CLXV.—*Catalytic Influences in Three-Carbon Tautomerism. Part I. Sodium Alkyloxides.*

By GEORGE ARMAND ROBERT KON and REGINALD PATRICK LINSTEAD.

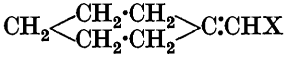
THE ionic mechanism of tautomeric change originally suggested by Wislicenus and Brühl and developed by Lapworth (J., 1901, **79**, 1265; 1902, **81**, 1508, *et cet.*) is understood to mean the separation of the " mobile " hydrogen in the form of a proton, leaving an anion in which the negative charge can be redistributed. The anion, on recombining with a proton, will then give rise either to the original compound or to an isomeride according to the changes which have taken place.

The further suggestion has been made by Ingold, Shoppee, and Thorpe (J., 1926, 1477) and developed by Ingold (*Ann. Reports*, 1927, 106 *et seq.*), that the separation of the proton is facilitated by potential intramolecular shifting of covalency electrons (" incipient ionisation ") capable of directing complete changes under suitable conditions (compare Allan, Oxford, Robinson, and Smith, J., 1926, 401) and that the redistribution of the negative charge in the anion is conditioned by similar factors.

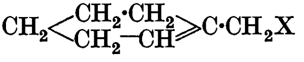
On the ionic view, the formation of the active form in a three-carbon * prototropic change—namely the anion—will be influenced, apart from structural factors, by the nature of the catalytic medium. The more affinity the medium has for the proton, the more ready will be the tautomeric interconversion. Experimental evidence on this point should be readily obtainable by examining the effect of different catalysts on a given system.

As a preliminary step it was necessary to standardise the conditions under which comparisons of mobility are made; and it was hoped at the same time to elaborate standard conditions for the comparison of the mobilities of different classes of tautomeric compounds. It had already been shown by one of us (Linstead, J., 1927, 2579) that comparisons of mobility could readily be made in a series of unsaturated acids, and it remained to elaborate a suitable method for neutral substances. Those selected as test substances for the purpose were the ketones (I and II, X = COMe)

(I.)



$$CH_2{<}\substack{CH_2\cdot CH_2\\ CH_2\cdot CH_2}{>}C{:}CHX$$



$$CH_2{<}\substack{CH_2\cdot CH_2\\ CH_2-CH}{\geqslant}C\cdot CH_2X$$

(II.)

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* We prefer a nomenclature based on *resultant*, as is customary in the classification of tautomerism, to one based on *mechanism*, *e.g.*, "pentad keto-enol," as suggested by Shoppee (J., 1928, 2568; compare Ingold and Rothstein, this vol., p. 9).

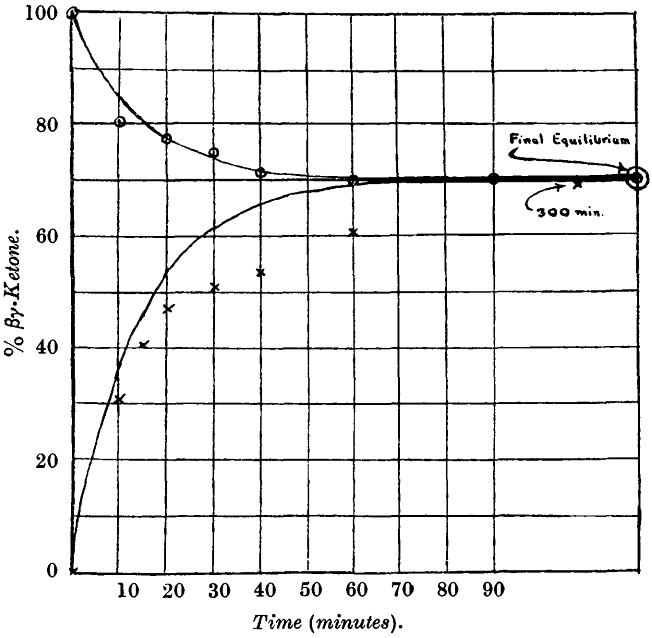
and esters (I and II, X = CO_2Et), the former exhibiting a high, and the latter a low degree of mobility. The conditions finally chosen as standard were : one equivalent of *N*-sodium ethoxide at 25°, the reagent being prepared from carefully dried alcohol. The mobility, as in the work on acids, can then be expressed in terms of the velocity coefficient (in minutes), $(k_1 + k_2) \times 10^4$, on the assumption of a unimolecular reversible reaction; or the half-change period, $t_{\frac{1}{2}} = 1/(k_1 + k_2) . \log_e 2$, can be used.

