S 38. *The Mutarotation of* lævo*Menthyl Benzoylformate in Alcoholic Solutions.*

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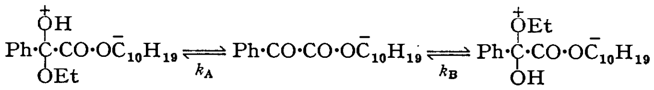
The mutarotation of *lævo*menthyl benzoylformate in primary alcohols is shown to be due to slow hemi-acetal formation. The kinetics of this reaction have been measured using both the polarimetric and the dilatometric method. The acid–base catalysis of such a reversible reaction is described and suitable mechanisms are proposed.

It is shown that the extent of hemi-acetal formation (and, therefore, the extent of mutarotation) is strongly dependent on the nature of the alcoholic solvent: thus MeOH > EtOH > Pr^{i}OH > Bu^{t}OH.

THE mutarotation of ethyl-alcoholic solutions of *lævo*menthyl benzoylformate was regarded by McKenzie and Mitchell (*Biochem. Z.*, 1929, **208**, 456), who first observed it, as probably being due to the establishment of an equilibrium: $\mathrm{Ph{\cdot}\overset{+}{C}O{\cdot}CO{\cdot}O\bar{C}_{10}H_{19}} \rightleftharpoons \mathrm{Ph{\cdot}\bar{C}O{\cdot}CO{\cdot}O\bar{C}_{10}H_{19}}$, " induced asymmetry " in the carbonyl group being postulated. An alternative explanation involving hemi-acetal formation was not ruled out but was not held to be so satisfactory. Jamison and Turner (*J.*, 1941, 538) regarded the first concept as untenable and the second as probable, first pointing out that the mutarotation could be explained most simply by postulating combination of ester and alcohol to form the two possible hemi-acetals and later (*Quarterly Reviews*, 1948, **1**, 299) drawing attention to the possibility of " first-order asymmetric transformation " between the diastereoisomeric hemi-acetals A and B :



$$\mathrm{Ph{\cdot}}\underset{\mathrm{OEt}}{\overset{\overset{+}{\mathrm{O}}\mathrm{H}}{\mathrm{C}}}\mathrm{{\cdot}CO{\cdot}\bar{O}C_{10}H_{19}} \underset{k_A}{\rightleftharpoons} \mathrm{Ph{\cdot}CO{\cdot}CO{\cdot}\bar{O}C_{10}H_{19}} \underset{k_B}{\rightleftharpoons} \mathrm{Ph{\cdot}}\underset{\mathrm{OH}}{\overset{\overset{+}{\mathrm{O}}\mathrm{Et}}{\mathrm{C}}}\mathrm{{\cdot}CO{\cdot}\bar{O}C_{10}H_{19}}$$

A *B*

The interaction of *lævo*menthyl benzoylformate and ethanol, if it leads to hemi-acetal formation, should give rise not only to mutarotational changes but also to other changes in physical properties. It has now been found that volume changes, which can be followed quantitatively by means of a dilatometer, accompany the interaction of *lævo*menthyl benzoylformate and ethanol, and moreover that, under comparable conditions, the velocity of the reaction as measured by the volume change is identical with that of the mutarotation. The reaction measured follows the first-order law, owing to the presence of ethanol in large excess.

It is further shown that an ethanol solution of ethyl benzoylformate, in which hemi-acetal formation can give rise only to enantiomorphs of identical molecular volume, undergoes a contractional change which can be followed dilatometrically, a result at once leading to the conclusion that the mutarotation of ethanol solutions of *lævo*menthyl benzoylformate could be sufficiently accounted for on the basis of hemi-acetal formation, superimposed " first-order asymmetric transformation " being neither indicated nor contra-indicated. The measured rate constant corresponding with the formation of diastereoisomerides such as A and B is the sum of two constants, k_A and k_B, which would usually be unequal : when *lævo*menthyl is replaced by ethyl, k_A and k_B become equal. The measured rate constant for the formation of the diastereoisomerides A and B could not register a fast asymmetric transformation A $\rightleftharpoons$ B proceeding contemporaneously with slow hemi-acetal formation and for the detection of such concealed first-order asymmetric transformation no method exists.

