Kinetics of the Addition of Anilines to Methyl Vinyl Ketone

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Rates of the addition of aniline (A) to methyl vinyl ketone (MVK) to form 4-anilinobutan-2-one (I) have been measured by ultraviolet spectrophotometry at 31·0°. The reaction in aqueous buffers follows second-order kinetics, and involves both general-acid and general-base catalysis. The rates of addition in unbuffered 40 vol. % aqueous dioxan also satisfy a similar rate equation for general-acid and -base catalysis, where aniline itself acts as a catalysing base. Mono- and di-basic phosphate ions show catalysis much more strongly than acetic acid or acetate ion probably because of bifunctional catalysis through a cyclic transition state. Electron-withdrawing group on aniline lower the rate, the substituent effect giving a Hammett ρ-value of −1·60. A mechanism which involves an activated complex of free aniline or aniline associated with base and hydrogen-bonded or free methyl vinyl ketone is postulated and discussed.

SUBSTITUTED quinolines are prepared by the Doebner–Miller synthesis [1,2] by heating acidified mixtures of anilines and αβ-unsaturated carbonyl compounds (or compounds leading to αβ-unsaturated carbonyls by dehydration etc.) with oxidising agents such as ferric chloride. The synthesis seems to involve the addition of the anilines to the double bond in the αβ-unsaturated carbonyl compounds. For example, the reaction of aniline with methyl vinyl ketone in an acidic solution is known to give a high yield of an adduct, 1-anilinobutan-2-one (I), without formation of an ordinary Schiff's base.

$$\mathrm{PhNH_2 + CH_2{:}CH{\cdot}CO{\cdot}Me \longrightarrow PhNH{\cdot}CH_2{\cdot}CH_2{\cdot}CO{\cdot}Me\ (I)} \qquad (1)$$

The adduct can then be converted into lepidine by heating with acid and an oxidising agent.[3,4]

Little has been known about the mechanism of the Doebner–Miller synthesis. As a first step in the elucidation of this type of reaction, an attempt was made to clarify the mechanism of addition of aniline to methyl vinyl ketone. Although the amine–carbonyl additions leading, for example, to oxime, semicarbazone, and Schiff's base have been extensively studied,[5] no report is available on the kinetics of additions of amines to αβ-unsaturated carbonyl compounds.

The present paper describes the kinetics and the effects of acid and base in the addition reaction of aniline to methyl vinyl ketone, and proposes a mechanism.

RESULTS AND DISCUSSION

The addition of aniline (A) to methyl vinyl ketone (MVK) is said to be reversible,[3] but the equilibrium shifts

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[1] A. Doebner and W. von Miller, *Ber.*, 1881, **14**, 2812; 1882, **15**, 3075; 1883, **16**, 1665; 1891, **24**, 1720; 1892, **25**, 2075.

[2] R. H. F. Manske and M. Kulka, *Org. Reactions*, 1953, **7**, 59.

[3] S. Tamura and M. Yamasaki, *J. Pharm. Soc. Japan*, 1956, **76**, 915.

[4] G. M. Badger, H. P. Crocker, B. C. Ennis, J. A. Gayler, W. E. Matthews, W. G. C. Raper, E. L. Samuel, and T. M. Spotstood, *Austral. J. Chem.*, 1963, **16**, 817.

[5] L. do Amaral, W. A. Sandstrom, and E. H. Cordes, *J. Amer. Chem. Soc.*, 1966, **88**, 2225.

largely to the right (product) side, since 4-anilinobutan-2-one did not decompose appreciably under the kinetic conditions. The conversion into 4-anilinobutan-2-one is almost quantitative. Hence, the rate calculation as a reversible reaction is virtually unnecessary.

Rate Law in Aqueous Buffers, and Acidity Effect.—When the reaction is carried out in an aqueous acetate or phosphate buffer, the rate of the formation of 4-anilinobutan-2-one fits the second-order equation:

$$d[\mathrm{Adduct}]/dt = k[\mathrm{MVK}][\mathrm{A}] \qquad (2)$$

Here, [MVK] and [A] are the stoicheiometric concentration of methyl vinyl ketone and the aniline, respectively. Typical results are in Table 1.

