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KINETICS AND MECHANISM OF THE REACTION OF DIPHENYLKETENE WITH SUBSTITUTED ANILINES IN BENZENE SOLUTION

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Abstract—Diphenylketene reacts with anilines in benzene solution to form diphenylacetanilides. The reaction is kinetically of the first-order in the ketene but contains both a first and a second-order term in aniline, the differential rate equation taking the form

$$-\mathrm{d}[\text{Ketene}]/\mathrm{d}t = [\text{Ketene}]\{k_1[\text{Aniline}] + k_2[\text{Aniline}]^2\}.$$

The constants k_1 and k_2 have been determined for a series of anilines and may be represented by the equations $\log k_1 = -0{\cdot}5 \log K_a - 1{\cdot}23$ and $\log k_2 = -1{\cdot}3 \log K_a - 2{\cdot}46$ respectively, where K_a represents the dissociation constant of the base's conjugate acid. Using N-deuterated derivatives the (approximate) isotope effects on k_1 and k_2 have also been found. The mechanisms of the overall second and third-order processes are discussed in the light of these data.

Ketenes add compounds of the form HX as in Eq. (1). Very little information is available about the kinetics and mechanisms of these

$$R_2C{=}C{=}O + HX \rightarrow R_2CHCOX \qquad (1)$$

reactions.[1] It has been presumed that when HX is a predominantly nucleophilic substance (e.g. ROH, RNH_2, etc.) there is initial attack on the carbonyl carbon atom, followed by the appropriate prototropic rearrangement. As part of a quantitative study aimed at throwing more light on these matters, and at establishing the reactivity of ketenes as compared with other acylating agents, we have examined the kinetics of the reaction of diphenylketene (R = Ph in Eq. (1)) with a series of anilines in benzene solution.

When HX represents an amine it is known[2] qualitatively that the more basic the amine the faster is reaction (1). This result is confirmed by our data which are in the tables. Experiments were conducted with the aniline in at least tenfold excess of the ketene, and under these conditions a first-order loss of ketene is observed. The first-order rate constant (k_{obs}) is a variable function of the aniline concentration but may be represented by an equation containing first and second-order terms in aniline:

$$\text{Rate} = -\mathrm{d}[\text{Ketene}]/\mathrm{d}t = [\text{Ketene}]\{k_1[\text{Aniline}] + k_2[\text{Aniline}]^2\} \qquad (2)$$

or

$$k_{obs} = k_1[\text{Aniline}] + k_2[\text{Aniline}]^2 \qquad (3)$$

Available evidence[3] indicates that amines form only very small amounts of hydrogen bonded dimers (or higher aggregates) in benzene and similar solvents, and the few

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[1] R. N. Lacey, *The Chemistry of Alkenes* (Ed. by S. Patai). Interscience (1964).

[2] H. Standinger, *Die Ketene*. F. Enke, Stuttgart (1912).

[3] J. L. Mateos, R. Cetina and O. Chao, *Chem. Comm.* 519 (1965); K. L. Wolf and G. Metzger, *Liebigs Ann.* **563**, 157 (1949); J. Feeney and L. H. Sutcliff, *J. Chem. Soc.* 1123 (1962).

TABLE 1. VALUES OF k_{obs} AT 25°

k_{obs} = observed first-order rate constant in min^{-1}; [Diphenylketene]$_{initial}$ ≃ 5 × 10^{-4} M; square brackets represent molarity throughout

