

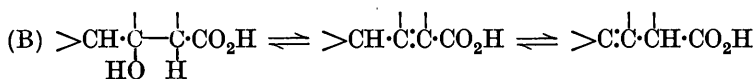
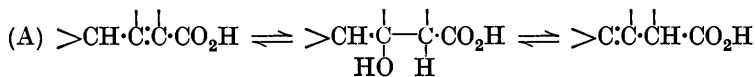
LVI.—*The Chemistry of the Three-carbon System.*
Part XI. The Mechanism of Isomeric Change in
Unsaturated Acids.

By REGINALD PATRICK LINSTEAD.

TAUTOMERIC compounds with retarded mobility may be regarded from the structural standpoint as insufficiently activated for complete mobility, or from the kinetic standpoint their inertia may be attributed to the infinitesimal velocities of the interconversion reactions under ordinary conditions. In such compounds, isomeric change can occur only in the presence of more or less powerful

reagents, and it is this peculiarity which has led to some doubt being cast on the genuineness of the tautomerism exhibited by them. It is held that such changes can be accounted for by the addition and splitting off of the catalyst. Support is given to these views by the production, side by side with the isomeric changes, of addition compounds which could function as such intermediates. Thus Butlerov (*Annalen*, 1877, **189**, 44) and Fittig (*ibid.*, 1894, **283**, 47) have observed the addition of water during changes in unsaturated hydrocarbons and acids, and Farmer that of methyl alcohol in the dihydromuconic esters (J., 1923, **123**, 3324). The ease with which a base may function in this way is shown by the work of Ruhemann (J., 1898, **73**, 723), who observed the readiness with which these substances can be added to unsaturated systems. Only in one example has it been shown that the addition product actually formed is not that which could act as a catalyst (Ingold, Shoppee, and Thorpe, J., 1926, 1477).

The interconversion of unsaturated acids in the presence of alkali furnishes a good example of retarded isomeric changes for the explanation of which two mechanisms can be suggested: (A) the β -hydroxy-acid functions as an intermediate product and the change proceeds by the addition and splitting off of water, or (B) tautomeric change occurs between the $\alpha\beta$ - and the $\beta\gamma$ -unsaturated acid, and at the same time water can be added to the $\alpha\beta$ -acid to give the β -hydroxy-acid, the process being reversible. Fittig



(*loc. cit.*), who first observed the change and the simultaneous formation of the β -hydroxy-acid, was unable to decide between these mechanisms, and with the exception of Knoevenagel's application of the Thiele hypothesis to the change (*Annalen*, 1900, **311**, 217) little further work appears to have been done either on the clearing up of this point or on the reaction as a whole.

If the tautomeric explanation (B) is correct, evidence in its favour will be forthcoming only when the additive reaction is very slow in comparison with the direct isomeric change. For example, if interconversion can be shown to occur under conditions which preclude the possibility of the presence of the β -hydroxy-acid, or the possibility of its dehydration is present, the tautomeric hypo-

thesis will receive strong support. In some of the work of Fittig (*Annalen*, 1894, **283**, 68, 132, 297), examples of acids can be found which cast doubt on the water-addition hypothesis. Thus the pentenoic and *isoheptenoic* acids undergo interconversion under conditions in which the β -hydroxy-acid is comparatively stable, whilst in the γ -phenylbutenoic acids the conversion of the $\beta\gamma$ - into the $\alpha\beta$ -form stops at a definite point and further action of alkali causes an increased addition of water without affecting this equilibrium (compare Linstead and Williams, J., 1926, 2736).

The interconversion of Δ^1 -*cyclohexenylacetic* acid and *cyclohexylideneacetic* acid now to be described is particularly suitable for investigation, as both the unsaturated acids and the corresponding β -hydroxy-acid, *cyclohexanolacetic* acid, $C_5H_{10}>C(OH)\cdot CH_2\cdot CO_2H$, are easily prepared and are crystalline, and the addition of water to the unsaturated system is extremely slow, the condition given above thus being satisfied.

Whilst the $\beta\gamma$ - is the more stable form, the $\alpha\beta$ - has considerable stability; *e.g.*, the sodium salt of the $\alpha\beta$ -acid resists interconversion in neutral solvents even at high temperatures, and the acid itself is unaffected by sodium bicarbonate and piperidine. It is only in the presence of hot alkali hydroxides that movement of the bond can occur.

