

Kinetics of the Base-Catalysed Condensation of Acetophenone with Benzaldehydes : A Quantitative Separation of Inductive, Resonance and Steric Effects

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The rate of base-catalysed condensation of acetophenone with substituted benzaldehydes has been studied in 90% alcohol. The reaction was first-order in each component. The Arrhenius parameters have been discussed. The applicability of Hammett equation has been studied. A quantitative separation of the inductive, resonance and steric effects has been attempted. The mechanism has been discussed.

The kinetics of the Claisen-Schmidt¹ reaction between substituted benzaldehydes and acetophenone have not been extensively studied. Gettler and Hammett² have investigated the base-catalysed reaction between benzaldehyde and methylethyl ketone. The self condensation of acetone in the presence of hydrogen chloride has been briefly examined³. Nikitin⁴ has studied the base-catalysed condensation of benzaldehyde and acetone and found the reaction to be second order.

In the present study we have chosen to examine the kinetics of the base-catalysed condensation of substituted benzaldehydes with acetophenone in the presence of a constant quantity of sodium ethoxide in 90% ethanol. The reaction was found kinetically bimolecular, and depends upon each reagent to the first power. The mechanism of the reaction has been illustrated in the discussion. The reaction should, therefore, be facilitated by factors which produce an electron deficit on the functional carbon atom. The specific reaction rate and energy of activation etc., have been illustrated in Table I. The reaction is facilitated by groups such as nitro, chloro in the phenyl nucleus of the aldehyde molecule and retarded by groups such as methyl and methoxy etc. A quantitative separation of inductive, resonance and steric effects has been attempted according to the method of Taft and Lewis⁵. A mechanism for the formation of benzalacetophenone (chalkone) has been suggested in light of the observation found by us.

EXPERIMENTAL

Most of the benzaldehydes were prepared and purified by the standard methods.

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Absolute ethyl alcohol was prepared by the method described by Vogel⁶ by using dry magnesium turnings. The 90% alcohol was prepared by suitably diluting absolute alcohol with distilled water.

An *N*/10 sodium ethoxide solution was prepared and stored by the method of Davis⁷ and Lewis⁷.

Kinetic procedure : Stock solutions of *M*/5 aldehyde, *M*/5 ketone and *N*/10 sodium ethoxide in 90% alcohol were prepared. The method of rate measurement and calculation of the specific reaction rates were similar to that of Coombs and Evans⁸. The specific reaction rate together with the Arrhenius parameters of different substituted benzaldehydes are illustrated in Table I.

TABLE I

No.	Name of the substituted benzaldehyde	$k_{35} \times 10^4$ in lit.mole ⁻¹ Sec. ⁻¹	E K.Cals/mole	log <i>PZ</i>	ΔS^\ddagger cal/deg.
1.	Unsubstituted	13.33	9.89	7.65	-41.42
2.	<i>p</i> -methoxy-	2.014	11.20	7.71	-36.96
3.	<i>p</i> -methyl-	4.69	11.97	8.67	-41.16
4.	<i>p</i> -chloro-	44.44	9.28	7.74	-44.45
5.	<i>p</i> -nitro-	291.70	7.83	7.55	-42.21
6.	<i>m</i> -nitro-	230.50	8.29	7.78	-40.66
7.	<i>m</i> -chloro-	37.50	11.50	9.40	-34.36
8.	<i>m</i> -bromo-	43.05	9.62	7.97	-35.63
9.	<i>m</i> -methoxy-	5.91	10.59	7.81	-40.98
10.	3-nitro, 4-methyl-	100.00	11.05	9.34	-32.29
11.	3-nitro, 4-methoxy-	33.34	9.21	7.47	-42.00
12.	3-nitro, 4-chloro-	167.20	8.29	7.62	-41.79
13.	2-chloro, 5-nitro-	222.30	8.74	8.06	-39.35
14.	2,4-dichloro-	66.68	8.29	7.54	-43.63
15.	<i>o</i> -chloro-	29.17	9.67	7.84	-40.82
16.	<i>o</i> -nitro-	144.40	9.21	8.20	-40.35

Cumulative effect of the substituents : The effect of the different substituents on the energy of activation in the formation of chalkones has been evaluated by the method of Rout *et al.*⁹.

In case of disubstituted benzaldehydes the resultant effect of the substituents is simply the sum of their individual effects. From the values of ΔE (Table II), the energy of activation of disubstituted benzaldehydes can be predicted as illustrated below, *i.e.*,

$$\begin{aligned} \text{3-Nitro, 4-methoxy benzaldehyde} &= 9,890 + (+1,310) + (-1,600) \\ &= 9,600 \text{ Cals/mole.} \end{aligned}$$

$$\text{Experimental value} = 9,212 \text{ Cals/mole.}$$

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TABLE II

Name of the substituent:	<i>m</i> -NO ₂	<i>O</i> -Cl	<i>p</i> -Cl	<i>p</i> -CH ₃	<i>p</i> -OCH ₃
ΔE Cals/mole :	-1,600	-218	-610	+2,085	+1,310

The energy of activation (E') calculated on the basis of the additive effect of the substituents of the disubstituted benzaldehydes together with the experimental value (E) of these compounds are given in Table III.