(a) 4-Methylaniline						
10^2[Aniline]	0·295	0·590	0·713	1·18		
k_{obs}	0·194	0·652	1·06	2·38		
(b) N,N-dideutro-4-methylaniline						
10^2[Aniline]	0·33	0·515	0·770	1·10		
k_{obs}	0·194	0·415	0·929	1·77		
(c) Aniline						
10^2[Aniline]	0·452	0·904	1·36	1·82	2·26	
k_{obs}	0·101	0·289	0·574	1·12	1·55	
(d) 4-Chloroaniline						
10^2[Aniline]	0·520	1·04	2·07	3·10	4·14	5·17
k_{obs}	0·050	0·106	0·290	0·465	0·970	1·45
(e) N,N-dideutero-4-chloroaniline						
10^2[Aniline]	0·490	1·47	2·45	3·42	4·89	
k_{obs}	0·039	0·196	0·385	0·710	1·23	
(f) 3-Chloroaniline						
10^2[Aniline]	1·02	2·04	3·51	5·02		
k_{obs}	0·036	0·097	0·242	0·516		
(g) 3,4-Dichloroaniline						
10^2[Aniline]	1·84	3·07	4·30	7·85	9·80	
k_{obs}	0·045	0·086	0·133	0·320	0·442	

TABLE 2. VALUES OF k_1 AND k_2 AT 25°

k_1 (l mole^{-1} min^{-1}) and k_2 (l^2 mole^{-2} min^{-1}) are defined by Eq. (3) and are accurate to ±7–10%. Isotope rate ratios k^H/k^D are accurate to ±15–20%. K_a = dissociation constant of anilinium ion in water at 25°

Aniline derivative	k_1	$10^{-2}k_2$	k_1^H/k_1^D	k_2^H/k_2^D	pK_a
4-methyl-	21	150	1·0 (5)	1·2 (5)	5·1
N,N-dideutero-4-methyl-	20	120			—
H-	13	21			4·6
4-chloro-	6·2	3·7	1·0	1·0	4·0
N,N-dideutero-4-chloro-	6·2	3·8			—
3-chloro-	2·3	1·5			3·5
3,4-dichloro-	1·9	0·29			3·0*

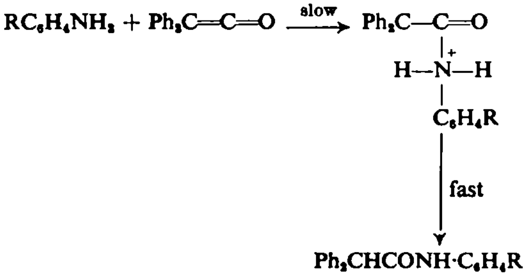
* Estimated using an equation given in Ref. 7.

equilibrium constants which have been obtained suggest that in the present experiments anilines will be predominantly monomeric in solution.

All the data in Table 1 can be fitted to an equation like (3) and average values of k_1 and k_2 for a particular aniline reproduce k_{obs} at any particular aniline concentration within ±10% (±7% for 3,4-dichloroaniline). Values of k_1 and k_2 are in Table 2. We studied also the N-deuterated anilines in two cases and by using the analysis above we were able to obtain the individual isotope effects (k_1^H/k_1^D and k_2^H/k_2^D)

on the first and second-order processes in aniline. The overall isotope effect, reflected in k_{obs} is, of course, in general a function of the aniline concentration because the isotope effects for the first and second-order processes are not necessarily the same and these processes contribute relatively different amounts to k_{obs} at different aniline concentrations. The following points emerge from the data in Tables 1 and 2.

(i) The reaction which is first-order in aniline is not very sensitive to the basicity of the base: k_1 only changes by a factor of 10 while K_a changes by a factor of 100. However, there is a clear relationship and k_1 may be represented to a good approximation by $\log k_1 = -0{\cdot}5 \log K_a - 1{\cdot}23$. The isotope effect (k_1^H/k_1^D) must be close to unity for 4-methyl- and 4-chloroanilines, and it seems probable that the transition state for the reaction between one molecule of base and the ketene is attained with only quite small net changes in the vibrational energy of the N—H bonds. Our values of k^H/k^D, being calculated from rate constants which are themselves averages derived from fitting k_{obs} to Eq. (3), are not sufficiently accurate (Table 2) to detect the presence, or absence, of secondary isotopic effects,[4] i.e. those in which the hydrogen atom concerned is not being in any way transferred to a new site during the rate determining step, for these very rarely disturb k^H/k^D from unity by more than 10–12%/H atom substituted by D. It is of particular interest that the isotope effect has been determined[5] accurately for a rather similar process to that under discussion—the bimolecular reaction between benzoyl chloride and aniline in benzene solution at 25°. By comparing N-dideutroaniline with the protio compound k^H/k^D was found to be 0·86 and this has been assumed to be a secondary isotope effect.[4,5] Such a value differs from unity by an amount which is within our limits of error. It therefore appears legitimate to consider that the process controlled by k_1 approximates to a slow attack by the nitrogen atom on the carbonyl carbon atom, followed by a relatively rapid prototropic rearrangement (4). Such a scheme is in keeping with previous suppositions about the mechanism[1].