While it was still possible to regard the " asymmetric induction " hypothesis as tenable, the statement (McKenzie and Mitchell, *loc. cit.*) that no mutarotation occurred with methanol solutions of *lævo*menthyl benzoylformate was surprising, but could not be challenged. With the acceptance of the hemi-acetal theory it constituted an anomaly necessitating investigation. It is now found that solutions of *lævo*menthyl benzoylformate in " commercial absolute " methanol do exhibit mutarotation, which is, moreover, even more rapid than is observed with a solution of the ester in ethanol of a similar degree of dryness. It is further shown that just as the rate of mutarotation shown by ethanol solutions of the ester is greatly increased (Jamison and Turner, 1941, *loc. cit.*) as complete absence of water is approached, so the apparently " negative " result obtained by McKenzie and Mitchell could be explained if their absolute methanol was drier than their ethanol. The following results of experiments on drying the solvent support this conclusion :

Methanol.	$k_1 \times 10^3$, min.$^{-1}$.	Final $[\alpha]_{5461}^{25°}$.
Commercial " absolute "	9·6	−75·3°
Dried by sodium and methyl phthalate	15·7	−73·4
Dried over calcium oxide and then with magnesium	21·6	−73·3
Dried over calcium oxide and twice with magnesium	170	−75·3

It may be noted that unless McKenzie and Mitchell had had occasion to suspect a very fast mutarotation with their methanol solutions, they would have taken no special precautions to avoid missing it. As can be calculated, the half-life period of our fastest mutarotation with methanol solutions is *ca.* 4 minutes, whereas when ethanol is the solvent the half-life period is *ca.* 4 hours.

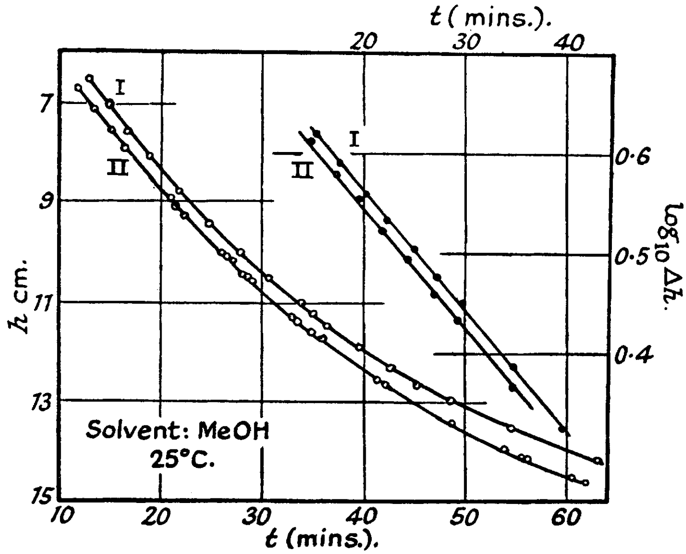
The volume change corresponding to mutarotation with a solution of *lævo*menthyl benzoylformate in commercial absolute methanol has been found to give a rate constant of $9{\cdot}9 \times 10^{-3}$ min.$^{-1}$, in good agreement with the figure $9{\cdot}6 \times 10^{-3}$ min.$^{-1}$ obtained by observing the mutarotation.

The dilatometric method permitted a comparison of the rates of hemi-acetal formation of ethyl and *lævo*menthyl benzoylformates in the two solvents, methanol and ethanol : the following results show that k_1 ethyl ester/k_1 *laevo*menthyl ester is, within experimental limits, a constant :

Benzoylformate.	Solvent.	$k_1 \times 10^4$, min.$^{-1}$.	k_1 ethyl ester / k_1 menthyl ester.
Ethyl	MeOH	270	2·7
*laevo*Menthyl	MeOH	99	
Ethyl	EtOH	72	2·5
*laevo*Menthyl	EtOH	29	

In order to illustrate the practicability of the dilatometric method, we show its application to a solution of ethyl benzoylformate in methanol; in Fig. 1 two experimental curves, together with their logarithmic plots of the Guggenheim type (*Phil. Mag.*, 1926, **2**, 538), show the first-order nature of the kinetics.

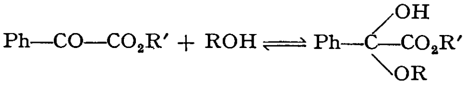
FIG. 1.



The dilatometric method having been established as an alternative to the polarimetric method for following hemi-acetal formation, it became possible, with advantage, to study by volume changes the combination of ethyl benzoylformate with alcohols of different types. In all of the solvents used, the rate of volume change followed the first-order law and it was therefore a simple calculation to deduce the initial height (by extrapolation back to zero time) and then find the height of the meniscus. The rate coefficients are shown for the sake of completeness, but are not strictly comparable between solvents since it is known that the rate (but not the extent) of reaction is extremely sensitive to traces of acid or basic catalysts. The presence of minute traces of water in an anhydrous-alcoholic solvent may exert a large, and therefore uncontrollable, effect on the reaction rate. Some results are set out below :

