

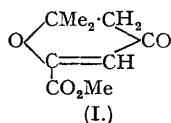
**6. Acid-Base Catalysis in Non-aqueous Solvents. Part X. The Isomerisation of Methyl Mesityl Oxide Oxalate in Chlorobenzene Solution at 99°.**

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Measurements are reported on the rate of conversion of the enolic  $\alpha$ -form of methyl mesityl oxide oxalate into the cyclic  $\beta$ -form. The reaction is of the first order, catalysed by acids and by bases, and data are given for catalysis by 11 amines and 8 carboxylic acids. The reaction velocity is proportional to the catalyst concentration at low concentrations, but at high concentrations tends to a limiting value which is independent of both the concentration and the nature of the catalyst. This is interpreted by supposing that the  $\alpha$ -form is first converted by the catalyst into the isomeric enol, which then changes to the  $\beta$ -form at a rate independent of the catalyst. The effectiveness of catalysts in the first stage of the reaction is closely related to their dissociation constants in water.

THE esters of mesityl oxide oxalic acid were first prepared by Claisen (*Annalen*, 1896, **291**, 132), and various properties of the  $\alpha$ - and  $\beta$ -forms were measured by Brühl (*Z. physikal. Chem.*, 1899, **30**, 12). Both these authors assigned the structures  $\text{CMe}_2\text{:CH}\cdot\text{CO}\cdot\text{CH}\cdot\text{C}(\text{OH})\cdot\text{CO}_2\text{Me}$  and  $\text{CMe}_2\text{:CH}\cdot\text{CO}\cdot\text{CH}_2\cdot\text{CO}\cdot\text{CO}_2\text{Me}$  to the  $\alpha$ - and the  $\beta$ -form respectively. Later, Dieckmann (*Ber.*, 1920, **53**, 1772) called attention to a number of points which do not accord well with the idea of a simple keto-enol tautomerism. In particular, the qualitative observations then available showed that the conversion of the  $\alpha$ - into the  $\beta$ -form was always slow, and was catalysed by acids more than by bases; both these points contrast with the known behaviour of simple keto-

enol tautomers.



Dieckmann agreed with the above structure for the  $\alpha$ -form, but suggested that the  $\beta$ -form is actually (I), and this formulation is now generally accepted, being supported by other chemical evidence (Borsche and Thiele, *Ber.*, 1923, 56, 2132) and by absorption spectra (Morton and Rogers, *J.*, 1926, 713). The reaction was selected for kinetic study because it is more convenient than the very labile keto-enol changes, and because it offers an opportunity of studying catalysis by amine bases. Although some of these bases have been

used extensively as catalysts in preparative organic chemistry, there is practically no quantitative information on their effectiveness as catalysts, since most of the existing kinetic work on basic catalysis deals with anion bases.

#### EXPERIMENTAL.

*Materials.*—Both forms of methyl mesityl oxide oxalic ester were prepared as described by Claisen (*loc. cit.*). The  $\alpha$ -ester was dissolved in dilute sodium carbonate solution and precipitated by a slight excess of dilute acetic acid at 0°: this was repeated several times, and the product recrystallised several times from ligroin (m. p. 84°). The  $\beta$ -ester was dissolved in ether and the solution shaken with sodium carbonate solution to remove any  $\alpha$ -ester. After distillation of the ether the  $\beta$ -ester was recrystallised from ligroin (m. p. 67°).

Benzylamine was a pure commercial product. Piperidine, diethylamine, triethylamine,  $\alpha$ -picoline and *s*-collidine were dried over solid potassium hydroxide and fractionally distilled. Diethyl-*p*-toluidine was fractionally distilled four times, and nicotine twice under reduced pressure. Diethylaniline was fractionally frozen (m. p. -34.5°) and then twice redistilled. Benzyl-diethylamine was prepared by heating diethylamine and benzyl chloride in a sealed tube: it was dried over solid sodium hydroxide and twice fractionally distilled. Trimethylamine was prepared by warming the hydrochloride with sodium hydroxide solution, and absorbed in chlorobenzene after passage through solid sodium hydroxide. Since the results with this base were anomalous, various methods of purification were tried, including repeated reconversion into the hydrochloride. All samples gave substantially the same kinetic results.