The study of the action of alkalis on the three acids is complicated by the fact that the β -hydroxy-acid readily undergoes hydrolytic fission in the presence of boiling potassium hydroxide solution with the formation of *cyclohexanone* and potassium acetate: $C_5H_{10}>C(OH)\cdot CH_2\cdot CO_2H \longrightarrow C_5H_{10}>CO + CH_3\cdot CO_2K$. The unsaturated acids yield these products only after more prolonged boiling with alkali, and it may therefore be supposed that addition of water to them precedes fission. The results resemble those obtained by Farrow and Kon (J., 1926, 2131) for some related unsaturated ketones.

The reactions were examined quantitatively under various conditions by the methods given on p. 369. After the requisite time of reaction, the product was divided in the usual way into a neutral fraction, containing the *cyclohexanone*, and an acid fraction, containing any or all of the four possible acids. The acetic acid was readily separated owing to its volatility, and the *cyclohexanolacetic* acid by its insolubility in light petroleum, in which the unsaturated acids are soluble. The unsaturated acids were estimated by the bromine addition method (preceding paper). The results are in Table I.

Some of the interconversion results obtained with the unsaturated

TABLE I.

Action of potassium hydroxide solution on cyclohexanolacetic acid.

Composition of product (as % of initial material).

| % KOH. | Time (hrs.). | Temp. | Composition of product (as % of initial material). | | | % Loss. | |
|--------|--------------|-------|--|--------------------|----------------|---------|--------------|
| | | | Unchanged acid. | Unsaturated acid.* | cyclohexanone. | | Acetic acid. |
| 1 | 48 | b. p. | 84.6 | 2.5 | 0 | 0 | 12.9 |
| „ | 100 | „ | 86.8 | 1.1 | „ | „ | 12.1 |
| 10 | 1 | „ | 92.0 | 4.3 | „ | „ | 3.7 |
| „ | 24 | „ | 85.2 | 2.7 | trace | „ | 12.1 |
| 60 | 24 | 20° | 83.4 | 8.4 | 0 | „ | 8.2 |
| „ | 1 | b. p. | 72.1 | 9.0 | 10.1; 11.3 | — | 8.8 |
| „ | 1.5 | „ | 22.9 | 18.1 | 25.6 | 9.0 | 33.4 |
| „ | 48 | „ | 20.0 † | | 36.4 | 25.6 | 43.6 |

* Total figure; proportion of components not estimated.

† Not separated.

TABLE II.

Action of potassium hydroxide on unsaturated acids.

(i) On cyclohexylideneacetic acid.

| Expt. No. | % KOH. | Time (hrs.). | Temp. | Composition of product (% initial material). | | % Loss. |
|-----------|--------|--------------|-------|--|----------------------|---------|
| | | | | $\alpha\beta$ -Acid. | $\beta\gamma$ -Acid. | |
| 1 | 1 | 24 | 20° | 98.8 | 0 | 1.2 |
| 2 | 10 | 24 | „ | 96.8 | 0 | 3.2 |
| 3 | „ | 1 | b. p. | 94.0 | 0 | 6.0 |
| 4 | „ | 24 | „ | 82.2 | 16.8 | 1.0 |
| 5 | 20 | 1 | „ | 94.8 | 2.9 | 2.3 |
| 6 | 30 | 1 | „ | 81.8 | 14.4 | 3.8 |
| 7 | 40 | 0.25 | „ | 93.3 | 6.4 | 0.3 |
| 8 | „ | 1 | „ | 55.3 | 28.5 | 16.2 |
| 9 | „ | 24 | „ | 12.5 | 83.3 | 4.2 |
| 10 | 50 | 0.5 | „ | 61.5 | 31.7 | 6.8 |
| 11 | „ | 1 | „ | 23.5 | 70.5 | 6.0 |
| 12 | „ | 1.55 | „ | 12.7 | 84.9 | 2.4 |
| 13 | „ | 24 | „ | 10.5 | 84.5 | 5.0 |
| 14 | 60 | 0.25 | „ | 74.5 | 22.7 | 2.8 |
| 15 | „ | 0.5 | „ | 19.9 | 58.1 | 22.0 |
| 16 | „ | 0.83 | „ | 15.7 | 76.7 | 7.6 |
| 17 | „ | 1 | „ | 12.5 | 83.5 | 4.0 |
| 18 | „ | 24 | „ | 8.0 | 64.4 | 25.2 |

(ii) On Δ^1 -cyclohexenylacetic acid.