Solvent.	Range of muta-rotation (*laevo*-menthyl ester).	$\Delta[\alpha]^{25°}_{5461}$.	ΔV, ml./g.-mol., ethyl ester.	ΔV, ml./g.-mol., menthyl ester.	$k_1 \times 10^4$, min.$^{-1}$, ethyl ester.
MeOH	−54 to −75°	21°	3·3	3·5	270
EtOH	−54 to −60	8	1·08	1·1	72
Pr^nOH	−54 to −61	7	0·87	—	37
Pr^iOH	−52 (no change)	0	0·28	—	25
Bu^nOH	−53 to −59	6	0·65	—	43
Bu^tOH	−49 (no change)	0	0	—	0
$EtO{\cdot}[CH_2]_2{\cdot}OH$	−49	0	0·23	—	15
$Cl{\cdot}[CH_2]_2{\cdot}OH$	−63 (no change)	0	0·06	—	23
$Cl{\cdot}[CH_2]_3{\cdot}OH$	—	—	0·24	—	14
$CO_2Et{\cdot}CH_2{\cdot}OH$	−51 (no change)	0	0·3	—	—
*dextro*Citronellol	—	—	0·57	—	59

The above results clearly show that in traversing the series of alcohols: methyl, ethyl, *iso*propyl, and *tert.*-butyl, there is a regular reduction in ΔV for ethyl benzoylformate. This is paralleled by a similar variation in $\Delta[\alpha]$ for *lævo*menthyl benzoylformate over the same range of alcohols. It follows, therefore, that the extent of hemi-acetal formation depends strongly on the nature of the alcohol, *i.e.* there is a displacement to the left in the equilibrium



$$\mathrm{Ph{-}CO{-}CO_2R'} + \mathrm{ROH} \rightleftharpoons \mathrm{Ph{-}C(OH)(OR){-}CO_2R'}$$

on passing up the series MeOH, EtOH, $\mathrm{Pr^iOH}$, $\mathrm{Bu^tOH}$. The change in ΔV between methanol and ethanol is not maintained for *n*-propanol and this is in contrast to *iso*propanol. In considering the effect of the structure of the alcohol, one may look either to steric effects or to electrical effects. The series $CH_3{\cdot}X$, $CH_3{\cdot}CH_2{\cdot}X$, $(CH_3)_2CH{\cdot}X$ and $(CH_3)_3C{\cdot}X$ is well known for the electron polarisations that take place towards the group X. This may well account for the shift in the equilibrium position for the above series where X = OH, although the possibility cannot be excluded that the increased bulk of the alkyl group reduces the thermodynamic stability of the corresponding hemi-acetal.

The main conclusion would appear to be what is expected, that primary alcohols combine more readily than other alcohols with benzoylformic esters. *tert.*-Butanol, which showed no reactivity, is unique among the alcohols examined, in being the least liable to undergo proton release by fission of the O—H bond, an essential step in any likely mechanism of non-catalysed hemi-acetal formation. In passing from *tert.*-butanol through *iso*propanol and ethanol to methanol, there is increasing ease of O—H bond fission, and so the observed increased extent of hemi-acetal formation is to be expected.

With the primary alcohol *dextro*citronellol, which might be expected to form hemi-acetals fairly readily, an apparently anomalous result was observed using ethyl benzoylformate. Dilatometric study showed that with the ethyl ester solution there was an appreciable contraction ($\Delta V = 0{\cdot}57$ ml./g.-mol; $k_1 = 0{\cdot}0059$ min.$^{-1}$); yet such a solution showed no mutarotation. This example, however, is complicated by the fact that the citronelloxyl group may make a cancelling contribution to the developing optical rotation of the hemi-acetals.

Hemi-acetal formation between *lævo*menthyl benzoylformate and an alcohol should be mechanistically bimolecular, as was pointed out by Jamison and Turner (1941, *loc. cit.*). *lævo*Menthyl benzoylformate dissolves readily in chloroform, the solution not exhibiting mutarotation. We have studied the combination of the ester with methanol, present in known proportions in admixture with chloroform. It was, however, not practicable to make observations with mixtures in which methanol was present in other than a large excess in relation to the *lævo*menthyl ester, and first-order kinetics were thus expected, and found. The results are summarised in Figs. 2 and 3. Fig. 2 shows the variation in the initial and final specific rotations of the ester with solvent composition, the initial rotations being obtained by extrapolation to zero time. It is seen that the rotations are linearly related to solvent composition. This is evidently due to a purely dielectric effect. The final rotations correspond to the equilibrium mixtures containing unchanged keto-ester and its hemi-acetals; their linear variation with the solvent is due to both the dielectric effect and the solvent-composition effect on the equilibrium. Increased methanol concentration is seen to have the expected result of displacing the equilibrium in favour of the hemi-acetals: thus there is a variation of 14° in the final rotations as compared with only 6° in the initial rotations.