Monochloroacetic, benzoic, and *o*-nitrobenzoic acids were used without further purification. "AnalaR" Acetic acid was four times fractionally frozen (m. p. 15.85°) and then gave kinetic results identical with the original sample. *m*-Nitrobenzoic acid was twice recrystallized from aqueous acetone mixture, and *p*-toluic acid from water. Dichloroacetic acid was fractionally distilled. Trimethylacetic acid was prepared from pinacol (*Org. Synth.*, Coll. Vol. I, p. 512) and dried by distilling it with benzene: it was then fractionated three times in a vacuum.

Chlorobenzene was dried over phosphoric oxide and fractionally distilled: it boiled within 0.2°.

*Estimation of the  $\alpha$ -Ester.*—This was effected by means of the colour reaction with alcoholic ferric chloride solution, which had been used by Knorr and Schubert (*Ber.*, 1911, 44, 2777) for equilibrium measurements. The colour measurements were carried out with a Hilger "Spekker" absorptiometer, using the green mercury line and micro-cells holding 0.7 c.c. Preliminary experiments showed that the absorption at this wave-length was independent of the excess ferric chloride concentration and of variations in room temperature, and that it remained unchanged over a period of several hours. The colour was destroyed by the presence of amine bases, but was unaffected by carboxylic acids. Even in the presence of amines the colour developed its normal value provided that trichloroacetic acid was present in more than sufficient quantity to neutralise the amine. Calibration with solutions containing known amounts of  $\alpha$ -ester and  $\beta$ -ester showed that the drum-reading was directly proportional to the concentration of  $\alpha$ -ester in the range 0—0.0015M, and that the concentration could be measured in this range with an error less than 10<sup>-5</sup>M. In all the kinetic measurements the comparison cell of the absorptiometer contained a solution of the same composition as that being investigated, with the omission of the  $\alpha$ -ester.

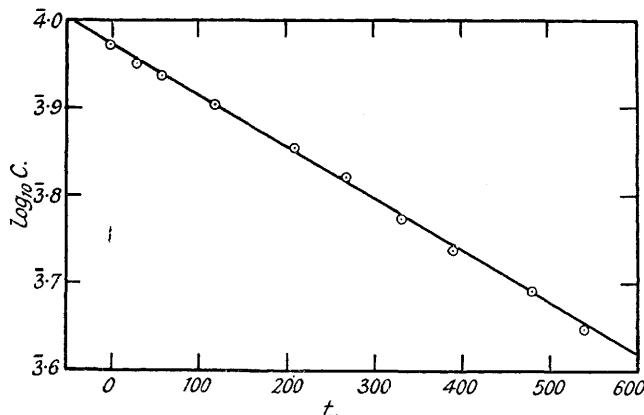
*Measurement of Reaction Velocity.*—Kinetic measurements were carried out in a steam-bath operating at slightly less than atmospheric pressure. The pressure was regulated by hand to compensate for variations in atmospheric pressure, and the temperature thus maintained at 99° ± 0.1°. The reaction mixture was initially 0.01M with respect to  $\alpha$ -ester, and contained the appropriate amount of catalyst in chlorobenzene solution. It was made up by weight, and samples of 0.2—0.5 c.c. transferred by an automatic pipette (Bell, Lidwell, and Vaughan-Jackson, *J.*, 1936, 1792) to 10—12 small glass bulbs, which were then sealed off and placed in the thermostat. Bulbs were removed at intervals, cooled to room temperature, and emptied into weighed tubes containing 1—3 c.c. of 0.006M-ferric chloride in alcohol together with the necessary amount of trichloroacetic acid.

The conversion of  $\alpha$ -ester into  $\beta$ -ester does not go quite to completion, experiments with different catalysts indicating 3—8% of  $\alpha$ -ester at equilibrium. (Knorr and Schubert, *loc. cit.*, found 3—5% in a number of solvents.) Owing to the slowness of the reaction it is difficult to determine the equilibrium position accurately, and we have therefore preferred to ignore the back-reaction and to study only about the first 60% of the change. Under these conditions a first-order reaction would be anticipated, and in fact a plot of the logarithm of the concentration (or drum-reading) against the time gave a straight line in almost all cases. Fig. 1 gives a typical plot of this kind. The first-order constants given subsequently were obtained graphically, and are defined by  $k = 2.303 \text{ d log}_{10} x / dt$ ,  $x$  being the concentration of  $\alpha$ -ester after  $t$  minutes. Preliminary experiments showed that the value of  $k$  was not appreciably changed by varying the ester concentration by a factor of 2 in either direction. The addition of water up to a concentration of 0.05M was also without effect, and no special precautions were therefore taken to exclude it.