TABLE III

Calculated and observed values of the energy of activation of substituted benzaldehyde

Name of the substituent :	3-NO ₂ , 4-CH ₃	3-NO ₂ , 4-Cl	2,4-Cl.	2-Cl, 5-NO ₂
E' (Calcd) Cals/mole	10,375	7,680	9,062	8,072
E (Obsvd.) Cals/mole	11,045	8,290	8,291	8,740

It is evident from the above table that there is a considerable agreement between the predicted and experimental values of activation energy. It can, thus, be concluded that the resultant effect of two substituents in the same benzene nucleus is very closely equal to the sum of the effects caused by each substituent separately.

A quantitative separation of Inductive, Resonance and Steric effects : The individual contributions due to inductive and resonance effects of a substituent have been determined by the method given by Taft and Lewis¹⁰⁻¹². The resonance interaction energies of meta and para-substituents have been evaluated by using the expressions $\Delta\Delta F_m = -2.303$ RT.Rm. and $\Delta\Delta F_p = -2.303$ RT. Rp, respectively. The steric interaction energy has been calculated by using the following expression¹².

$$\Delta\Delta F_s = -2.303 \text{ RT. } (\delta E_s)$$

TABLE IV

Substituent	-CH ₃	-OCH ₃	-Cl	-NO ₂
I	+0.0149	+0.0749	-0.149	-0.1889
Rm	—	-0.0756	-0.2867	-0.9736
R _p	-0.3797	-0.6956	-0.5065	-1.0292
$\Delta\Delta F_m$ in K.cals/mole	—	+0.1106	-0.420	-0.1426
$\Delta\Delta F_p$ in K.Cals/mole	-0.1508	-0.7418	-0.5562	+0.1019
δE_s	—	—	-0.3748	-0.3726
$\Delta\Delta F_s$ in K.Cals/mole	—	—	+0.549	+0.541

The $\Delta\Delta F_s$ values for the nitro and chloro groups are positive, indicating a steric destabilisation in the transition state¹³. Chloro and nitro groups, when ortho substituted react slower than the corresponding para isomers. This may be due to their steric effects.

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Relationship between Energy of Activation and Entropy of activation—Isokinetic Relationship: A linear relationship between the entropy of activation and energy of activation has been found for the reaction between substituted benzaldehydes and acetophenone. In the equation^{14, 15}

$$\Delta^{\ddagger}H(E) = \Delta^{\ddagger}H(E)_0 + \beta \Delta^{\ddagger}S$$

E_0 has the value 29.2 K.Cals and β , the isokinetic temperature is equal to 478°K. At this temperature if the above equation holds good the rate coefficient for all the different benzaldehydes would be the same. The linear nature of the plot between E and $\Delta^{\ddagger}S$ signifies that the same mechanism (at least in so far as the main details are concerned) operates in the whole series.

Mechanism of the Reaction: A survey of literature reveals that no definite mechanism is available for the condensation of aromatic ketones with aromatic aldehydes. Two alternative mechanisms¹⁶⁻¹⁷ have been suggested for the formation of chalkones.

In the present investigation we have interpreted our results in the light of the mechanism suggested by Lapworth¹⁶ by considering the resonance interaction energy of the various groups at the transition state.

The initial step of the reaction is the formation of the carbanion by the attack of the base followed by the rate determining condensation step, the rate being proportional to the concentration of acetophenone and benzaldehyde. The same conclusion has been furnished by Noyce and Coworkers¹⁸ for the base catalysed condensation of acetone with benzaldehyde.

The effect of the substituent is more pronounced in the phenyl nucleus of the aldehyde than in the phenyl nucleus of the acetophenone¹⁹. Further, the change from *p*-nitrobenzaldehyde to anisaldehyde results in a pronounced change in rate, the nitro group enhancing and the methyl group retarding the rate. This arises due to the basicity of the aldehyde. Due to the interaction of the *p*-methoxy group with the carbonyl group of the aldehyde, the amount of positive charge on the carbonyl carbon atom is considerably reduced and hence the attack of the carbanion on the keto group of the benzaldehyde moiety is not favoured. But the case is just the reverse in case of para nitro benzaldehyde. The rate is therefore, greater in case of para nitrobenzaldehyde than anisaldehyde.

The resonance interaction values for the para nitro group is -0.246 K.Cal/mole and para methyl group is +0.563 K.Cals per mole¹⁹. The negative value of the paranitro group confirms the fact that there is pronounced interaction in the transition state than in the reactant state¹³. The positive sign of the resonance interaction value for the paramethoxy group indicates that it destabilises the transition state. These facts provide further evidences in favour of the mechanism discussed by us.

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