Fig. 3 illustrates the variation in rate of mutarotation with solvent composition. The first-order rate coefficient shows a marked dependence on the methanol concentration. Although the relationship is not linear (not to be expected over such a large range of solvent variation), it is clear that the methanol is playing a fundamental part in the process. The relationship is of the type $v = k{\cdot}[E]{\cdot}f([MeOH])$, where v is the velocity of mutarotation, k is the bimolecular-rate coefficient, and [E] is the keto-ester concentration. This is in harmony with the concept of a bimolecular reaction between *lævo*menthyl benzoylformate and methanol and is therefore explicable on the slow, hemi-acetal formation hypothesis.

It was not possible to carry out kinetic experiments with a solvent of less than 25% (v/v) methanol, since the extent of mutarotation became too small to measure accurately. The curve in Fig. 3 has therefore been extrapolated to zero methanol concentration, where, as is known, the rate of mutarotation is zero. The results show, however, that there is an increasing dependence of the rate coefficient on the methanol concentration as the latter is increased. The evidence lends strong support to the hemi-acetal theory and conflicts with the predictions of the " induced asymmetry " hypothesis, since on the latter view addition of a solvent in which mutarotation is observed to one in which it is not should decrease, not increase, the rate of mutarotation.

McKenzie and Mitchell (*Biochem. Z.*, 1930, **224**, 242) observed that the mutarotation of an ethanol solution of *lævo*menthyl benzoylformate was accelerated by aqueous hydrochloric acid or by pyridine. It is now found that the rate coefficient (25°) for the mutarotation of *lævo*menthyl benzoylformate in methanol is very considerably increased in the presence of pyridine :

Solvent.	Method.	$k_1 \times 10$ mins.$^{-1}$.
MeOH	Polarimetric	96
,,	Dilatometric	99
0·015M-pyridine in MeOH	Polarimetric	480
,, ,,	Dilatometric	510

FIG. 2.

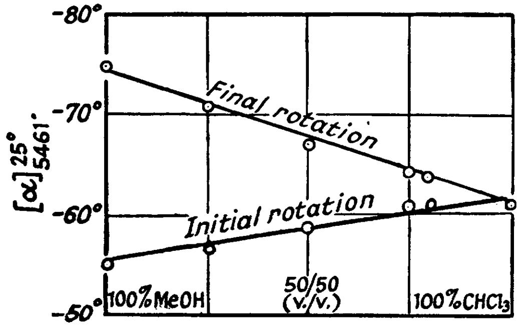
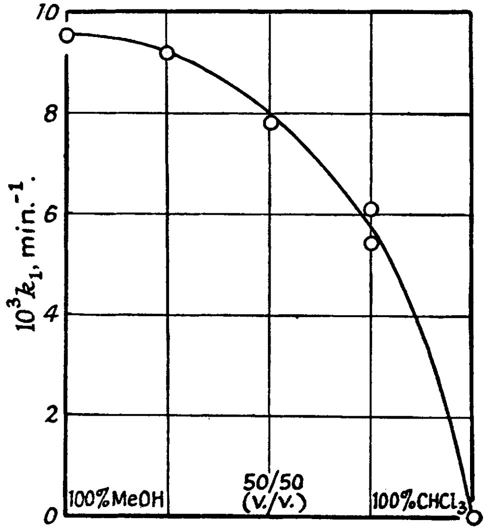


FIG. 3.



With ethanol solutions of *lævo*menthyl benzoylformate measurements were made over a considerable range of pyridine concentrations, and it is seen from Fig. 4 (top curve) that the catalytic effect tends to attain a constant value after a certain concentration is reached. It is concluded, therefore, that the catalyst is not the pyridine molecule, but the ethoxide ion, formed in the equilibrium :

$$C_5H_5N + EtOH \rightleftharpoons C_5H_5\overset{\oplus}{N}H + \overset{\ominus}{O}Et.$$

Using α for the " degree of ionisation " of the weak base pyridine, in the sense of this equation, $\alpha \sim \sqrt{K/c}$, K being the equilibrium constant and c the analytical concentration of pyridine. It follows that $[\overset{\ominus}{O}Et] \sim \sqrt{K.c}$, so that the catalytic effect, if arising from the ethoxide ion, should bear a linear relationship to $\sqrt{c}$. That this is indeed so is shown by the lower curve in Fig. 4.

Catalysis of the mutarotation of methanolic solutions of *lævo*menthyl benzoylformate by pyridine proceeds on similar lines (Fig. 5).