TABLE 1

The apparent second-order rate constants for the addition of aniline (A) to methyl vinyl ketone (MVK) in a phosphate buffer with the ratio of $[H_2PO_4^-]/[HPO_4^{2-}]$ 1/4, $[HPO_4^{2-}]$ 2·00 × 10^{-2}M, pH 7·30, and ionic strength 0·20 at 31·0°, with various initial concentrations of reactants (the value of k is nearly equal to k_f at this pH)

Initial concn. (10^{-2}M)		10^2k
[MVK]	[A]	(M^{-1} sec.$^{-1}$)
1·60	1·60	1·94
1·60	0·80	1·83
0·80	1·60	1·87
0·80	0·80	1·79

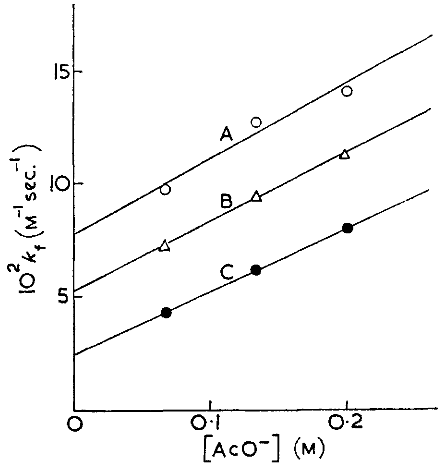

FIGURE 1 Plot of the second-order rate constant, k_f, against [AcO⁻] for the addition of aniline to methyl vinyl ketone in acetate buffers of ionic strength 0·20 at 31·0°

A, [AcOH]/[AcO⁻] 4/1, pH 4·05; B, 2/1, 4·25; C, 1/1, 4·60

If a protonated aniline is unreactive as in ordinary amine–carbonyl reactions, the rate constant k should be expressed as:

$$k = k_f/\{1 + ([H^+]/K_a)\} \qquad (3)$$

where k_f is the rate constant for the reaction of free aniline, and K_a is the acidity constant for anilinium ion. The observed slope (—0·95) of a line in a plot of log k_f at zero buffer concentration against pH (below 5) suggests hydronium ion catalysis. Practically, $k = k_f$ at pH above 7, since pK_a of anilinium ion is 4·58.

Figure 1 shows the results obtained in acetate buffers with the initial concentration of each reactant at 0·0100M.

TABLE 2

Catalytic constants for the addition of aniline to methyl vinyl ketone at 31·0°

Catalyst	Solvent	
	Water	40 vol. % dioxan–water
$MeCO_2H$	0·02	—
$MeCO_2^-$	0·26	—
$H_2PO_4^-$	0·45	—
HPO_4^{2-}	0·42	—
H^+	*ca.* 10^3 *	—
H_2O	5·5 × 10^{-3}	1·6 × 10^{-4}
$PhNH_2$	—	4·3 × 10^{-3}
Pyridine	—	7·0 × 10^{-2}

* For free aniline.

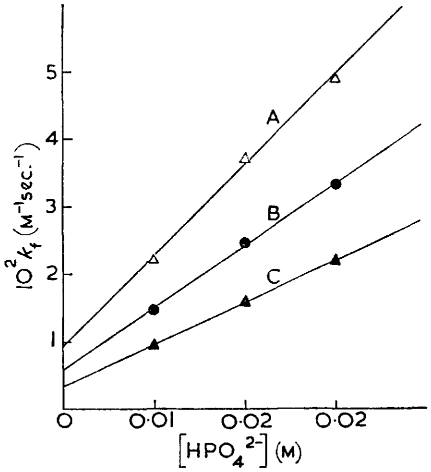

FIGURE 2 Plot of the second-order rate constant, k_f, against $[HPO_4^{2-}]$ for the addition of aniline to methyl vinyl ketone in phosphate buffers of ionic strength 0·20 at 31·0°

A, $[H_2PO_4^-]/[HPO_4^{2-}]$ 2/1, pH 6·50; B, 1/1, 6·80; C, 1/4, 7·30

As is apparent from Figure 1, the value of k_f at a constant value of the ratio [AcOH]/[AcO⁻] varies linearly on changing the buffer concentration, while the slope of the plotted line varies with change in the ratio. These results indicate the operation of both general-acid (AcOH) and general-base (AcO⁻) catalysis.[6-8] However, the acid catalysis by acetic acid is very weak.

Figure 2 shows the results obtained with phosphate buffers, where both general-acid ($H_2PO_4^-$) and general-base (HPO_4^{2-}) catalysis is also observed. These catalytic constants are shown in Table 2. The catalytic constant for monobasic phosphate ion is much larger than for acetic acid of stronger acidity. Dibasic phosphate ion shows catalysis comparable with that of monobasic phosphate ion.