| | | | | | | |
|----|----|----|-------|------|------|--------|
| 19 | 10 | 1 | b. p. | 0 | 94.2 | 5.8 |
| 20 | 40 | 1 | „ | 0 | 90.6 | 9.4 |
| 21 | „ | 24 | „ | 12.2 | 81.4 | 6.4 |
| 22 | 50 | 1 | „ | 7.8 | 78.2 | 14.2 * |
| 23 | „ | 24 | „ | 12.4 | 82.6 | 5.0 |
| 24 | 60 | 1 | „ | 7.0 | 63.4 | 29.6 * |
| 25 | „ | 23 | „ | 7.9 | 63.9 | 26.3 * |

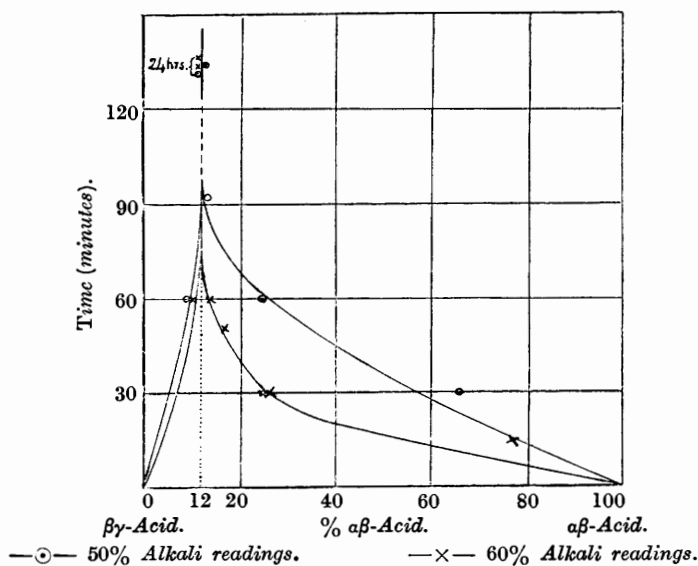
In experiment 18, the product also contained a trace of the β -hydroxy-acid, 2.6% of cyclohexanone, and 1.6% of acetic acid. In experiment 25, the quantities of the same three products were a trace, 0.4%, and 2.9%, respectively. Traces of the β -hydroxy-acid were detected in experiments 22 and 24.

* Acid product distilled.

acids are given graphically in Fig. 1, where the percentage of $\alpha\beta$ -acid in the mixture is plotted against time. The asymptotic approach to equilibrium is clearly shown.

The first point of interest that emerges from the results is the small loss which is experienced throughout, except where a large amount of fission has occurred, and in those experiments where the acid product was distilled under reduced pressure. This ensures the trustworthiness of the results as a whole. In the experiments on the unsaturated acids, no addition of water occurred, the absence of hydroxy-acid being proved in all cases by the nascent bromine method (see preceding paper). The slow rate of hydration is

FIG. 1.



clearly shown by the results of some of the experiments with 60% alkali acting for 23 or 24 hours, where 36% of fission takes place from the hydroxy-acid, but only 2—3% when the unsaturated acids are used. This may possibly be due to the slowness with which the negative hydroxyl ion is added to the ion of the dissociated salt of the acid (compare Higginbotham and Lapworth, J., 1922, 121, 49). The steric effect of the *cyclohexane* ring also may inhibit addition. The absence of β -hydroxy-acid from the final product cannot in itself be taken as a proof that the acid does not intervene in the isomerisation, but it is clear from some of the above results that if it were formed it could not be dehydrated in quantity sufficient to account for the rapid interconversion of the unsaturated

acids. Thus the 1-hour readings with 60% alkali show that 84% of interconversion occurs under conditions in which only 9% of hydroxy-acid is dehydrated, and the 24-hour readings with 10% alkali show that 17% of interconversion occurs where the β -hydroxy-acid is almost completely unaffected.

Under ideal conditions, the interconversion reaction should be unimolecular if it is due to tautomerism and bimolecular if dependent on the addition and splitting off of water. In an infinite excess of water, however, the rate of interconversion would depend only on the concentration of the acid, whichever mechanism were true. Experimental evidence on this point, therefore, can hardly be conclusive, for a considerable excess of water was present, even in the 60% alkali experiments, where the molecular proportions of acid, potassium hydroxide, and water were 1 : 10 : 20.7.