Effect of Sodium Ethoxide on the Ketones.—This reaction has already been studied by Dickins, Hugh, and Kon (J., 1928, 1630), using less than one equivalent of catalyst. It is now found that under the standard conditions both ketones pass rapidly into the equilibrium mixture, which contains 30% of the αβ-form (I). (In these and subsequent figures we are deliberately neglecting the small amounts of saturated impurity, not separable by fractionation, which are present.) The rate of equilibration and the point of equilibrium are the same when commercial " absolute " alcohol is used in place of the specially dried solvent, but large amounts of water diminish the rate of equilibration. It is, however, apparent that, whereas the βγ-ketone reaches equilibrium in about 60 minutes, the αβ-ketone takes very much longer. A similar difference is seen in the curves accompanying the previous paper (*loc. cit.*) and also in the figures for the homomesitones (Abbott, Kon, and Satchell, J., 1928, 2514) and can be illustrated by evaluating the equation for a unimolecular reversible change, $k_1 + k_2 = 1/t . \log_e \xi/(\xi - x)$. The change from the βγ-side gives an approximate value for $(k_1 + k_2) \times 10^4 = 700$ with a half-change period of 9·9 minutes. From this the amount of change in time *t* can be calculated by substituting it in the original equation for the change both from the αβ- and from the βγ-side. The figures so obtained are compared with those found experimentally in Fig. 1. The difference in the rates of equilibration of the two ketones is even more marked when sodium methoxide is employed; in fact an equilibrium mixture is not produced from the αβ-ketone even at the end of 48 hours. The reason for this must be sought in the slow addition of the elements of ethyl (or methyl) alcohol to the αβ-ketone with the production of an ethoxy(or methoxy)-derivative, doubtless of the structure $C_5H_{10}{>}C(OR){\cdot}CH_2{\cdot}COMe$; we have actually isolated such derivatives in both cases. Their formation is slow in comparison with the rate of tautomeric change and can practically be disregarded when one is dealing with the equilibration of the βγ-ketone, as shown by the agreement of the experimental and the calculated curve; the addition product is, however, formed in small amount when the reaction mixture is kept for, say, 20 hours. There is probably a definite equilibrium, αβ-ketone + EtOH $\rightleftharpoons$ ethoxy-ketone, which accounts for the small amount of the latter formed.

It is clear from the foregoing that in determinations of the mobility of a system small errors are always to be expected, which will be minimised by measuring the rate of equilibration of the βγ-isomeride.

Effect of Other Alkyloxides.—Sodium methoxide, propoxide and *iso*propoxide all produce the same equilibrium mixture, containing 30% of αβ- and 70% of βγ-ketone, but the rates of equilibration are very different. The order of efficiency of these catalysts is *iso*propoxide>propoxide>ethoxide>methoxide. The activity of the *iso*propoxide could not be compared directly with that of the others, because the strongest solution obtainable was 0·183 *N*; but even this is much more effective than *N*-ethoxide and about equal to *N*-propoxide; a comparison with 0·183 *N*-ethoxide and -propoxide also confirms the order of activity given and is apparent from the approximate times required for half-change (calculated for the αβ-ketone) :

FIG. 1.



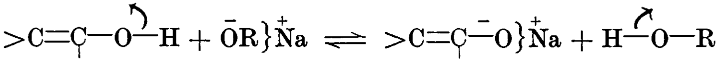
Full lines = theoretical curves for $(k_1 + k_2) \times 10^4 = 700$.
⊙ *and* × *= mean observed values from the βγ- and the αβ-side, respectively.*

Alcohol.	Concentration : $N/1$.	$N \times 0{\cdot}183$.
MeOH	180 mins.	—
EtOH	12 ,,	60 mins.
$Pr^{\alpha}OH$	5 ,,	40 ,,
$Pr^{\beta}OH$	—	9 ,,

In all these experiments the amounts of ketone and sodium remain constant and the differences are therefore due to the alcohols.*

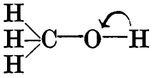
Such a result can readily be interpreted in the light of the ionic mechanism of tautomeric change and is regarded as significant evidence in support of the views discussed at the beginning of this paper.

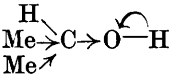
The rate of change may be considered as dependent on the concentration of the electromeric anion and hence on the ease of removal of the proton, either in solvated form or, as is more probable in the present case, in combination with the negative alkoxyl ion :



$$>\mathrm{C}=\underset{|}{\mathrm{C}}-\mathrm{O}-\mathrm{H}+\overset{-}{\mathrm{O}}\mathrm{R}\}\overset{+}{\mathrm{Na}} \rightleftharpoons >\mathrm{C}=\underset{|}{\mathrm{C}}-\overset{-}{\mathrm{O}}\}\overset{+}{\mathrm{Na}}+\mathrm{H}-\mathrm{O}-\mathrm{R}$$