We have also made quantitative measurements at 25° of the acid (hydrochloric; sulphuric) catalysis of mutarotations of methanol and ethanol solutions of *lævo*menthyl benzoylformate. It is known that small traces of water cause a marked retardation of the mutarotation rate in ethanol, this retardation becoming progressively less marked as the amount of water increases and the rate coefficient attaining a constant value after the addition of 0·15% of water (Jamison and Turner, 1941, *loc. cit.*). It was therefore not desirable to use anhydrous ethanol as a stock solvent, but instead, commercial " absolute " ethanol which had been once distilled without being dried. The rate coefficient in this solvent underwent no perceptible change over the period of months during which the various catalytic effects were measured.

Hydrochloric Acid as Catalyst in Ethanol.—A series of kinetic runs was performed in which the hydrochloric acid concentration was varied up to 1·3 × 10⁻³N. Beyond this the rate became too large to measure (half-life about 2 minutes). The results (Fig. 6) show a linear relationship of the type $k_1 = k_1^0 + k_{H^\oplus}$ [HCl], where k_1 is the first-order rate coefficient, k_1^0 is the rate coefficient for the solvent only, and $k_{H^\oplus}$ is the catalytic constant.

FIG. 4.

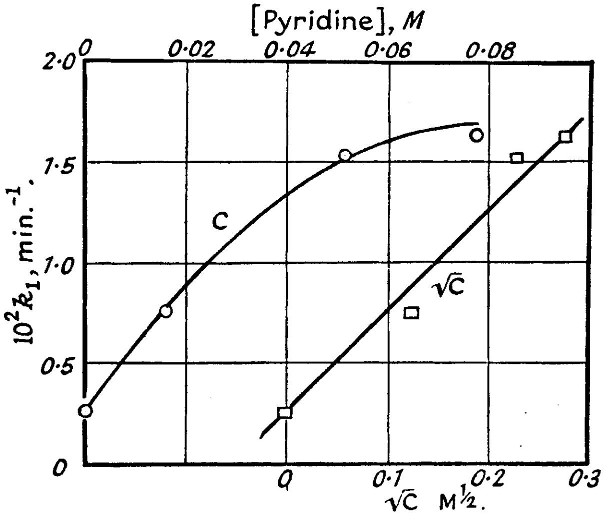
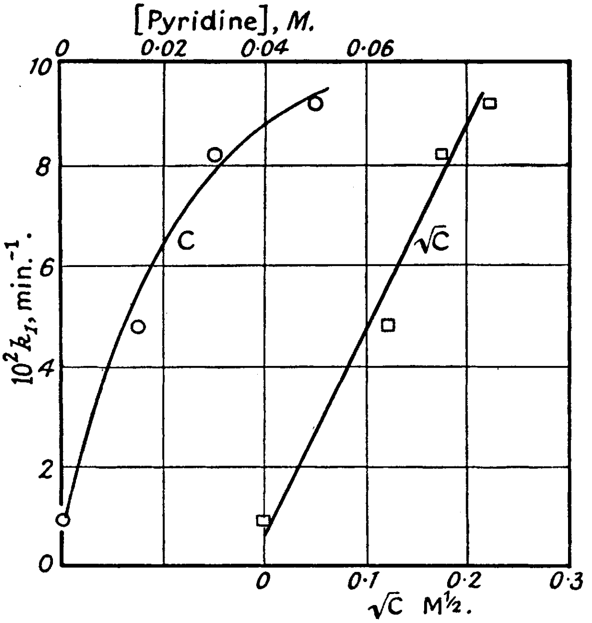


FIG. 5.



The Water-retardation Effect in the Acid-catalysed Reaction in Ethanol.—In view of the established water-retardation effect for the non-catalysed reaction in ethanol, a parallel investigation was made for the acid-catalysed reaction. The solvent used was $3{\cdot}8 \times 10^{-4}$N-HCl/EtOH and the added water concentration was varied up to 0·75M. It was found that the retardation decreased progressively as the water concentration was increased. Moreover, the retardation was of the inverse type, *i.e.*

$$k_1 = \frac{k_1^0}{1 + k_{H_2O}\,[H_2O]}$$

where k_1^0 is the rate coefficient for the solvent ($3{\cdot}8 \times 10^{-4}$N-HCl) and k_{H_2O} is the catalytic constant for water in this solvent. The above relationship may be re-written as

$$1/k_1 = 1/k_1^0 + k_{H_2O}[H_2O]/k_1^0$$

so that a plot of $1/k_1$ against $[H_2O]$ should yield a linear relationship the slope of which is equal to k_{H_2O}/k_1^0 and the intercept of which on the $1/k_1$ axis is equal to $1/k_1^0$. Figure 7 shows this.

FIG. 6.