*Glass Catalysis.*—In the absence of any added catalyst the reaction velocity is very small and not very reproducible. Successive experiments in bulbs with an internal area of about 3.5 sq. cm. gave values of

$10^5k = 8.2, 13.2, 5.0, 6.2, 8.1, 6.8, 7.2, 8.1, 9.1, 7.4$  (mean 7.9). In a second experiment the surface was increased to 39 sq. cm. by packing with glass capillaries and the mean velocity constant was  $7.6 \times 10^{-4}$ , while a third experiment with 44 sq. cm. surface gave  $k = 9.0 \times 10^{-4}$ . These values are approximately proportional to the extent of the glass surface, and the "spontaneous" reaction is thus clearly due to a heterogeneous reaction. It was found that the reaction catalyzed by bases is not measurably affected by increase of surface, and it is therefore possible to correct for the surface reaction by subtracting the "spontaneous" rate from the observed rate in presence of basic catalysts. This correction has been applied to all the velocity constants in Table I, an amount of  $2.1 \times 10^{-5}$  per sq. cm. being subtracted from the observed values. This correction was usually only a small fraction of the whole, but for the weakest tertiary amines the surface reaction contributed as much as half the total velocity, and the results for these bases are therefore less reliable.

FIG. 1.



*Catalysis by Bases.*—The data obtained are given in Table I, and Fig. 2 shows the dependence of velocity on catalyst concentration for some of the tertiary bases. The slope of the plots falls off rapidly

TABLE I.

## Catalysis by bases.

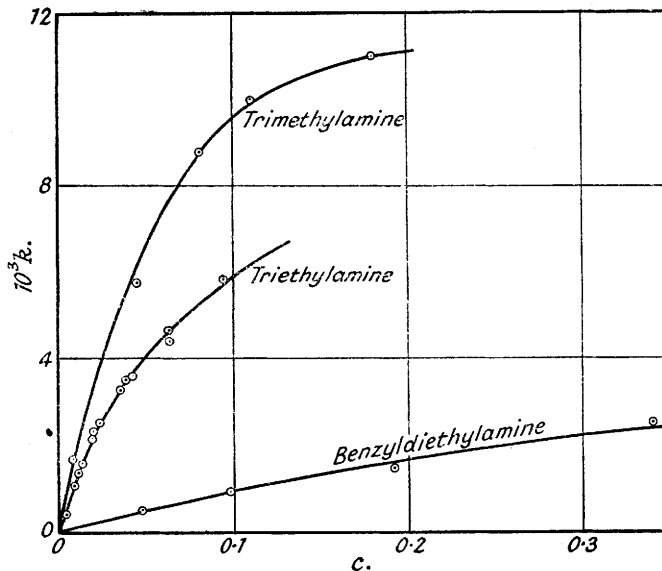
<i>Triethylamine</i> : $k_c = 0.142$ ; $k_\infty = 0.0102$ .														
$10^4c$ .....	32	87	109	127	170	188	196	230	349	372	414	618	630	944
$10^5k$ { obs. ....	44	104	123	160	220	235	271	247	332	353	360	470	440	584
{ calc. ....	44	110	135	154	196	213	220	248	335	357	374	473	478	581
<i>Trimethylamine</i> : $k_c = 0.206$ ; $k_\infty = 0.0175$ .														
$10^4c$ .....	92	460			806			868		884		927		1830
$10^4k$ { obs. ....	17		58		88			97		100		108		119
{ calc. ....	17		62		86			89		89		91		120
<i>Benzyl-diethylamine</i> : $k_c = 0.0118$ ; $k_\infty = 0.0067$ .														
$10^3c$ .....	48	95	191	343										
$10^5k$ { obs. ....	53	95	146	257										
{ calc. ....	52	96	168	251										
<i>Nicotine</i> : $k_c = 0.0078$ ; $k_\infty = 0.0100$ .														
$10^3c$ .....	46	92	132	137										
$10^5k$ { obs. ....	36	63	92	93										
{ calc. ....	28	67	94	97										
<i>s-Collidine</i> : $k_c = 0.0021$ .				<i>Diethyl-p-toluidine</i> : $k_c = 0.00086$ .				<i>Diethylaniline</i> : $k_c = 0.00036$ .						
$10^3c$ .....	49	100	198		$10^3c$ .....	100	200	302		$10^3c$ .....	90	270	452	
$10^5k$ (obs.) .....	9	16	23		$10^5k$ (obs.) .....	73	105	128		$10^5k$ (obs.) .....	3	7	9	
$10^4k/c$ .....	18	16	12		$10^5k/c$ .....	73	52	43		$10^5k/c$ .....	33	26	20	
<i>α-Picoline</i> : $k_c = 0.00046$ .				<i>Piperidine</i> : $k_c = 0.497$ .										
$10^3c$ .....	91	183	325		$10^4c$ .....	44	89	135	152					
$10^5k$ (obs.) .....	4	5	8.5		$10^5k$ (obs.) .....	210	401	579	637					
$10^5k/c$ .....	44	27	26		$10^3k/c$ .....	474	452	428	420					
<i>Diethylamine</i> : $k_c = 0.234$ .				<i>Benzylamine</i> : $k_c = 0.057$ .										
$10^4c$ .....	150	303	604	920	$10^4c$ .....	151	333	566	903					
$10^4k$ (obs.) .....	32	57	91	136	$10^4k$ (obs.) .....	7.7	17	28	46					
$10^3k/c$ .....	215	187	151	148	$10^3k/c$ .....	56	54	51	50					