(The ketone is here shown in its enolic form for the sake of simplicity; it is not intended to imply the extent of enolisation.) The extent to which the alkyloxy-ion $\overset{-}{O}R$ will be able to bring about this change will be determined by the toleration of its oxygen atom for the negative charge; the more stable the ion, *i.e.*, the greater the acidity of the alcohol, the less will be its tendency to remove a proton. The difference is well illustrated by comparing methyl alcohol with *iso*propyl alcohol :





In the latter the oxygen has a greater control of the C—O covalency electrons owing to the inductive effect of the two methyl groups and therefore its toleration for the negative charge is lowered (compare Allan and Robinson, J., 1926, 376; Robinson and Smith, *ibid.*, p. 392). The order of the activities of the alkoxyl ion already given is readily deduced from these considerations. The efficiency of the alcohols is the reverse of that expected from their dissociating powers as measured by their dielectric constants.

This explanation is also in good agreement with the observation that *cyclo*hexenylacetone cannot be methylated in presence of methyl alcohol, although it is readily ethylated in presence of ethyl alcohol (Kon, J., 1926, 1792). In the same way, sodium hydroxide

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* Since the above was written, Ingold and Shoppee have described a similar difference in the catalytic activities of sodium methoxide and ethoxide (this vol., p. 447, footnote).

should be less effective than sodium methoxide in causing tautomeric interchange, but difficulties arise owing to the fact that the ketone is practically insoluble in water, and, if enough alcohol is added, some of the alkoxyl ion may be formed. The only experiment performed shows that sodium hydroxide in 75% ethyl alcohol is much less effective than sodium ethoxide in its action on the αβ-ketone; a comparison with sodium methoxide is difficult owing to the addition which occurs with the latter.

Effect of Sodium Ethoxide on the Esters.—The conversion of the αβ-ester (I, $X = CO_2Et$) into a mixture of the two in presence of potassium hydrogen sulphate was shown by Birch, Kon, and Norris (J., 1923, **123**, 1361), and an interconversion in presence of sodium ethoxide at 60° was demonstrated by Linstead and May (J., 1927, 2565), but the point of equilibrium was not known with certainty.

It did not appear practicable to study the effect of sodium alkyloxides other than the ethoxide on the esters owing to the probability of replacement of the ester group.

The action of sodium ethoxide produces a slow equilibration and the rate of change is greatly affected by conditions. For instance, when the pure αβ-ester is treated with sodium ethoxide prepared from commercial absolute alcohol, a gradual change continues for some 250 hours; the mixture then contains 57% of the βγ-ester. At the same time there is considerable hydrolysis with the production of the corresponding acids (I and II, $X = CO_2H$), and 10% of a higher-boiling neutral fraction is also produced. This contains about half its weight of the β-ethoxy-ester, $C_5H_{10}{>}C(OEt){\cdot}CH_2{\cdot}CO_2Et$, formed in the same way as the corresponding ketone.

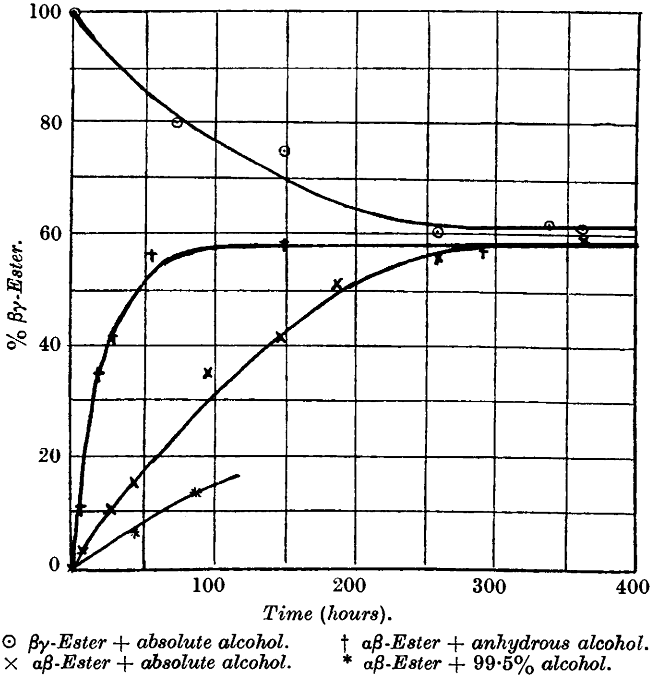
Under similar conditions the βγ-ester gives an equilibrium mixture containing 62% of the βγ-ester; the amount of addition product is very small and considerable hydrolysis again occurs.