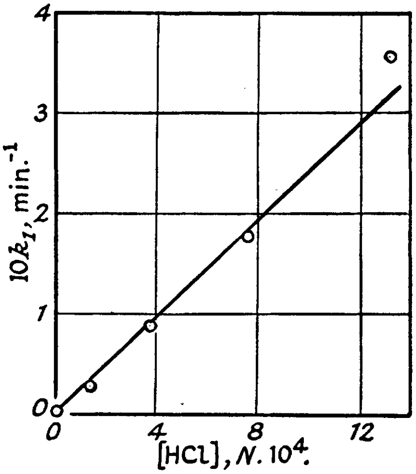


FIG. 7.

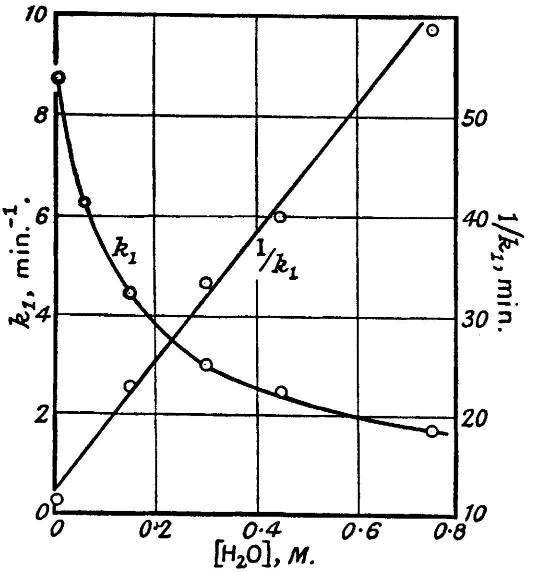
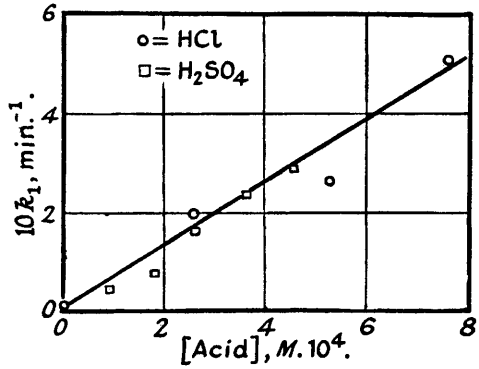


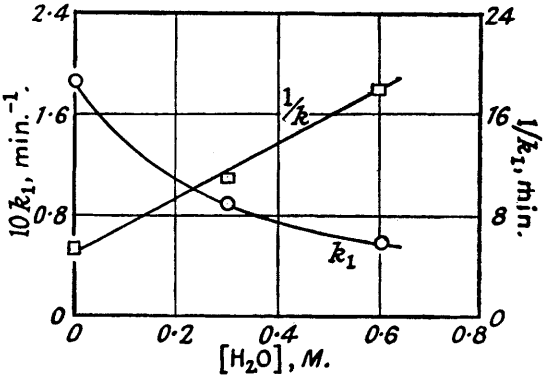
FIG. 8.



Acid catalysis of the reaction between *lævo*menthyl benzoylformate and methanol has also been studied quantitatively. With either hydrochloric or sulphuric acid a linear relationship was found between catalytic effect and concentration of catalyst. When acid concentration was plotted as a *normality*, the catalytic constants for hydrochloric and sulphuric acid were found to be in the ratio 2 : 1, but plotting acid concentrations as a *molarity*, identical catalytic constants were obtained (Fig. 8). This is to be expected if $\overset{+}{R}OH_2$ is the effective catalyst, the second dissociation of sulphuric acid being very small compared with the first.

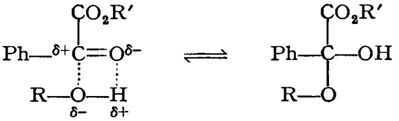
The water-retardation reaction in methanol was examined in 2·6 × 10^{-4}N-HCl/MeOH, the added-water concentration being varied up to 0·06M. The effect was found to be strictly analogous to that found with ethanol, the rate coefficient tending to a constant value. A plot of $1/k_1$ against $[H_2O]$ showed that the inverse law was operative, *i.e.* $k_1 = k_1^0/1 + k_{H_2O}[H_2O]$, where k_1^0 is the rate coefficient for the solvent (2·6 × 10^{-4}N-HCl/MeOH) and k_{H_2O} is the catalytic constant for water in this solvent (Fig. 9).

FIG. 9.



Water was found to exert no significant retardation on the base-catalysed reaction.