$$\mathrm{RC_6H_4NH_2 + Ph_2C{=}C{=}O \xrightarrow{slow} \begin{array}{c} Ph_2C{-}C{=}O \\ |^{+} \\ H{-}N{-}H \\ | \\ C_6H_4R \\ \big\downarrow \text{fast} \\ Ph_2CHCONH{\cdot}C_6H_4R \end{array}} \qquad (4)$$

(ii) The rate constant k_2 (Table 2) for the reactions involving two molecules of aniline shows a much greater dependence on the basicity of the aniline than does k_1 and may be represented by $\log k_2 = -1{\cdot}3 \log K_a - 2{\cdot}46$. The different relationships between k_1 and k_2 and K_a mean that the relative reactivity of any two anilines is a function of the aniline concentration chosen for the comparison, and that at high concentrations (e.g. normal preparative conditions) where the second-order term is kinetically dominant, the most basic anilines are especially favoured. It appears likely that the second aniline molecule acts as a base and helps to enhance the nucleophilicity of the first molecule as it attacks the carbonyl carbon atom.

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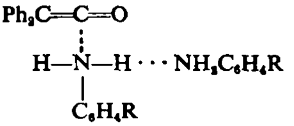
[4] E. A. Halevi, *Progress in Physical Organic Chemistry* Vol. 1, p. 109 (1963).

[5] J. J. Elliott and S. F. Mason, *Chem. and Ind.* 488 (1959).

For this reaction the isotope effect, k_2^H/k_2^D, varies a little more than does k_1^H/k_1^D. The value of 1·25 for 4-methylaniline probably implies a decelleration on deuterium substitution in this instance. The value for 3,4-dichloroaniline may be less than unity, but this is not yet certain. In the absence of information about the effect of deuterium substitution on hydrogen bonding between amines it would be unwise to speculate in any detail about our data. We suggest that the transition state is here concerned with the slow attack of a hydrogen-bonded dimeric aniline species on the carbonyl carbon atom (5).



$$\begin{array}{l} \quad Ph_2C{=}C{=}O \\ \qquad\quad \vdots \\ H{-}N{-}H\cdots NH_2C_6H_4R \\ \qquad | \\ \quad C_6H_4R \end{array} \qquad (5)$$

EXPERIMENTAL

Materials. Diphenylketene was prepared by Smith and Hoehn's method,[6] except that nickel peroxide replaced HgO. Nickel oxide is more convenient to use, does not have to be freshly prepared, and repeatedly gave yields comparable with those quoted by Smith and Hoehn. Redistilled diphenyl ketene (b.p. 120°/3 mm) was stored under N_2 at −30° in a vessel sealed by a silicone-rubber septum, samples for use in kinetic experiments being withdrawn when needed with a Hamilton micro-syringe. Even under these conditions the ketene deteriorates slowly owing to polymerization reactions and fresh batches were made as required.