The equilibration of the αβ-ester with sodium ethoxide prepared from specially dried alcohol gives the same final position of equilibrium (57% βγ-), but this value is attained in 63 hours. The same small amount of addition product is found, but the extent of hydrolysis is greatly reduced, being only 9% in 6 days and 16% in 12 days. Conversely, the addition of 0·5% of water to the ordinary absolute alcohol greatly increases hydrolysis and retards tautomeric change. These results are illustrated in Fig. 2.

In the light of the experiments on ketones, the retarding effect of water in the present instance is not attributed to a specific anti-catalytic action but merely to greatly increased hydrolysis which removes both the ester and the catalyst and thus rapidly decreases the concentration of the reactants; it is significant that the presence of water does not affect the final equilibrium point.

The βγ-ester appears to be hydrolysed more rapidly than the αβ, and there is always more βγ-acid in the mixed acids than βγ-ester in the neutral portion in the same experiments. This does not, however, affect the equilibrium (compare above) and we can therefore suppose that tautomeric change is more rapid than hydrolysis or, alternatively, the rates of hydrolysis of the two esters are of the same order as the proportion of the esters in the equilibrium mixture (4 : 6).

FIG. 2.



The ethoxy-ester is formed rapidly although in small amount, and this does not increase appreciably on standing; apparently an equilibrium is rapidly set up between the ethoxy- and the αβ-ester and is not disturbed.

The ethoxy-ester has been isolated in a pure state by repeated fractionation and hydrolysed to the corresponding solid acid; we have not yet demonstrated the position of the ethoxy-group with certainty, although it is presumably on the β-carbon. The ethoxy-ester boils some 15° higher than the αβ-ester and shows a definite though small reaction with iodine chloride; its presence in somewhat greater amount in the equilibrium mixture obtained from the αβ-side is understandable and probably accounts for the slightly divergent equilibrium values found from the two sides.

The true equilibrium is considered to be that found from the βγ-side, namely 62% of βγ-ester. The mobility is $(k_1 + k_2) \times 10^4 =$ 8·1 (in minutes), with a half-change period of 14·1 hours.

The correctness of the figures obtained for the equilibrium from the αβ-side was confirmed by the hydrolysis of an ester with an iodine addition corresponding to an αβ-content of 43·5%, under conditions precluding isomeric change. The acid obtained had an iodine addition corresponding to an αβ-content of 42%. The reversibility of the change was also confirmed satisfactorily by the isolation of pure βγ-acid from an equilibrated αβ-ester and of pure αβ-acid from an equilibrated βγ-ester (p. 1280).

EXPERIMENTAL.

A. *Ketones.*

*cyclo*Hexylideneacetone (I, X = COMe) was prepared as described by Dickins, Hugh, and Kon (*loc. cit.*) and purified by fractionation. The specimen used had b. p. 83—84°/12 mm., $d_{4°}^{15·6°}$ 0·95188, $n_D^{15·6°}$ 1·49224, whence $[R_L]_D = 42·11$. *cyclo*Hexenylacetone (II, X = COMe) was regenerated from the semicarbazone and treated with aluminium amalgam (compare Abbott, Kon, and Satchell, *loc. cit.*), the product having a somewhat higher iodine addition than the best previously obtained; it had b. p. 77°/11 mm., $d_{4°}^{19·0°}$ 0·93760, $n_D^{19·0°}$ 1·47389, whence $[R_L]_D = 41·39$. The alcohols used were dehydrated by digesting them twice with calcium (Winkler, *Ber.*, 1905, **38**, 3612).

Procedure.—A weighed quantity of the ketone, and the requisite amount of a titrated solution of sodium in the appropriate alcohol (slightly stronger than normal), together with the additional quantity of the alcohol required to bring the concentration to normal, were separately brought to 25° (thermostat), and then thoroughly mixed. At intervals, test portions, containing 1·5—2 g. of the ketone, were run into 200 c.c. of water containing enough acetic acid to neutralise the alkali formed, and the ketone was twice extracted with ether. The extract (about 150 c.c.) was shaken four times with an equal volume of water and dried over calcium chloride and the ether was removed through a column; the residue was distilled under reduced pressure, a fraction covering the b. p.'s of both ketones being collected. The yields were good (over 80%). The fractions were analysed iodometrically by the method of Linstead and May (*loc. cit.*). A new reference curve was constructed from the following values :

% αβ-Ketone	100	90	75	50	25	10	0
% Iodine addition ...	16·9	26·6	41·0	62·0	77·6	83·4	85·8

Accuracy of the Method.—In some experiments the test portions were halved and the ketone in each half was isolated and analysed separately as a check on the accuracy of the method (Expts. 16 and 17, Table I). The values did not diverge by more than 0·5% in the iodine addition. The agreement between corresponding values obtained in different experiments is of the order of ± 1% (compare Table I).