In experiments at higher pH, *e.g. ca.* 11 in a carbonate

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[6] A. A. Frost and R. G. Pearson, ' Kinetics and Mechanism,' Wiley, New York, 1952, ch. 9.

[7] Y. Ogata, A. Kawasaki, and N. Okumura, *J. Org. Chem.*, 1965, **30**, 1636; *Tetrahedron*, 1966, **22**, 1731.

[8] Y. Ogata and A. Kawasaki, *J. Chem. Soc. Japan, Ind. Chem. Sect.*, 1966, **69**, 811.

buffer or a triethylamine–hydrochloride buffer, the yields of product (I) were lower and the second-order rate law failed, probably because methyl vinyl ketone was consumed by polymerisation at these high pH values.[9] A complete pH–rate profile cannot be obtained because of side-reactions at extreme pH.

Effect of Temperature.—The Arrhenius plot for the reaction holding the ratio $[H_2PO_4^-]/[HPO_4^{2-}]$ constant and with the initial concentration of each reactant at $8{\cdot}00 \times 10^{-3}$M in the temperature range 20—50° gave the Arrhenius parameters in Table 3.

TABLE 3

Arrehenius parameters for the addition of aniline to methyl vinyl ketone in a phosphate buffer with $[H_2PO_4^-]/[HPO_4^-]$ 1/1, pH 6·80, and ionic strength 0·20

$[H_2PO_4^-]$ (M)	10^2k_2 (M^{-1} sec.$^{-1}$) 21°	31°	41°	50°	E_a (kcal. mole^{-1})	$\Delta S^\ddagger$ (e.u.)
0·0200	3·04	3·90	5·12	6·71	5·2	−50
0·0133	2·21	2·88	4·06	5·50	5·8	−48
0·0067	1·27	1·60	2·48	2·96	6·1	−49

The observed energies and entropies of activation resemble those for the additions of amines to aryl vinyl sulphone,[10] *i.e.*, E_a 6·6 kcal./mole and $\Delta S^\ddagger$ −41 e.u., which suggests an analogous transition state for the present reaction.

Substituent Effect.—The reactions of substituted anilines with methyl vinyl ketone were carried out in a phosphate buffer of 5 vol. % aqueous dioxan at pH 6·90 and 31·0°. The electron-withdrawing groups on aniline decrease the rate, as is the case in ordinary amine–carbonyl additions, suggesting that the nitrogen atom of the amine becomes more positive in the transition state of the rate-determining step such as in a nucleophilic attack of amine. The second-order rate constants 10^2k_f (M^{-1} sec.$^{-1}$) are as follows: *p*-MeO, 9·00; *p*-Me, 4·44; unsubstituted, 2·55; *p*-Cl, 1·85; *p*-NO$_2$, 0·151. The Hammett plot (Figure 3) gives a value of ρ −1·60 ($r = 0{\cdot}998$, $s = 0{\cdot}09$). Even if the reaction is acid-catalysed, the reactions of substituted anilines with benzaldehyde, benzoin, and nitrosoaniline have been shown to have negative overall ρ-values.[11]

Rate Law in Unbuffered Aqueous Dioxan.—When the reaction is carried out in an unbuffered medium, it is expected that the reaction may be catalysed by aniline itself. For the clarification of this situation, the reaction was conducted at 31·0° in a 2 : 3 (v/v) mixture of dioxan and water, which was employed because of the low solubility of (I) in pure water.

The observed rate fits the equation:

$$v = (k_0 + k_A[A])[MVK][A] \qquad (4)$$

where k_0 is an uncatalysed or solvent-catalysed rate constant and is calculated to be $1{\cdot}6 \times 10^{-4}$ M^{-1} sec.$^{-1}$, and k_A is an aniline-catalysed rate constant with a value of $4{\cdot}3 \times 10^{-3}$ M^{-2} sec.$^{-1}$. [A] is practically equal to the concentration of free aniline at this pH of *ca.* 7. These k_0 and k_A values were calculated graphically.

As an example of another organic base, 0·005—0·04M-pyridine was added to the reaction mixture. Similar base catalysis was observed, the rates satisfying the equation:

$$v = (k_0 + k_H[A] + k_P[P])[MVK][A] \qquad (5)$$

where P represents pyridine, and the pyridine-catalysing constant k_P is calculated graphically to be $3{\cdot}5 \times 10^{-2}$ M^{-2} sec.$^{-1}$.