Reagent grade aniline and 3-chloro-, 4-methyl-, 4-chloro-, and 3,4-dichloroaniline were purified by standard methods. They had b.p. 184°, 230° and m.p. 45°, 71° and 73° respectively. N,N-Dideuterated anilines were prepared by the following general method. Purified aniline (ca. 1 g) was dissolved in ether (Na-dried, 5 ml) and shaken with D_2O (3 ml, 99·9% D) for 30 min. The water layer was removed and shaking continued for a further 30 min with fresh D_2O (3 ml). The phases were finally separated and evaporation of the ether *in vacuo* left the N,N-dideutero product. The deuterium derivatives of 4-methyl- and 4-chloroaniline had m.p. 40°, and 68–69° respectively. NMR (in CCl_4) showed that >90% of the N-bound protium had been replaced.

AnalaR benzene was refluxed over calcium hydride (3 hr) and about 10% of the volume then removed by distillation. The next 50% was distilled from the calcium hydride, and under dry (O_2-free) N_2, when required for preparing reaction mixtures.

Kinetic arrangements. In benzene solution diphenylketene has an absorption band of medium intensity centred at 4050 Å. This band is absent from spectra of the addition products and the rate of disappearance of the ketene can therefore be followed spectrophotometrically. Reaction mixtures were prepared in the following way. A known wt of aniline was placed in a 25-ml graduated flask fitted with a B.10 ground-glass socket and the flask made a receiver in the benzene distillation apparatus. An adaptor fitted with a tap permitted the flask to be made up accurately to the mark with solvent. A portion of the solution was transferred to a stoppered spectrophotometer cell in a dry atmosphere and the cell placed in a thermostatted (25°) housing in a Unicam S.P. 500 UV spectrophotometer. After ca. 20 min reaction was initiated by the addition of a suitable amount (ca. 1·2 μl) of diphenylketene from a Hamilton micro-syringe. With the ketene in at least a 10-fold deficit compared with the aniline, the loss of ketene was always an accurately first-order process, the observed rate constant, k_{obs}, being calculated from a plot of $\log (D_t - D_\infty)$ against time, where D_t and D_∞ represent the optical densities at 4050 Å at times $t = t$ and $t = \infty$ respectively. D_∞ was always very small compared with the initial optical density. Even in the absence of added aniline the ketene absorption falls slowly (owing to dimerization and to reaction with dissolved O_2, this being the reason for distilling the solvent in a stream of N_2). However, at the concentrations we employed the rate of this spontaneous loss was negligible compared with that resulting from reaction with the anilines. The values of k_{obs}, in Table 1, were reproducible to within ±3%.

Reaction products and stoichiometry. The kinetic experiments suggest that the reaction between ketene and the aniline is virtually quantitative. This was checked in four cases by preparative scale

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[6] L. I. Smith and H. H. Hoehn, *Organic Syntheses*, Coll. Vol. III, p. 356.

[7] J. Clark and D. D. Perrin, *Quart. Revs.* **18**, 295 (1964).

experiments which, as far as possible, simulated the kinetic conditions. Three of the resulting anilides do not appear to have been prepared previously. All gave analyses (detailed below) in good agreement with expected values. Diphenylacetanilide had m.p. 185° (lit. 180°). (Found: C, 83·5; H, 6·02; N, 4·94; $C_{20}H_{17}ON$ requires: C, 83·6; H, 5·97; N, 4·98%.) Diphenylacet-4-methylanilide had m.p. ca. 175° (solidifies and melts again at 185–186°). (Found: C, 83·4; H, 6·27; N, 4·85; $C_{21}H_{19}ON$ requires: C, 83·7; H, 6·36; N, 4·65%.) Diphenylacet-4-chloroanilide had m.p. 204°. (Found; C, 74·9; H, 5·07; N, 4·28; Cl, 10·95; $C_{20}H_{16}ONCl$ requires: C, 74·6; H, 5·00; N, 4·34; Cl, 11·01.) Diphenylacet-3,4-dichloroanilide had m.p. 182–183°. (Found: C, 67·7; H, 4·46; N, 3·95; Cl, 19·75; $C_{20}H_{15}ONCl_2$ requires: C, 67·5; H, 4·25; N, 3·93; Cl, 19·90%.)