with increasing concentration, and the reaction velocity approaches a limiting value at high concentrations of base. This can be expressed by the equation

$$k = k_c k_\infty c / (k_\infty + k_c c) \dots \dots \dots (1)$$

where  $c$  is the base concentration,  $k_c$  the catalytic constant in very dilute solutions, and  $k_\infty$  the limiting velocity at high concentrations. In the case of triethylamine, trimethylamine, benzyl-diethylamine and nicotine the values of  $k(\text{calc.})$  are derived from this equation, the values of  $k_c$  and  $k_\infty$  being given at the head of the data for each base. The weaker tertiary amines *s*-collidine, diethyl-*p*-toluidine, diethyl-aniline, and  $\alpha$ -picoline also show a decrease of catalytic constant with increasing concentration, but the practicable concentration range is not great enough to obtain the limiting velocity or to apply equation (1). For these four amines, therefore, the observed values of  $k/c$  were plotted against  $c$ , and  $k_c$  obtained by extrapolating to  $c = 0$ .

FIG. 2.



The position is less simple for the primary and secondary amines, since they undoubtedly condense with the ester under our experimental conditions. However, it seemed possible that the condensation was preceded by the catalysed conversion of the  $\alpha$ - into the  $\beta$ -ester, or to some intermediate involved in the conversion into  $\beta$ -ester, so that the rate of disappearance of the  $\alpha$ -ester would be comparable with its rate of isomerisation in presence of tertiary bases. (It will be shown in the discussion that this supposition was justified.) Since the primary and secondary amines are removed by condensation, the reactions are no longer of the first order, but they do not depart from this as much as might be expected, probably because the condensation products (of the Schiff's base type) also act as catalysts. The velocity constants given in the table represent the initial slopes of the first-order plots, and the values of  $k_c$  were obtained by extrapolating to  $c = 0$  the plot of  $k/c$  against  $c$ .

*Catalysis by Acids.*—In most respects this resembled catalysis by tertiary bases, but a new surface phenomenon appears at low acid concentrations. For example, with solutions of dichloroacetic acid between 0.2 and 0.001M the observed velocity constant fell off steadily but slowly with decreasing concentration, but on decreasing the concentration below 0.001M the velocity decreased rapidly, and became almost zero for concentrations below 0.0003M. It is believed that this behaviour is due to the adsorption of acid on the glass surface, thus reducing the effective catalyst concentration. This view was confirmed by an experiment with 0.001M-dichloroacetic acid in which the glass surface was increased ten-fold by packing with glass capillaries: the effect was to decrease the velocity constant from  $8 \times 10^{-3}$  to  $7 \times 10^{-4}$ . We have therefore assumed that in each unpacked bulb the acid concentration is diminished by adsorption by an amount  $3.4 \times 10^{-4}$ M, and the values of  $c(\text{corr.})$  in Table II were obtained

TABLE II.

*Catalysis by acids.*

*Dichloroacetic acid*:  $k_c = 25$ ;  $k_\infty = 0.0145$ ;  $A = 0.07$ .

