caused by the *o*′- and *p*′-substituents are strong evidence in favour of electromeric assistance in the reaction. On the other hand, it is impossible to write conventionally bonded excited states for *o*′- and *p*′-nitrochalcones, which show nitro-group polarisation and a formal positive charge on the β-carbon atom. In spite of the difficulty, we believe that a rather weak electromeric effect is being transmitted to the β-carbon atom *via* the cross-conjugated carbonyl group in these compounds, the inductive effects being negligible.

EXPERIMENTAL

Preparation.—The chalcones were prepared by the standard method outlined earlier.[8] Constant-boiling ethyl alcohol, used as solvent for kinetic work, was prepared in large quantity by Baker and Hemming's method.[10]

Catalyst Solution.—The catalyst solution was 0·5M-sodium hydroxide in the solvent alcohol. It was prepared in small quantities and not stored for any length of time. A slight excess of the hydroxide pellets was dissolved in 100 ml. of constant-boiling alcohol; this solution showed a carbonate deposit which was removed by drawing the solution off through a sintered-glass filter into a protected flask. The strength of the final solution, determined by titration with standard hydrochloric acid, showed no carbonate by differential titration.

Rate Measurement.—The chalcone (2—4 mg.) in a 25 ml. flask was treated with *ca.* 19 ml. of solvent and immersed in a thermostat at the reaction temperature; catalyst and pure solvent were similarly stored. Dissolution of the chalcone was normally complete in 30 min. by which time the contents had reached the bath-temperature. Catalyst solution (5 ml.) was added

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[8] Walker and Young, preceding paper.
[9] Braude and Waight, *J.*, 1953, 419.
[10] Baker and Hemming, *J.*, 1942, 191.

and the volume rapidly made up to the mark with solvent at the bath-temperature. The whole was mixed by short vigorous shaking. About 5 min. were allowed for the reaction to settle down after mixing, and the first 1 ml. sample was then removed for analysis, followed by others later. All samples were run into *ca.* 8 ml. of solvent in a 10 ml. graduated flask, the time intervals being measured from the commencement of delivery. The diluted solution was made up to 10 ml. and the optical density of this solution was measured (Unicam SP500 Spectrophotometer) in a 0·5 cm. silica cell at the $\lambda_{\max.}$ for the chalcone against a control of pure solvent and at a constant slit width of 0·1 mm.

Variations in the catalyst concentration were made both by changing the concentration of the catalyst solution and by altering the amount added to the reaction mixture.

The results for a typical experiment are given below.

o′-*Nitrochalcone at* 35°.

0·0032 g. in 25 ml. of solution containing 5 ml. of 0·357M-NaOH. 1 ml. samples, determined at 298 mμ, gave the following readings.

Time (min.)	0	7	14	21	28	35	42	50	57	64
$\log I_0/I$ (= K)	0·563	0·553	0·544	0·533	0·521	0·511	0·503	0·490	0·484	0·474
$-\log K$	0·249	0·257	0·264	0·273	0·283	0·291	0·298	0·309	0·315	0·324

$k' = k[\text{Catalyst}] = 1{\cdot}15 \times 10^{-3}$.
$k = 1{\cdot}61 \times 10^{-2}$ mole^{-1} l. min.$^{-1}$ (uncorr.).

Correction for k. ε at 298 mμ are: *o*′-nitrochalcone 22,600; Ph·CHO 150; *o* $NO_2{\cdot}C_6H_4{\cdot}COMe$ 1300. Thus:

$$K_{\text{corr.}} = K_0 - \Delta K_{\text{obs.}}[22{,}600/(22{,}600 - 150 - 1300)]$$
$$= K_0 - 1{\cdot}07\Delta K_{\text{obs.}}$$

Whence, from the Table: $k_{\text{corr.}} = 1{\cdot}76 \times 10^{-2}$ mole^{-1} l. min.$^{-1}$.

The individual measurements of k showed standard deviations of ±3% (*e.g.*, for chalcone $10^2 k_{35}$ were 0·436, 0·449, 0·459, and 0·454). This rather low accuracy arises from two causes: first, the correction procedure adopted is not strictly accurate since it assumes that the K_0 (*i.e.*, the optical density at zero time) is entirely due to chalcone whereas some slight reaction has already occurred; this reduces the final k. Secondly, there is curvature towards infinite slope of the plot of log K against time which is caused by the approach to equilibrium; in most cases the early linear portion was unmistakable but in others a tendency to curvature could be detected after 15% change; in order to avoid this the measurements had to be restricted to the first 20% of reaction which meant compressing the whole experiment into an optical-density range of approx. 0·1 (*i.e.*, from 0·5 to 0·4) with a consequent loss of accuracy.

The few experiments on acid-catalysis employed a similar method and a catalyst solution of 0·5M-hydrogen chloride in the kinetic solvent, which was prepared by passing dry gas into the constant-boiling alcohol. For example, sealed samples consisting of an acid chalcone solution (7×10^{-4}M-chalcone, 0·1M-HCl) and a neutral solution of the same concentration were kept at 35° for 30 days. Spectrographic analysis of both series at four selected wavelengths showed no significant absolute or relative changes throughout this period. A complete spectrum at the end indicated a possibly slightly greater degree of decomposition in the neutral sample. The experiments on the nitrochalcones were shorter and simpler, but just as conclusive.

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