Table I gives the results obtained. There is no difference, within the limits of experimental error, between the effect of sodium ethoxide prepared from dry (Expts. 1—3) and commercial "absolute" alcohol (Expts. 4 and 5).

The strongest solution of sodium in *iso*propyl alcohol which did not deposit solid sodium *iso*propoxide was about *N*/5; in order to ensure a comparison with sodium ethoxide and propoxide, a series of experiments (8—10) was carried out with 0·183 *N*-solutions of sodium in the appropriate alcohol. These experiments suffice to show the order of the reaction and incidentally illustrate the effect of dilution.

The point of equilibrium was determined for each alcohol separately and the agreement is satisfactory, the value being 30% of αβ-ketone. The equilibrium mixture derived from the αβ-ketone was also analysed (Found: C, 77·6; H, 10·1. Calc. for $C_9H_{14}O$: C, 78·2; H, 10·2%).

The high fraction obtained from the sodium ethoxide experiments was redistilled; a definite fraction, b. p. 99—101°/9 mm., was obtained which appeared to consist of 30% of unsaturated ketone and 70% of *ethoxy-ketone* (Found: C, 73·3; H, 10·5. $C_{11}H_{20}O_2$ requires C, 71·7; H, 10·9%). When treated with semicarbazide, it gave the *semicarbazone* of 1-ethoxy*cyclo*hexylacetone, which formed fine plates, m. p. 174°, from methyl alcohol (Found: C, 59·5; H, 9·4. $C_{12}H_{23}O_2N_3$ requires C, 59·7; H, 9·6%).

A similar high fraction was obtained in the sodium methoxide experiments; the *semicarbazone* of the methoxy-ketone isolated from it formed plates, m. p. 181—182° (Found: C, 57·9; H, 9·3. $C_{11}H_{21}O_2N_3$ requires C, 58·1; H, 9·3%).

B. *Esters.*

Materials.—Ethyl *cyclo*hexylideneacetate (I, X = CO_2Et) was prepared from the corresponding acid either through the acid chloride—the product then contained sub-analytical traces of chlorine—or by boiling with 4% alcoholic hydrogen chloride for 2¼ hours. Ethyl Δ^1-*cyclo*hexenylacetate (II, X = CO_2Et) was prepared from the corresponding acid through the acid chloride or by keeping it at room temperature with twice its volume of

TABLE I.

Equilibration of Ketones.

Expt.	Reagent.	Material.	Time (mins.) 10	15	20	30	40	60
1	*N*-NaOEt anhydrous	$\alpha\beta$	—	—	—	—	—	69·0
2	,, ,,	$\alpha\beta$	Lost	54·1	59·4	61·9	64·9	—
3	,, ,,	$\alpha\beta$	45·2	—	59·0	—	65·8	68·5
4	,, {from commercial absolute alcohol}	$\alpha\beta$	47·9	—	60·0	62·2	64·1	—
5	,,	$\alpha\beta$	47·6	—	—	—	—	69·1
6	*N*-NaOPr$^{\alpha}$ anhydrous	$\alpha\beta$	64·6	—	67·5	73·6	—	—
7	,, ,,	$\alpha\beta$	—	—	—	*74·8*	—	—
8	0·183*N*-NaOPr$^{\alpha}$ anhydrous	$\alpha\beta$	27·4	—	37·2	—	—	—
9	,, NaOPr$^{\beta}$,,	$\alpha\beta$	51·1	—	63·7	—	—	—
10	,, NaOEt ,,	$\alpha\beta$	Lost	—	28·1	—	—	—
11	*N*-NaOEt anhydrous	$\beta\gamma$	80·2	—	78·7	77·5	75·3 *74·9*	*74·4* (90 minutes)

Expt.	Reagent.	Material.	Time (mins.) 60	120	240	360
12	*N*-NaOMe anhydrous	$\alpha\beta$	41·5	44·7	55·1	60·0
13	,, ,,	$\beta\gamma$	—	79·4	77·0	*74·3*

Other experiments.

Expt.	Reagent.	Material.	
14	*N*-NaOH in 75% EtOH	$\alpha\beta$	60·3 (95 minutes)
15	,, (approx) NaOPr$^{\beta}$	$\alpha\beta$	*74·8* (360 minutes)
16	,, NaOPr$^{\alpha}$ [combined fractions of (6)]		*74·5*, *74·5* (240 minutes)
17	,, NaOEt ,, ,, ,, (2) and (4)		73·7, 73·2 (300 minutes)
18	,, ,, ,, ,, ,, (3)		*74·6* (1200 minutes)
19	,, NaOMe ,, ,, ,, (12)		66·5 (3200 minutes)
20	,, ,, ,, ,, ,, (13)		*74·2* (1440 minutes)

The figures refer to iodine additions. Those italicised represent equilibrium values. The mean figures in Expts. 1, 2, 3, 4, 5, and 11 were used in plotting Fig. 1.