$10^4 c(\text{corr.})$ .....	7.2	7.7	15.2	22.7	37.6	89	417	774	879	1823
$10^4 k$ { obs. ....	84	81	106	115	126	138	184	200	210	258
{ calc. ....	81	83	105	116	126	141	172	198	205	272

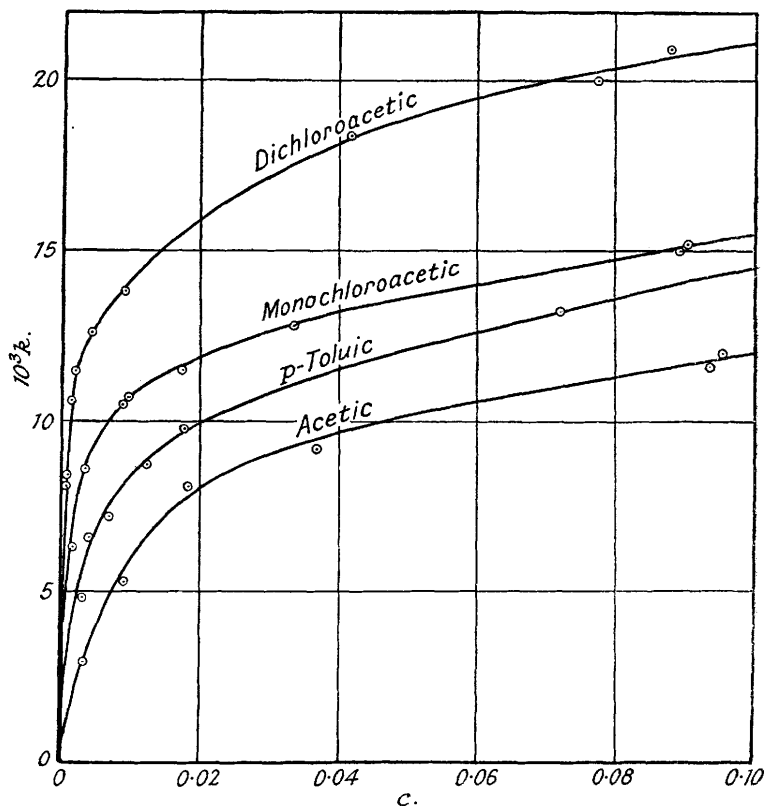
*o*-Nitrobenzoic acid:  $k_c = 11.5$ ;  $k_\infty = 0.0143$ .

$10^5 c(\text{corr.})$ .....	135	219	239	388	802
$10^4 k$ { obs. ....	72	97	100	108	124
{ calc. ....	74	91	94	108	124

TABLE II—contd.

<i>Monochloroacetic acid</i> : $k_c = 7.87$ ; $k_\infty = 0.0125$ ; $A = 0.027$ .									
$10^4 c$ (corr.)	16.1	35.9	89	94	176	330	895	902	1804
$10^4 k$ { obs.	63	86	105	107	115	128	150	152	170
{ calc.	63	87	106	107	119	128	147	147	173
<i>m-Nitrobenzoic acid</i> : $k_c = 7.12$ ; $k_\infty = 0.0125$ .									
$10^4 c$ (corr.)	20.5	21.9	31.7	46.4	71	97	197	495	
$10^4 k$ { obs.	71	66	83	91	95	109	113	131	
{ calc.	67	70	81	91	100	106	115	121	
<i>Benzoic acid</i> : $k_c = 2.51$ ; $k_\infty = 0.0138$ .									
$10^4 c$ (corr.)	34	49	69	359	902	1806			
$10^4 k$ { obs.	52	62	79	113	129	142			
{ calc.	53	65	77	120	130	134			
<i>p-Toluic acid</i> : $k_c = 2.44$ ; $k_\infty = 0.0125$ .									
$10^4 c$ (corr.)	33	39	69	89	123	176	720		
$10^4 k$ { obs.	48	66	72	77	88	98	132		
{ calc.	49	54	72	80	88	97	117		
<i>Acetic acid</i> : $k_c = 1.07$ ; $k_\infty = 0.0133$ .									
$10^4 c$ (corr.)	34	90	183	368	936	951	1735		
$10^4 k$ { obs.	29	53	81	92	116	120	127		
{ calc.	29	56	79	100	118	118	125		
<i>Trimethylacetic acid</i> : $k_c = 2.25$ ; $k_\infty = 0.0132$ .									
$10^4 c$ (corr.)	34	86	89	93	98	184	441	924	1885
$10^4 k$ { obs.	49	80	85	79	79	96	117	120	130
{ calc.	48	78	79	81	82	102	116	124	128
<i>Trimethylacetic acid + pyridine</i> .									
$10^4 c$ (acid)	37	45	45	927	906	904	907	1165	
$10^4 c$ (base)	0	11	215	0	109	215	323	326	
$10^4 k$ (obs.)	49	56	56	120	125	139	153	163	

FIG. 3.



by subtracting this amount from the stoichiometric concentrations. Since each bulb contained 0.45 c.c. of solution and had an internal surface of 3.5 sq. cm., this corresponds to about  $3 \times 10^{16}$  molecules per sq. cm. This figure is not unreasonable, since the true surface of the glass is probably considerably greater than its geometrical area, and carboxylic acids are known to be strongly adsorbed from the vapour phase by glass at temperatures near 100°.