In general, the rate may be expressed as:

$$v = (k_0 + k_{HA}[HA] + k_B[B])[MVK][A] \qquad (6)$$

where k_{HA} and k_B are catalytic constants for acid (HA) and base (B), respectively.

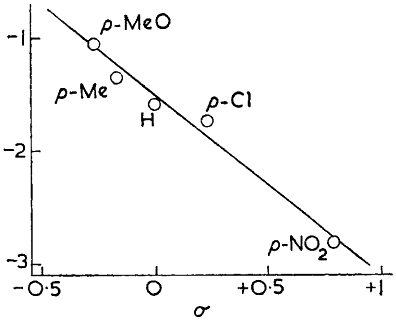
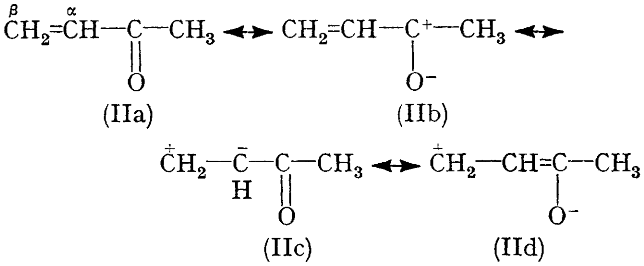


FIGURE 3 Hammett plot for the addition of substituted anilines to methyl vinyl ketone in a phosphate buffer of 5 vol. % aqueous dioxan with $[H_2PO_4^-]/[HPO_4^{2-}]$ 1/1, $[HPO_4^{2-}]$ $2{\cdot}00 \times 10^{-2}$M, pH 6·90, and ionic strength 0·20 at 31·0°, with the initial concentrations of reactants at 0·003—0·006M for anilines and 0·003—0·03M for methyl vinyl ketone

Mechanism.—The resonance forms (IIa—d) rationalise the nucleophilic attack of aniline on the β-carbon atom of methyl vinyl ketone.[12]



$$\overset{\beta}{C}H_2{=}\overset{\alpha}{C}H{-}C({=}O){-}CH_3 \longleftrightarrow CH_2{=}CH{-}C^+(O^-){-}CH_3 \longleftrightarrow \overset{+}{C}H_2{-}\overset{-}{C}H{-}C({=}O){-}CH_3 \longleftrightarrow \overset{+}{C}H_2{-}CH{=}C(O^-){-}CH_3$$

The acid catalysis suggests the participation of proton or general-acid in the transition state; the protonation or co-ordination of acid may occur at a carbonyl oxygen atom.

Since the pK_a value of the conjugate acid of methyl vinyl ketone may be *ca.* −6, by analogy with other

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[9] N. Murata, H. Arai, and Y. Tashima, *J. Chem. Soc. Japan, Ind. Chem. Sect.*, 1953, **56**, 709.

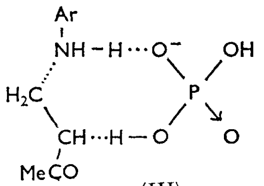
[10] S. T. McDowell and C. J. M. Stirling, *J. Chem. Soc.* (*B*), 1967, 343, 348, 351.

[11] E. F. Pratt and M. J. Kammlet, *J. Org. Chem.*, 1961, **26**, 4029; 1963, **28**, 1366; Y. Ogata and Y. Takagi, *J. Amer. Chem. Soc.*, 1958, **80**, 3591.

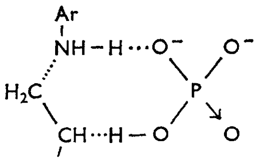
[12] M. Friedman and J. S. Wall, *J. Org. Chem.*, 1966, **31**, 2888.

ketones,[13] the concentration of protonated methyl vinyl ketone under these reaction conditions (0·01M-MVK at pH 4—7) may be 10^{-12}—10^{-15}M. On account of the observed rate constant 10^{-2} M^{-1} sec.$^{-1}$ at 31·0°, the rate constant for the reaction of protonated methyl vinyl ketone is calculated to be *ca.* 10^{8}—10^{11} M^{-1} sec.$^{-1}$ which is close to the diffusion-controlled rate constant,[14] $1\cdot4 \times 10^{11}$ M^{-1} sec.$^{-1}$. Therefore, the protonated methyl vinyl ketone is improbable as a main reactive species in the rate-determining step, although a very rapid attack by amine on protonated methyl vinyl ketone cannot completely be ruled out.