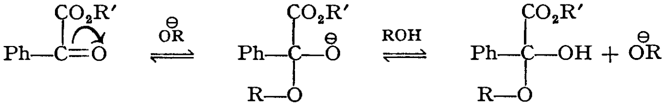
The intimate mechanisms proposed for hemi-acetal formation are essentially identical with those suggested by Bell (*Trans. Faraday Soc.*, 1941, **37**, 716). It should, however, be emphasised that the proton denoted below by $H^{\oplus}$ is really the solvated analogue ($R^{\oplus}OH_2$). The non-catalysed solvolytic reaction may be due to the one-stage addition of the alcohol to the ketone, thus



$$\begin{array}{c}\mathrm{CO_2R'}\\ |\\ \mathrm{Ph}-{}^{\delta+}\mathrm{C}=\mathrm{O}^{\delta-}\\ \vdots\qquad\vdots\\ \mathrm{R}-\underset{\delta-}{\mathrm{O}}-\underset{\delta+}{\mathrm{H}}\end{array} \rightleftharpoons \begin{array}{c}\mathrm{CO_2R'}\\ |\\ \mathrm{Ph}-\mathrm{C}-\mathrm{OH}\\ |\\ \mathrm{R}-\mathrm{O}\end{array}$$

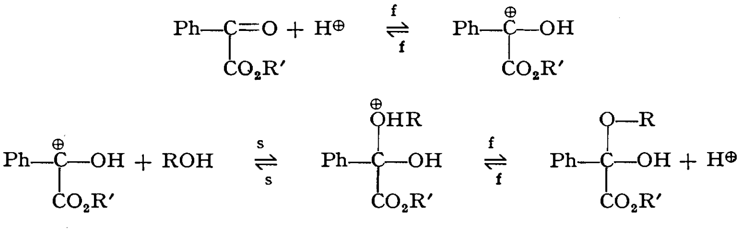
This mechanism may become the effective one in strictly anhydrous solvents where the possibility of a hydrogen bonded complex, acting as an intermediate, cannot be excluded.

The base-catalysed reaction is believed to involve nucleophilic attack at the polarised carbonyl group by the alkoxide ion,



$$\begin{array}{c}\mathrm{CO_2R'}\\ |\\ \mathrm{Ph}-\mathrm{C}=\mathrm{O}\end{array} \overset{\overset{\ominus}{\mathrm{OR}}}{\rightleftharpoons} \begin{array}{c}\mathrm{CO_2R'}\\ |\\ \mathrm{Ph}-\mathrm{C}-\overset{\ominus}{\mathrm{O}}\\ |\\ \mathrm{R}-\mathrm{O}\end{array} \overset{\mathrm{ROH}}{\rightleftharpoons} \begin{array}{c}\mathrm{CO_2R'}\\ |\\ \mathrm{Ph}-\mathrm{C}-\mathrm{OH}\\ |\\ \mathrm{R}-\mathrm{O}\end{array} + \overset{\ominus}{\mathrm{OR}}$$

while the acid-catalysed reaction would proceed along the following lines :



$$\begin{array}{c}\mathrm{Ph}-\mathrm{C}=\mathrm{O}\\ |\\ \mathrm{CO_2R'}\end{array} + \mathrm{H}^{\oplus} \underset{f}{\overset{f}{\rightleftharpoons}} \begin{array}{c}\oplus\\ \mathrm{Ph}-\mathrm{C}-\mathrm{OH}\\ |\\ \mathrm{CO_2R'}\end{array}$$

$$\begin{array}{c}\oplus\\ \mathrm{Ph}-\mathrm{C}-\mathrm{OH}\\ |\\ \mathrm{CO_2R'}\end{array} + \mathrm{ROH} \underset{s}{\overset{s}{\rightleftharpoons}} \begin{array}{c}\oplus\\ \mathrm{OHR}\\ |\\ \mathrm{Ph}-\mathrm{C}-\mathrm{OH}\\ |\\ \mathrm{CO_2R'}\end{array} \underset{f}{\overset{f}{\rightleftharpoons}} \begin{array}{c}\mathrm{O}-\mathrm{R}\\ |\\ \mathrm{Ph}-\mathrm{C}-\mathrm{OH}\\ |\\ \mathrm{CO_2R'}\end{array} + \mathrm{H}^{\oplus}$$

It is assumed that the proton transfer reactions are instantaneous, and that the rate-determining stages, in each case, are the heterolytic formation and fission of covalent bonds.