N-alcoholic hydrogen chloride and six times its volume of absolute alcohol for 4 hours. The properties of these esters were as follows :

Ester.	Preparation.	$n_{\mathrm{D}}^{t^\circ}$.	$D_{4^\circ}^{t^\circ}$.	B. p.	% Iodine addition.
αβ (1)	Alcoholic HCl	1·47986/17·9°	0·9829/17·9°	112—114°/16 mm.	7·4
αβ (2)	Acid chloride	1·47986/18·0	0·9877/18	114·5—115·5/14	6·9
αβ (3)	Acid chloride	1·47889/18·0	0·9857/18	108/13	7·3
βγ (1)	Acid chloride	1·4621/24·3	—	113—114/26	75·8
βγ (2)	Alcoholic HCl	1·4639/18·0	0·9785/18	98/13	76·3

The iodine additions given in this section refer to the % addition in 60 minutes under the conditions of Linstead and May (*loc. cit.*, p. 2578).

In the present work the three preparations of the αβ-ester were mixed, also the two of the βγ-ester (Found : for the αβ-ester, C, 71·1 ; H, 9·3 ; for the βγ-ester, C, 70·9 ; H, 9·4. Calc. : C, 71·4 ; H, 9·6%). Mixtures of the αβ(1)- and the βγ(2)-ester gave the following iodine additions, which were used in plotting the reference curve :

% *αβ*-Ester …………	75	60	50	40	33·3	20	14·3
% Addition …………	29·4	41·8	49·6	56·8	61·0	68·8	71·7

Action of Sodium Ethoxide on the Esters.—A weighed quantity of the ester was treated with an equivalent amount of sodium ethoxide (in the form of a solution slightly stronger than normal) as described for the ketones. In general, about 10 g. of ester were used in each experiment. The reaction was allowed to proceed at 25° in a thermostat. After a suitable interval of time a portion of the solution (v c.c.), with an ester content of 3—6 g., was withdrawn, immediately treated with *N*/2-sulphuric acid ($3v$ c.c.), and then extracted with ether ($6v$ c.c.) in three portions. The united extracts were freed from ether and the residue was heated on the steam-bath for ½ hour to remove the bulk of the alcohol. The residual oil was shaken with 100 c.c. of 10% sodium carbonate solution until effervescence ceased ; the neutral portion was then extracted with ether ($6v$ c.c.), the extract dried and freed from solvent, and the residue fractionally distilled under reduced pressure, the apparatus used being the same throughout the work. None of the material boiled below the boiling range of the unsaturated esters. The liquid boiling above 115°/14 mm. was collected separately and is referred to in Table II as " ethoxy-ester fraction," although it contained a considerable amount of unsaturated esters. The sodium carbonate extract of the neutral substance was extracted once more with ether to remove traces of ester, acidified, and thoroughly extracted with ether. The dried solution was freed from solvent on the steam-bath and finally in a vacuum desiccator.

TABLE II.

Action of Sodium Ethoxide on Esters.