The present reaction is different from the ordinary general-acid and general-base catalysis effective for the addition of weak amines to carbonyl carbon atoms,[8] since the simple Brönsted catalysis law fails for this reaction, as is obvious from the observed catalytic constants. A much higher catalytic effect for monobasic phosphate ion, $H_2PO_4^-$, which has lower acidity than acetic acid, strongly suggests a specific bifunctional catalysis by monobasic phosphate ion both as an acid and a base through an activated complex (III). Also, similar catalysis (IV) is probable with dibasic phosphate ion, HPO_4^{2-}.

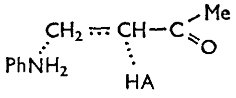


(III)

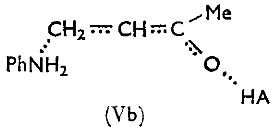


(IV)

The similarity between the catalytic constant for dibasic phosphate ion and that for monobasic phosphate ion supports these mechanisms. The observed value of activation parameters in phosphate buffers (E_a 5·2—6·1 kcal. mole^{-1}; $\Delta S^{\ddagger}$ —48 to —50 e.u.) are analogous to those for the addition of amines to aryl vinyl sulphone in ethanol (E_a 6·6 kcal. mole^{-1}; $\Delta S^{\ddagger}$ —41 e.u.), in which an analogous cyclic transition state has been postulated. On the contrary, the acid catalysis by acetic acid may be a simple proton-transfer from the acid either to the α-carbon atom (Va) concerted with the attack of aniline or to a carbonyl oxygen atom (Vb). The catalysis (Va) resembles the phosphate catalysis (III) and (IV) mentioned above.



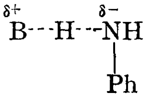
(Va)



(Vb)

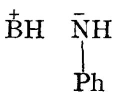
The acid catalysis might take part in a proton-transfer from acid to carbonyl oxygen, leading to an enolic intermediate. However, the mechanism involving this intermediate is less probable, since the absorption of the keto-form of 4-anilinobutan-2-ones seems to be almost the same as that of the enol form, and the measured rates are those of the addition step. For example, the absorption spectrum of *N*-but-2-enylaniline in ethanol ($\lambda_{max.}$ 249 and 295 mμ; log ε 4·10 and 3·30) is almost identical with that of 4-anilinobutan-2-one (247 and 295 mμ; log ε 4·07 and 3·37). Furthermore, the spectra of *N*-alkylanilines do not vary significantly with unconjugated substituents, *e.g.*, methylaniline (241 and 287 mμ; log ε 3·96 and 3·20), ethylaniline (241 and 287 mμ; log ε 3·96 and 3·16), isopropylaniline (243 and 288 mμ; log ε 3·91 and 3·06), butylaniline (242 and 290 mμ; log ε 4·11 and 3·28), and isobutylaniline (245 and 292 mμ; log ε 4·02 and 3·20) in 0·004N-sodium hydroxide–48% ethanol mixture. Therefore, the rate-determining step is the addition of anilines to methyl vinyl ketone, and not the isomerisation of the enol to the keto-form of the adduct. Furthermore, the phosphate ion catalysis suggests that the acid catalysis is a proton-transfer from acid to the α-carbon atom of methyl vinyl ketone (IV), since the phosphate ion catalysis involving a bridge from N to O (ten-membered ring) is unlikely.

On the other hand, the base catalysis suggests a pull by hydrogen-bonding (VIa) or the abstraction of a proton (VIb) from an aniline molecule by base B, where the base may be aniline itself. However, (VIb) is probably ruled out for the base catalysis, since the concentration of the conjugate base of aniline is too low for the condensation to occur (pK_a for aniline is 27).[15]



$$\overset{\delta+}{B}\cdots H\cdots\underset{Ph}{\overset{\delta-}{N}}H$$

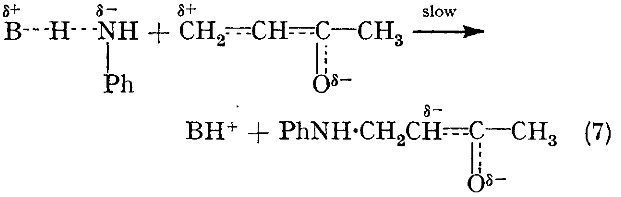
(VIa)