The kinetics of unimolecular reversible reactions have been investigated by Küster (*Z. physikal. Chem.*, 1895, **18**, 171) and by Lowry (*J.*, 1899, **75**, 224), and the equation proposed by Küster has been successfully applied to tautomeric equilibria. This connects the change in concentration of the substance, A, initially present (x) with the time (t) by the expression

$$t(k_1 + k_2) = \log_e \left\{ \frac{\xi}{(\xi - x)} \right\} \dots \dots (1)$$

where ξ is the value of x at equilibrium and k_1 and k_2 are the velocity coefficients of the forward and the back reaction respectively. The values of k_1 and k_2 can then be found from the equilibrium values for the concentration of A :

$$K = k_1/k_2 = \xi/(a - \xi) \dots \dots (2)$$

where a is the initial concentration of A.

The equilibrium in the pair of acids now under discussion being taken as 12% $\alpha\beta$ -acid \rightleftharpoons 88% $\beta\gamma$ -acid (see preceding paper), the application of the Küster equation gives the results in Table III.

TABLE III.

60% Alkali (ten times the quantity required for neutralisation).

Concentrations in g./c.c. Time in minutes.

| A. | t . | x . | $\xi - x$. | $k_1 + k_2$. |
|---------------------|-------|--------|-------------|---------------|
| $\alpha\beta$ -Acid | 15 | 0.0865 | 0.2444 | (0.020) |
| " | 30 | 0.2801 | 0.0508 | 0.062 |
| " | 50 | 0.3121 | 0.0188 | 0.057 |
| " | 60 | 0.3271 | 0.0038 | 0.075 |
| $\beta\gamma$ -Acid | 60 | 0.0376 | 0.0075 | 0.068 |

50% Alkali (ten times the quantity required for neutralisation).

| | | | | |
|---------------------|----|--------|--------|---------|
| $\alpha\beta$ -Acid | 30 | 0.0850 | 0.1351 | (0.016) |
| " | 60 | 0.1875 | 0.0326 | 0.032 |
| " | 93 | 0.2150 | 0.0051 | 0.040 |

When the severe conditions and the powerful nature of the catalyst are taken into consideration, the agreement between the figures for the constants must be regarded as good.

The individual values of k_1 and k_2 can be calculated from equation (2), the mean values for $k_1 + k_2$, 0.066 (60% alkali) and 0.036 (50% alkali), and the known value, 88 : 12, for the ratio of the quantities of the acids at equilibrium, being used. These are :

| | | |
|--|-------|-------|
| % Alkali | 60% | 50% |
| $k_1(\alpha\beta \longrightarrow \beta\gamma)$ | 0.058 | 0.032 |
| $k_2(\beta\gamma \longrightarrow \alpha\beta)$ | 0.008 | 0.004 |

These figures furnish the first quantitative values for the mobility of a system of this type under specified conditions. Comparison between them and similar figures for other series would be of real significance in the study, *e.g.*, of the effect of positive groups on mobility. For such a purpose the conditions of the equilibration would have to be standardised—those used in the present work would be unsuitable because (1) the concentrations of the reagents are so high that in many series dissolution of the potassium salt would probably be incomplete, and the presence of a solid phase would affect the determinations of reaction velocity (the potassium salts of the two *cyclohexane* acids are only just dissolved by the boiling 60% alkali solution); (2) the unstable acids might decompose at the high reaction temperature; (3) the change in the *cyclohexane* series is comparatively slow (see preceding paper). In a very mobile series the change might proceed at a rate too fast for experimental measurement, under the conditions which produce complete equilibration in some 65 minutes in the present series.

By decreasing the concentrations of the reactants and reducing the severity of the reaction, it is hoped to arrive at a standard set of conditions capable of general use.

The Effect of Conditions on Interconversion.

The experimental results show that the rate of isomeric change depends on the concentration of alkali. This may function in two ways. In the first place, increase in alkali concentration decreases the amount of water and increases the concentration of the potassium salt of the acid. Secondly, the experiments are carried out at the boiling point of the solution, and this rises with increasing concentration, the 60% solution boiling at about 145°. The experimental figures available do not at present allow of a distinction being made between the temperature and the concentration effects.

The concentration of alkali does not appear to have any effect

on the ultimate position of equilibrium, as there is close agreement between the results obtained with 40, 50, and 60% alkali (compare preceding paper). Johnson and Kon (J., 1926, 2748) reached the same conclusion in their investigation on the movement of the double bond in substituted cinnamic acids. From the theoretical standpoint this is unexpected, as change in temperature should displace the equilibrium in all systems except those in which the heat of reaction is zero for the tautomeric change. Küster (*loc. cit.*) showed that the position of equilibrium between the isomeric ketopentachlorocyclopentenes was considerably affected by temperature. A more accurate experimental method for the study of these and similar isomeric changes at constant temperature has now been devised and the influence of temperature on these reactions is being studied.