The water retardation for the acid-catalysed reaction, being of the inverse linear type, is probably due to its acting as a base towards the solvated proton, thus

$$\overset{\oplus}{\mathrm{ROH_2}} + \mathrm{H_2O} \rightleftharpoons \mathrm{H_3O^{\oplus}} + \mathrm{ROH},$$

and since the addition of water causes no change in the final equilibrium rotation value, it must be supposed that $H_3O^{\oplus}$ does not react with the keto-ester, *i.e.* a displacement to the right is completely unproductive and serves only to reduce the concentration of an effective reagent ($\overset{\oplus}{R}OH_2$). The retardation caused by water in the non-catalysed reaction may be due to interaction between the water molecule and the keto-ester, thereby partially preventing the formation of the alcohol–ester complex.

EXPERIMENTAL.

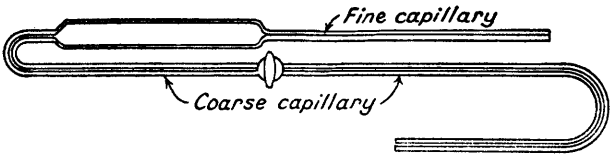
*lævo*Menthyl benzoylformate was prepared by the method of McKenzie (*J.*, 1904, 1249), crystallised from aqueous acetone, and dried in a vacuum over phosphorus pentoxide.

Ethyl benzoylformate was prepared by distilling a mixture of benzoylformic acid (40 g.), toluene (25 c.c.), ethanol (50 c.c.), and concentrated sulphuric acid (3 c.c.). The distillate was dried (potassium carbonate), poured back, and the mixture redistilled twice after drying. The mixture was shaken with dilute sodium carbonate followed by water, and extracted with toluene. The hydrogen sulphite compound was prepared, washed with alcohol, and decomposed by warming with dilute hydrochloric acid. The yellow oil thus obtained was extracted with ether, washed, and dried (sodium sulphate) and distilled, b. p. 256°/730 mm., yield 29 g.

The solvents were all redistilled immediately before use, with the already-mentioned exception of methanol and ethanol. The *dextro*citronellol was a gift from Messrs. A. Boake, Roberts and Co., Ltd.; it was distilled before use (b. p. 216°/745 mm.) and gave the following rotations (no solvent): $[\alpha]_{5461}^{25^\circ}$ $+5{\cdot}22^\circ$, $[\alpha]_{5780}^{25^\circ}$ $+4{\cdot}57^\circ$. Methanol was distilled once and retained as stock solvent. It was further dried by boiling under reflux a mixture of sodium (2 g.), dimethyl phthalate (6 g.), and methanol (100 c.c.) for one hour, followed by immediate distillation. Precautions were taken to exclude moisture and the methanol was used at once. A more anhydrous solvent was prepared by standing over freshly ignited quicklime for three days and then distilling. The distillate (200 c.c.) was allowed to stand for 12 hours over pure magnesium (2 g.) and redistilled. This distillate was again allowed to stand over magnesium until the metal had dissolved, when the solution was redistilled and used immediately.

The dilatometer is shown in Fig. 10. The inclusion of a tap results in greater sensitivity combined with quicker filling than would otherwise be possible. The dilatometer was filled by placing the end of the coarse capillary in the reaction solution and applying suction through the fine capillary. Preliminary blank runs showed that no leaking was detectable when vaseline was used as a tap lubricant. All of the kinetic runs were carried out in a precision thermostat (sensitivity ± 0·005°) at 25·0°, heated by a permanent (60 watt) heater together with an intermittent (100 watt) lamp connected through a "Sun-vic" relay to a toluene regulator. The height of the meniscus was read through a telescope to avoid errors due to parallax.

FIG. 10.



The polarimeter tube (2 dcm.) was enclosed in a lagged metal jacket through which thermostat water was pumped. All rotations were observed for the mercury green line ($\lambda = 5461$ A.). Where the accuracy was sufficiently high, the Guggenheim method of analysis for first-order kinetics was used; otherwise, the rate coefficient was obtained by the normal graphical method. The values of all rate coefficients are given in natural logarithms.

The total volume change undergone by one gram-molecule of the keto-ester during its reaction with the alcohol solvent (ΔV ml./g.-mol.) was derived in the following manner. If we dissolve x g. of the keto-ester (molecular weight $= M$) in y ml. of solution and place z ml. of this solution in a dilatometer of that volume (*i.e.* z ml.), then we observe a change in height h cm. of the capillary meniscus. This height h corresponds to a volume change $\pi r^2 h$ ml. where r cm. is the capillary radius. This volume change is due to reaction involving xz/My g.-mol. of keto-ester, whence it follows that the volume change due to reaction involving one g.-mol. of ester (ΔV) is equal to $\frac{\pi r^2 h M y}{xz}$ ml./g.-mol. of ester.

In all kinetic experiments, whether polarimetric or dilatometric, the reaction solution was 0·1 molar with respect to the keto-ester.

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