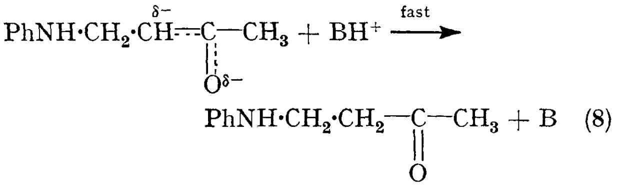
$$\overset{+}{B}H\quad \underset{Ph}{\overset{-}{N}}H$$

(VIb)

Complex (VIa) is similar to the complex for the phosphate catalysis, (III) and (IV). This consideration leads to a mechanism for the base catalysis. Since the simple



$$\overset{\delta+}{B}\cdots H\cdots\underset{Ph}{\overset{\delta-}{N}}H + \overset{\delta+}{C}H_2\overset{\cdots}{=}CH\overset{\cdots}{=}\underset{O^{\delta-}}{C}-CH_3 \xrightarrow{\text{slow}} BH^+ + PhNH\cdot CH_2CH\overset{\cdots}{=}\underset{O^{\delta-}}{\overset{\delta-}{C}}-CH_3 \quad (7)$$



$$PhNH\cdot CH_2\cdot CH\overset{\cdots}{=}\underset{O^{\delta-}}{\overset{\delta-}{C}}-CH_3 + BH^+ \xrightarrow{\text{fast}} PhNH\cdot CH_2\cdot CH_2-\underset{O}{\overset{}{C}}-CH_3 + B \quad (8)$$

proton-transfer from catalyst acid to anionic α-carbon atom (8) may be fast, the attack of aniline on methyl vinyl ketone (7) is probably rate-determining. The observed negative ρ-value with *para*-substituted anilines

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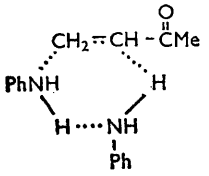
[13] H. J. Cambell and J. T. Edward, *Canad. J. Chem.*, 1960, **38**, 2109; R. T. Stewart and K. Yates, *J. Amer. Chem. Soc.*, 1958, **80**, 6355.

[14] M. Eigen and L. de Maeyer, *Z. Elektrochem.*, 1955, **59**, 986.

[15] W. K. McEwen, *J. Amer. Chem. Soc.*, 1936, **58**, 1124.

agrees with a nucleophilic attack of anilines on the methyl vinyl ketone in the rate-determining step.

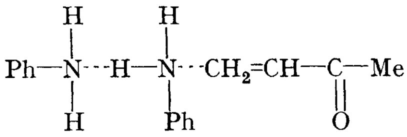
A cyclic transition state has been postulated for the aminolysis of ester [16] and the addition of amines to aryl vinyl sulphone.[10] An analogous transition state (VII), however, is less plausible, since the stronger base



(VII)

catalysis is observed with pyridine having no effective hydrogen atom in comparison with aniline.

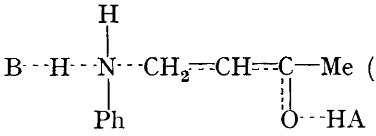
Amines are known to dimerise in non-aqueous solvents such as carbon tetrachloride,[17] and attack of dimeric aniline on dimethylketen in ether has been postulated.[18] The observed kinetic second-order term with respect to aniline can better be described as a base-catalysis rather than an attack of dimerised aniline, since the mixture solvent (40 vol. % aq. dioxan) has greater dissociating power, and since pyridine can act as an effective catalyst. Anyway, attack of dimeric aniline on methyl vinyl ketone (VIII) is no more than a kind of general-base catalysis with aniline itself.



$$\mathrm{Ph{-}\overset{H}{\underset{H}{N}}{\cdots}H{-}\overset{H}{\underset{Ph}{N}}{\cdots}CH_2{=}CH{-}\underset{O}{\underset{\|}{C}}{-}Me}$$

(VIII)

Finally, a concerted mechanism through a transition state (IX) cannot be ruled out on the basis of the observed kinetics.



$$\mathrm{B{\cdots}H{\cdots}\overset{H}{\underset{Ph}{N}}{\cdots}CH_2{=}CH{=}\underset{O\cdots HA}{\underset{\vdots}{C}}{-}Me}$$

(IX)

This reaction of αβ-unsaturated carbonyls with amine is analogous to the cyanoethylation of ethanolamine [19] or the addition of piperidine to aryl vinyl sulphone.[10] However, no base-catalysis has been observed for these additions. This is probably due to the stronger basicity of these amines which needs no activation by the basic catalyst for the addition.