The Mechanism of the Reaction.

The experimental results already described provide strong support for the tautomeric nature of the reaction, but the inner mechanism of such a change is not yet clear. It can be interpreted on the lines suggested by Ingold, Shoppee, and Thorpe's application of Robinson's theory (*loc. cit.*) as an example of a highly polar catalyst facilitating the removal of the mobile hydrogen atom from the system in the form of a proton. This new hypothesis, whilst accounting for many of the experimental facts, would appear to disregard the close connexion between the enolising power of activating groups and mobility (compare Farrow and Kon, J., 1926, 2128).

EXPERIMENTAL.

Materials.—The acids used were prepared by the methods given in the preceding paper, and had the properties recorded there. *cyclo*Hexanolacetic acid was prepared by Wallach's method (*Annalen*, 1906, 347, 329); it crystallised from hot petroleum (b. p. 60—80°) in laminæ, m. p. 64°.

Reaction with Alkali.—The acid (5 g.) was added to a hot solution of potassium hydroxide (ten times the quantity required for neutralisation) in the requisite amount of water. Except in the experiments of very short duration, a copper reaction vessel was used, fitted with a double-surface condenser and with a soda-lime tube to eliminate carbon dioxide. The time of reaction was taken from the commencement of boiling, and at its conclusion the reaction vessel was plunged into ice and the contents were extracted with ether. The *cyclo*hexanone in the dried ethereal extract was slowly freed from solvent under a long column and was weighed and identi-

fied by conversion into its semicarbazone. The alkaline liquid was acidified, cooled, and extracted with an equal volume of ether divided in several portions, the ether being subsequently removed from the dried solution through a column. If the residue contained acetic acid, this was distilled off and estimated by titration with standard alkali. The residual acid was freed from the last traces of solvent in a good vacuum. In the experiments on *cyclohexanol-acetic acid*, the unchanged acid invariably crystallised and was freed from unsaturated acid by washing it with petroleum (b. p. 40—60°). The insoluble acid which remained melted sharply, in all cases between 56 and 64°, and was identified by mixed melting-point determinations. The soluble, unsaturated acid was freed from solvent and weighed. The amount usually obtained was insufficient for a determination of the proportion of the isomerides. When the initial material was an unsaturated acid, the acid product was tested for hydroxy-acid by the nascent bromine method and was then examined by the bromine addition method (see preceding paper). The conditions used were: concentration, 1/60 g.-mol. per litre; solvent, carbon tetrachloride; temperature, 25°. The compositions of the mixtures were found by reference to the standard curves. In some of the earlier experiments, the product was distilled under reduced pressure before examination, but this resulted in loss and served no useful purpose.

The results of these observations are in Tables I and II. The accuracy of the methods of extraction and estimation was checked by blank experiments; *e.g.*, under the conditions used, 85% of the *cyclohexanone* was recovered and the figures given in the tables are therefore the experimental figures multiplied by a factor (1.2). Similarly, 95% of the hydroxy-acid can be isolated by the petroleum separation method mentioned above, giving a factor of 1.05, which has been used in compiling the tables. One of the analyses of the mixed unsaturated acids was kindly checked by Mr. C. J. May by Bougault's method; the results are given below.

| | % $\beta\gamma$ -Acid found. | % $\alpha\beta$ -Acid found. | % Loss. |
|----------------------------|------------------------------|------------------------------|---------|
| By bromine method | 81.8 | 14.4 | 3.8 |
| By Bougault's method | 77.9 | 18.3 | 3.8 |

The quantitative separation of mixtures of the unsaturated acids and of several of their salts by fractional crystallisation from a variety of solvents was attempted, but no process was discovered of sufficient accuracy to check the figures obtained by the bromine method.

Sodium cyclohexylideneacetate was prepared in theoretical yield by the action of "molecular" sodium on the acid in benzene solution. The gelatinous product was washed with ether and dried.

The pure salt forms fine, white needles, m. p. 276° (decomp.), from ethyl alcohol (Found : Na, 13.9. $C_8H_{11}O_2Na$ requires Na, 14.2%). It is insoluble in most organic solvents, soluble in water, and very soluble in methyl alcohol.

The pure salt was unaffected after being boiled with xylene, alcohol or water for 24 hours; pure *cyclohexylideneacetic acid* was obtained on acidification.

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IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY,
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