			Acid product.		Neutral product.						
						Unsaturated ester.					
Initial ester.	Time (hours).	Amount used (g.).	G.	Composition, % $\beta\gamma$.	Ethoxy-ester fraction (g.).	G.	B. p. °/14 mm.	$n_D^{t^\circ}$.	$d_{4^\circ}^{t^\circ}$.	% Iodine addition.	% $\beta\gamma$ Ester.
1 $\alpha\beta$	6·72	3·25	—	—	0·2 (6%)	2·0 (62%)	102—111°	1·4763/19·1°	0·9777	10·3	3
2 $\alpha\beta$	28·75	3·27	—	—	0·25 (8%)	1·6 (49%)	98—111	1·4698/24·3	0·9747	17·7	11
3 $\alpha\beta$	45	3·33	1·4 (51%)	65	0·2 (6%)	1·2 (36%)	104—115	1·4703/16·8	—	21·5	15·5
4 $\alpha\beta$	97·25	3·27	1·75(33%)	64	0·25 (8%)	1·7 (52%)	91—106	1·4618/24·2	0·9753	38·6	36
5 $\alpha\beta$	144·5	3·54	—	—	—	1·1 (31%)	91—113	1·4606/24·0	0·9730	43·2	41·5
6 $\alpha\beta$	185	5·28	2·1 (40%)	62	0·35 (7%)	2·4 (45%)	100—116	1·4632/18·4	0·9787	49·4	50·5
7 $\alpha\beta$	266	4·75	—	—	0·2 (4%)	1·5 (32%)	105—114	1·4598/21·6	0·9747	54·2	56
8 $\alpha\beta$	360	4·75	—	—	0·35 (7%)	1·4 (30%)	103—113	1·4626/19·8	0·9760	56·0	59
9 $\alpha\beta$	8	3·31	Nil	—	Nil	1·9 (58%)	104—115	1·4750/16·8	—	19·6	13
10 $\alpha\beta$	17	5·43	Trace	—	0·2 (4%)	4·25(78%)	98—108	1·4695/19·5	0·9786	37·9	35
11 $\alpha\beta$	28·75	5·22	,,	—	0·2 (4%)	3·35(64%)	100—112	1·4670/20·3	0·9778	43·0	41·5
12 $\alpha\beta$	63·5	5·43	,,	—	0·75(13%)	4·0 (74%)	95—110	1·4643/19·5	0·9794	54·5	56·5
13 $\alpha\beta$	148	5·22	0·4 (9%)	—	0·7 (13%)	3·4 (65%)	103—116	1·4654/17·0	—	56·0	59
14 $\alpha\beta$	290	6·61	0·9 (16%)	78	0·7 (11%)	4·52(69%)	98—115	1·4645/16·7	0·9822	54·5	56·5
15 $\alpha\beta$	45	3·20	—	—	Nil	0·8 (25%)	104—112	1·4724/15·2	0·9843	13·7	6·5
16 $\alpha\beta$	90	3·20	—	—	,,	0·7 (22%)	104—108	1·4685/13·8	0·9855	20·3	14·5
17 $\beta\gamma$	70	3·74	1·4 (45%)	94	0·1 (2%)	1·3 (35%)	96—116	1·4656/17·0	—	69·1	80
18 $\beta\gamma$	148·5	3·74	1·5 (48%)	91	0·12 (3%)	1·3 (35%)	93—115	1·4653/16·7	0·9788	66·2	75·5
19 $\beta\gamma$	266	3·26	—	—	0·3 (9%)	1·9 (58%)	103—116	1·4630/19·4	0·9770	57·6	61
20 $\beta\gamma$	337	7·92	3·5 (53%)	90	0·2 (3%)	2·62(33%)	94—115	1·4643/16·7	0·9822	58·6	62·5
21 $\beta\gamma$	360	3·26	—	—	0·3 (9%)	1·5 (46%)	102—112	1·4630/19·7	0·9757	58·0	61·5

The alcohol used in these experiments was: (1—8) commercial absolute alcohol; (9—14) anhydrous alcohol; (15—16) absolute alcohol + $\frac{1}{2}$% of water; (17—21) commercial absolute alcohol.

Examination of the Products.—The neutral distillates—main and high fractions—were weighed and the physical properties and iodine addition of the main fraction were taken. In several cases the neutral product was distilled in two portions, the results obtained agreeing closely. The acid product was weighed and, where the amount was sufficient, the iodine value was determined by Linstead and May's interpolation method (*loc. cit.*, p. 2568). In these determinations the alkaline solutions were acidified before titration (*loc. cit.*, footnote, p. 2574) and it was therefore necessary to construct a new reference curve, mixtures of the two pure acids (I and II, X = CO_2H) being used. The figures obtained under the new conditions for a 10-minute reaction were :

% αβ-Acid ...	100	80	50	33·3	25	10	0 (βγ-acid)
% Addition ...	1·0	18·0	35	45·3	48·2	54·0	55·6

The results are summarised in Table II and the main inferences from them have already been made.

Purity of the Unsaturated Ester Fraction.—The refractive index of the ester drops progressively on equilibration (column 10) and the mean value for the equilibrated product (1·4643/17°) is almost identical with that of the βγ-form. This is an indication of the presence of the less refractive ethoxy-ester which is confirmed by analysis [Found : (Expt. 12) C, 70·0, 70·1; H, 9·7, 9·8%]. The figures in the last column are obtained from the iodine addition of the corresponding unsaturated ester fraction by means of the reference figures given on p. 1278. It is obvious that if this fraction contains saturated impurity the observed iodine addition will give an almost correct value for the βγ-content, but will be unable to distinguish between the two non-reactive substances present. Hence the values in the last column in Table II represent the percentage of βγ-ester in the total product and the true percentage—in equilibrium with αβ-ester—will be greater than this. On the other hand, a small amount of unsaturated ester is undoubtedly present in the ethoxy-ester fraction, and of the two unsaturated esters there will be a larger proportion of the higher-boiling αβ-ester in this fraction than in the main fraction in the corresponding experiment. Hence, on this basis, the observed αβ-content in the unsaturated ester fraction will be too low. As the former source of error probably exceeds the latter, the recorded percentage of αβ-ester in the equilibrium mixture represents a maximum.