The dependence of reaction velocity on catalyst concentration resembled that found for the stronger bases, and typical plots are shown in Fig. 3. However, with monochloro- and dichloro-acetic acids the velocity did not quite reach a limiting value at high concentrations, but continued to increase slowly with increasing concentration. This can be expressed by adding a linear term to equation (1), giving

$$k = k_e k_{\infty} c / (k_{\infty} + k_e c) + A c \dots \dots \dots (2)$$

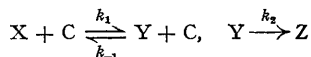
The linear term was not necessary for the weaker acids, or for those which were insufficiently soluble for high concentrations to be studied.

*Catalysis in Mixtures of Acid and Base.*—The data given at the end of Table II show that the addition of pyridine has no effect on catalysis by trimethylacetic acid. (Pyridine is too weak a base to have a measurable catalytic effect alone.) This contrasts with the often-quoted observations of Richards and Lowry (*J.*, 1925, 127, 1385) for the mutarotation of tetramethylglucose in mixtures of pyridine and cresol, and offers no support for the view that the interconversion of keto-enol isomers takes place by a simultaneous reaction of both acid and base with the substrate.

#### DISCUSSION.

The particular feature of this reaction, common to both basic and acidic catalysis, is the fact that the reaction velocity is proportional to the catalyst concentration only at very low concentrations, and approaches a constant limiting value at high concentrations. This behaviour can be best explained by the following reaction scheme.

Let X be the  $\alpha$ -ester, Z the  $\beta$ -ester, C the catalyst, and Y some intermediate form of the ester present only in very small concentration. If the reaction takes place in two consecutive steps

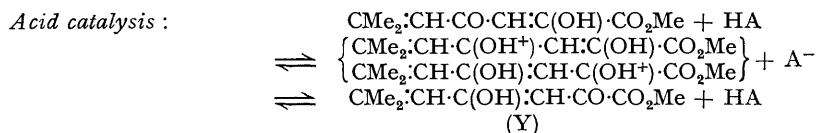
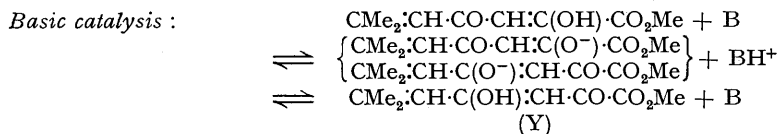


then the conditions for a stationary concentration of Y give

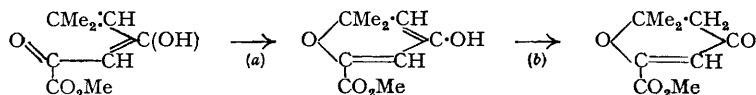
$$k = - \frac{1}{[X]} \frac{d[X]}{dt} = \frac{k_1 k_2 [C]}{k_2 + k_{-1} [C]} \dots \dots \dots (3)$$

which is identical with equation (1) if we write  $k_1 = k_e$ ,  $k_1 k_2 / k_{-1} = k_{\infty}$ . Moreover, since both  $k_2$  and the ratio  $k_1/k_{-1}$  are independent of the catalyst, the value of  $k_{\infty}$  should be the same throughout. This is borne out by the experimental data, since although the effectiveness of the eight acid catalysts at low concentrations varies by a factor of 25, the extreme values of  $k_{\infty}$  are 0.0125 and 0.0145. For basic catalysts the data are less satisfactory, since it was only possible to evaluate the maximum rate for triethylamine (0.0102), trimethylamine (0.0175), benzyl-diethylamine (0.0067), and nicotine (0.0100), and these values are of low accuracy. However, they show no trend with basic strength and are close to the limiting value for acid catalysis, so that there is substantial evidence for the above reaction scheme.