EXPERIMENTAL

Materials.—Methyl vinyl ketone was prepared by the dehydration of 4-hydroxybutan-2-one [9] which was obtained by the condensation of acetone with formaldehyde. The product was dried over calcium chloride and distilled, b.p. 79—81°. Substituted anilines were purified by distillation in a nitrogen atmosphere or by recrystallisation until their b.p.s or m.p.s agreed with literature values: *p*-anisidine, b.p. 94·5—94·8°/1·5 mm.; *p*-toluidine, b.p. 69·5—71·5°/4 mm.; aniline, b.p. 85·8—86·2°/25 mm.; *p*-chloroaniline, b.p. 85·0—86·0°/3 mm.; *p*-nitroaniline, m.p. 146·5—147·5°. Dioxan was distilled from sodium, b.p. 101—102°. Other, commercial liquid materials were redistilled before use.

Authentic 4-anilinobutan-2-ones were prepared by a modification of Tamura's procedure.[3] Methyl vinyl ketone (0·1 mole) was added dropwise to a mixture of the substituted aniline (0·1 mole), conc. hydrochloric acid (20 ml.), and water (100 ml.) during 0·5 hr. at room temperature. The flask was warmed to 50° for 5 hr., neutralised with 1N-sodium hydroxide, and extracted with ether. The ether extract, after evaporation of solvent, was worked up in the usual way. The crude products were purified by chromatography (on silicic acid) or by distillation followed by recrystallisation. The yield of the isolated 4-anilinobutan-2-ones was 30—50% because of its decomposition with hydrochloric acid together with the loss on purification. However, in the absence of hydrochloric acid, 4-anilinobutan-2-one (60 g.) was obtained in a better yield (75·8%) from the reaction of aniline (50 g.) with methyl vinyl ketone (34 g.) at 40° for 4 hr. On the other hand, spectrophotometry showed that the yield under the kinetic conditions reached over 80% except for 4-(4-nitroanilino)butan-2-one; the precipitate of the adduct was observed as the reaction proceeded. The products were confirmed by the identity of the ultraviolet spectra of diluted reaction mixture with that of a mixture of aniline and 4-anilinobutan-2-one of known composition.

Reaction Products.—Under kinetic conditions, *i.e.*, in 50 vol. % dioxan–0·025M-phosphate buffer solutions (16 ml.), the yields of the adducts isolated from each amine (0·56 mole) and methyl vinyl ketone (0·67 mole) at room temperature for 2—4 hr. are shown in Table 4. The reaction product was extracted twice with ether (5 and then 10 ml.), washed with water, and dried over anhydrous sodium sulphate. The solvent and excess of methyl vinyl ketone were distilled off in a vacuum, and the residue was cooled, to give solid. The crude adduct was obtained in 90—99% yield and recrystallised twice from light petroleum. The yields of the recrystallised product are listed in Table 4. All melting points and infrared spectra of adducts are consistent with those obtained in an aqueous solution.

TABLE 4

The aniline–methyl vinyl ketone adducts obtained in 50 vol. % dioxan–0·025M-phosphate buffer solutions (16 ml.) at 20° [a]

R in	Yield[b]			Infrared spectra [e] (cm.$^{-1}$)		
RNH·CH$_2$·CH$_2$·CO·Me	(g.)	(%)	M.p.	ν(NH)	ν(C=O)	Others
Ph	0·87	53·4	33—35°	3370	1715	740, 865
p-MeC$_6$H$_4$	1·14	64·5	39—40	3380	1710	810
p-ClC$_6$H$_4$	1·37	65·8	70—72	3380	1710	815
p-MeOC$_6$H$_4$	1·30 [c]	67·4	Liquid	3375 [d]	1715 [d]	820 [d]
p-O$_2$NC$_6$H$_4$	0·83	79·8	84—85°	3350	1710	836

[a] MVK = 0·012 mole, RNH$_2$ = 0·01 mole; *p*-nitroaniline used was 0·005 mole. [b] Based on RNH$_2$. [c] Purified by chromatography on silicic acid. [d] Liquid film on NaCl. [e] KBr disc.

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The addition of aliphatic amines to methyl vinyl ketone occurs analogously with aliphatic amines. For example, benzylamine gave 4-benzylaminobutan-2-one (62·4%) and butylamine gave 4-butylaminobutan-2-one (57·6%) under the same conditions; the infrared spectra (film) showed NH (3425 cm.$^{-1}$, singlet) and strong C=O (1705 cm.$^{-1}$) bands.