The intermediate Y is probably the isomeric enol ester, formed from the  $\alpha$ -ester by mechanisms resembling those for other prototropic changes, *i.e.*



where the brackets { } indicate mesomeric ions with a charge distribution intermediate between those represented by the two formulæ. The enol Y thus formed can then pass into the  $\beta$ -ester by the steps



Step (a) involves only a bond shift, but it demands a special configuration of the molecule and is likely to be a slow reaction. Step (b) is a simple enol-keto change which would be expected to take place rapidly under our experimental conditions. It may be noted that in both the open-chain enols and in the enol and the keto-ring compound all the double bonds form part of a conjugated system. This is not so for the open-chain keto-form, which may account for its non-occurrence.

This scheme explains why the formation of  $\beta$ -ester is much less facile than a simple keto-enol tautomerism, and also why there is greater equality between the catalytic effects of acids and bases, since the mechanism given above for acid catalysis cannot operate in a simple keto-enol change. The slight increase in rate at high concentrations of strong acids [represented by the linear term in equation (2)] is probably due to the attachment of a proton to one of the basic oxygen atoms in the enol Y: this would no doubt affect the rate of ring closure, though it is difficult to predict whether an increase or a decrease is to be expected.

According to the above interpretation, the values of  $k_c$  represent the catalytic constants of acids and bases for the interconversion of the two open-chain enols by a prototropic mechanism. It is therefore of interest to compare these catalytic constants with the dissociation constants of the catalysts in water, since it has been shown (Griffiths, *J.*, 1938, 818) that the strengths of acids and bases in chlorobenzene run parallel with those in water. For the bases, values are only available at 25°, and these are given in Table III, while Fig. 4 shows a plot of  $\log_{10} k_c$  against  $\log_{10} K_d$ .

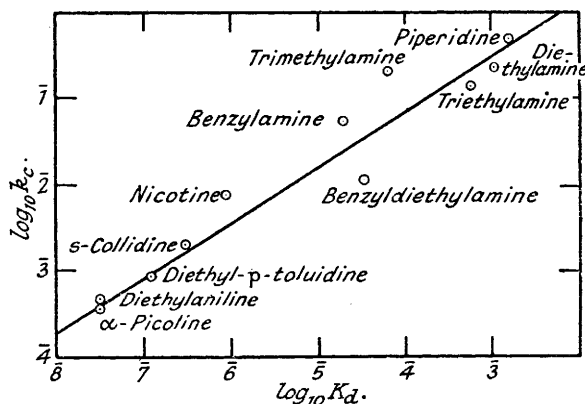
TABLE III.

*Catalytic power and basic strength.*

Catalyst.	$k_c$ (99°).	$K_d$ (25°).	Ref.	Catalyst.	$k_c$ (99°).	$K_d$ (25°).	Ref.
Piperidine .....	0.497	$1.6 \times 10^{-3}$	(1)	Nicotine .....	0.0078	$9 \times 10^{-7}$	(5)
Diethylamine .....	0.234	$1.1 \times 10^{-3}$	(2)	<i>s</i> -Collidine .....	0.0021	$2.1 \times 10^{-7}$	(6)
Triethylamine .....	0.142	$5.9 \times 10^{-4}$	(3)	Diethyl- <i>p</i> -toluidine .....	0.00086	$1.2 \times 10^{-7}$	(2)
Trimethylamine ...	0.206	$6.5 \times 10^{-5}$	(4)	Diethylaniline .....	0.00036	$3.0 \times 10^{-8}$	(2)
Benzyl-diethylamine .....	0.0118	$3.3 \times 10^{-5}$	(2)	$\alpha$ -Picoline .....	0.00046	$3.0 \times 10^{-8}$	(7)
Benzylamine .....	0.057	$2.2 \times 10^{-5}$	(2)				

References for dissociation constants: (1) Bredig, *Z. physikal. Chem.*, 1894, **13**, 191. (2) Hall and Sprinkle, *J. Amer. Chem. Soc.*, 1932, **54**, 3469. (3) Winmill and Moore, *J.*, 1912, 1635. (4) Everett and Wynne-Jones, *Proc. Roy. Soc.*, 1944, **177**, A, 499. (5) Craig and Nixon, *J. Amer. Chem. Soc.*, 1931, **53**, 4370. (6) Lunden, *J. Physical Chem.*, 1907, **5**, 574. (7) Constam and White, *Amer. Chem. J.*, 1903, **5**, 574.

FIG. 4.