TABLE 5

Third-order rate constants ($v = k_3$[MVK][A^2]) in unbuffered solutions at 31°

[MVK]$_0$ (M)	[A]$_0$ (M)	[Pyridine]$_0$ (M)	$10^3 k_3$ (M^{-2} sec.$^{-1}$)
0·10	0·15	0	5·5
0·10	0·10	0	6·0
0·10	0·075	0	6·1
0·10	0·10	0·040	33·8
0·10	0·10	0·020	18·8
0·10	0·10	0·005	10·0

The observed rate was determined by following the increase in absorbance of the adducts, 4-anilinobutan-2-ones, at appropriate wavelengths. Therefore, it is certain that the reactions whose rate were determined gave the expected products.

4-Anilinobutan-2-one had b.p. 117—119°/2 mm., m.p. 35·0—35·5° (lit.,[3] 36°), $\lambda_{\text{max.}}$ (buffer, pH 7) 239 mμ (log ε 3·99).

4-(4-Methylanilino)butan-2-one had b.p. 128—133°/2 mm., m.p. 40·0—41·0° (lit.,[3] 41—41·5°), $\lambda_{\text{max.}}$ (buffer, pH 7) 239·5 mμ (log ε 3·97).

4-(4-Chloroanilino)butan-2-one formed *needles*, m.p. 69·2—70·0°, $\lambda_{\text{max.}}$ (buffer, pH 7) 247 mμ (log ε 4·12), $\nu_{\text{max.}}$ (KBr) 3380 (>NH), 1710 (C=O), and 820 cm.$^{-1}$ (1,4-substitution) (Found: C, 60·4; H, 6·0; N, 7·15. $C_{10}H_{12}ClNO$ requires C, 60·45; H, 6·1; N, 7·05%).

4-(4-Nitroanilino)butan-2-one formed yellow *needles*, m.p. 154—156°, $\lambda_{\text{max.}}$ (buffer, pH 7) 408 mμ (log ε 4·26), $\nu_{\text{max.}}$ (KBr) 3370 (>NH), 1720 (C=O), and 848 cm.$^{-1}$ (1,4-substitution) Found: C, 58·2; H, 5·9; N, 13·15. $C_{10}H_{12}N_2O_3$ requires C, 57·7; H, 5·8; N, 13·45%).

4-(4-Methoxyanilino)butan-2-one was a yellow *liquid* (isolated by chromatography), $\lambda_{\text{max.}}$ (buffer, pH 7) 238 mμ (log ε 4·02), $\nu_{\text{max.}}$ (film) 3380 (>NH), 1720 (C=O), 1245 (OMe), and 825 cm.$^{-1}$ (1,4-substitution) (Found: C, 68·2; H, 7·65; N, 7·5. $C_{11}H_{15}NO_2$ requires C, 68·35; H, 7·8; N, 7·25%).

Rate Measurement.—The reaction was followed by ultraviolet spectrophotometry using a Shimadzu SV-50A spectrophotometer. After starting the reaction by mixing thermostatted solutions of reactants, aliquots were taken out at appropriate intervals, diluted with a phosphate buffer of pH 7, and the absorbance at a given wavelength measured to calculate the conversion. A blank test confirmed the additivity of the absorbance of the three components in the reaction mixture. The wave-lengths and molar extinction coefficients used for the determination of the rate are listed together with *para*-substituents (λ, log ε of substituted aniline and 4-anilinobutane-2-one): H, 250 mμ (3·068, 3·737); Cl, 260 mμ (3·145, 3·857); NO_2, 260 mμ (3·332, 3·462), 320 mμ (3·602, 3·049); MeO 260 mμ (2·703, 3·514); Me 260 mμ (2·753, 3·396). In the reaction with aqueous buffers (pH 4—8), the second-order plot of $(\ln[A]/[A]_0 - \ln[MVK]/[MVK]_0)/([A]_0 - [MVK]_0)$ against time gave straight lines. On the other hand, for the reactions in unbuffered media with initial concentrations of $[A]_0 = 0{\cdot}18$—$0{\cdot}20$M and $[MVK]_0 = 0{\cdot}10$—$0{\cdot}30$M, third-order kinetics, $v = k_3[MVK][A]^2$, were satisfied (Table 4). The observed third-order rate constant k_3 decreased with increasing [A], and hence k_A was evaluated from the intercept of plot of k_3 against 1/[A]. The value for the pyridine-catalysing constant k_P was calculated from a plot of k_3 against [P].

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