It will be seen that there is a rough linear relation between these two quantities, the slope of the straight line in the figure being 0.66. The most serious discrepancy is for trimethylamine, and it is of interest that other workers (Brown, *J. Amer. Chem. Soc.*, 1944, **66**, 431) have concluded that the true basic strength of this molecule is not satisfactorily represented by its dissociation constant in water. On the other hand, the kinetic measurements relate to a temperature of 99°, and it is possible that some of the discrepancies would be removed if dissociation constants at this temperature were available.

The primary and secondary amines fall well on the same straight line as the tertiary amines. This confirms the view that their condensation reaction with the ester involves a prototropic change and is kinetically allied to the transformation of  $\alpha$ -ester into  $\beta$ -ester. Since for these amines the initial rate is roughly proportional to the amine concentration, it seems likely that the condensation takes place rapidly with the intermediate enol isomer  $\text{CMe}_2\text{:CH}\cdot\text{C}(\text{OH})\text{:CH}\cdot\text{CO}\cdot\text{CO}_2\text{Et}$ , in which the carbonyl group would be especially reactive.

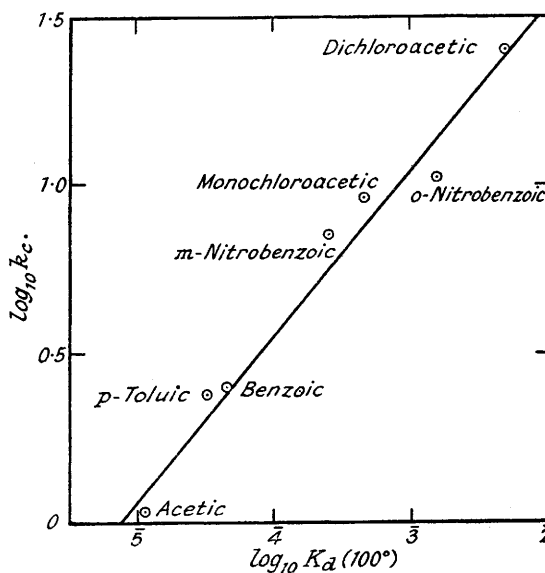
For most of the acid catalysts, dissociation constants in water at  $100^\circ$  are either directly available or can be estimated by extrapolation. Table IV and Fig. 5 show how the dissociation constants at  $25^\circ$  and  $100^\circ$  compare with the observed values of  $k_c$ .

TABLE IV.  
Catalytic power and acid strength.

Acid.	$k_c$ .	$K_a$		Ref.
		$25^\circ$ .	$100^\circ$	
Dichloroacetic .....	25	$5.1 \times 10^{-2}$	$5.0 \times 10^{-3}$	(1)
<i>o</i> -Nitrobenzoic .....	11.5	$6.3 \times 10^{-3}$	$1.6 \times 10^{-3}$	(2)
Monochloroacetic .....	7.87	$1.38 \times 10^{-3}$	$4.7 \times 10^{-3}$	(3)
<i>m</i> -Nitrobenzoic .....	7.12	$3.4 \times 10^{-4}$	$2.6 \times 10^{-4}$	(2)
Benzoic .....	2.51	$6.6 \times 10^{-5}$	$4.5 \times 10^{-5}$	(2)
<i>p</i> -Toluic .....	2.44	$4.3 \times 10^{-5}$	$3.3 \times 10^{-5}$	(2)
Acetic .....	1.07	$1.75 \times 10^{-5}$	$1.11 \times 10^{-5}$	(4)
Trimethylacetic .....	2.25	$9.1 \times 10^{-6}$	—	(5)

References for dissociation constants: (1) Ostwald, *Z. physikal. Chem.*, 1889, **3**, 177. Value at  $100^\circ$  extrapolated from kinetic data (Baughan and Bell, *Proc. Roy. Soc.*, 1937, **156**, A, 464). (2) Schaller, *ibid.*, 1898, **25**, 519. (3) Wright, *J. Amer. Chem. Soc.*, 1934, **56**, 314 ( $100^\circ$  value extrapolated). (4) Noyes, *ibid.*, 1904, **30**, 318. (5) Dippy, *J.*, 1938, 1222.

FIG. 5.



It will be seen that there is a fairly close relation between the catalytic constants at  $99^\circ$  and the dissociation constants at  $100^\circ$ , the slope of the line in Fig. 5 being 0.49. If dissociation constants at  $25^\circ$  are used the agreement is somewhat less satisfactory, and a serious discrepancy is shown by trimethylacetic acid: unfortunately, the dissociation constant of this acid is only known at a single temperature ( $25^\circ$ ).

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