Hydrolysis of the Equilibrated Esters.—In order to confirm the essential change αβ-ester $\rightleftharpoons$ βγ-ester, the equilibrated αβ-ester was hydrolysed to the βγ-acid, and the equilibrated βγ-ester to the αβ-acid. (1) The αβ-ester (6·67 g.) was equilibrated for 381 hours in the usual way. The neutral product was fractionated twice and a fraction of b. p. 102—105°/16 mm. finally collected. This was hydrolysed with 50% excess of 10% sodium hydroxide solution in the cold for 24 hours, alcohol being added until the mixture was homogeneous (compare Linstead, J., 1927, 2579). The acid fraction was isolated in the usual way and solidified almost completely in a vacuum desiccator. The acid melted at 35—37° alone and at 37—38° when mixed with pure Δ^1-*cyclo*hexenylacetic acid. (2) A sample of equilibrated βγ-ester (Expt. 20, Table II) was refractionated, and the fraction boiling at 112—114°/15 mm. hydrolysed by the method given above. When the alkaline liquid was acidified, *cyclo*hexylideneacetic acid crystallised in long needles, which, alone or when mixed with an authentic sample, melted at 90—91°.

To confirm the composition of the equilibrium mixture of esters, a sample (3·8 g.) obtained from the αβ-ester (Expt. 14, Table II) was hydrolysed with 120 c.c. of 10% sodium hydroxide solution in the manner already described, 3·0 g. of a liquid mixture of acids being obtained. This had an iodine addition of 41·2%, corresponding to an αβ-content of 42%, which agrees well with that (43·5% of αβ) obtained by analysis of the original ester. The nature of the acids was confirmed by treating the mixture with a concentrated solution of iodine under Bougault's conditions (*Ann. Chim. Phys.*, 1908, **14**, 145): 0·80 g. of the mixture then gave 0·16 g. of the αβ-acid (20%) (m. p. and mixed m. p. 90—91°) and 0·85 g. (60%) of the γ-lactone of 1-iodo-2-hydroxy*cyclo*hexyl-1-acetic acid (m. p. 56°, alone or when mixed with a specimen prepared from authentic βγ-acid). These substances were isolated by the method previously used (Linstead and May, *loc. cit.*).

The Acid Products.—In the earlier experiments (1, 2, 5, 7, and 8) the acid products obtained by the hydrolysis of the esters during equilibration were not collected separately (this accounts for the gaps in Table II) but were accumulated in bulk. The mixture so obtained, which was completely soluble in sodium bicarbonate solution, did not solidify in a vacuum desiccator and when fractionated (5 g.) under reduced pressure boiled entirely within the range of the two unsaturated acids. Two fractions were obtained: (1) 145°/22 mm.—150°/17 mm. (2·5 g.) and (2) 150°/17 mm.—158°/21 mm. (1·6 g.). Fraction (1) in ice gave plates of the βγ-acid, m. p. 37°; fraction (2) on long standing gave the αβ-acid as a crystalline powder, m. p. 86—88°, and on subsequent cooling in ice gave the βγ-acid.

In subsequent experiments in which the acid fractions were isolated separately the product often wholly or partly solidified after complete removal of the solvent (Expts. 6, 14, 17, 18, and 20).

In every case the solid was the βγ-acid (m. p. 37°). These results support those obtained from analysis by the iodine method.

The Ethoxy-ester Fraction.—This was accumulated, and the whole distilled from a Claisen flask with a fractionating column in the side arm. The fraction boiling above 121°/15 mm. (2·1 g.) was collected separately and redistilled; 1·7 g. were then obtained, boiling steadily at 128°/15 mm. This was pure *ethyl* 1-*ethoxy*cyclo*hexylacetate* (Found: C, 67·2; H, 10·2. $C_{12}H_{22}O_3$ requires C, 67·2; H, 10·4%). The ester is a colourless liquid noticeably less mobile and less odorous than the unsaturated esters. It has b. p. 122°/11 mm., $n_D^{17·4°}$ 1·45753, $d_4^{17·4°}$ 0·9865. Under standard conditions it has a slight reaction with iodine chloride (13·4%).

Hydrolysis of the ester with potassium hydroxide gave a good yield of the corresponding acid, m. p. 43°; recrystallised from ether, this formed flattened needles, m. p. 50—51°. It was immediately soluble in aqueous sodium bicarbonate, and the solution did not reduce permanganate. The *silver* salt was appreciably soluble in hot water, from which it crystallised in fine needles, m. p. 216° (decomp.) (Found: Ag, 37·0. $C_{10}H_{17}O_3Ag$ requires Ag, 36·8%).

In an attempt to confirm the β-position of the ethoxyl group (assumed above) the ester was heated in a sealed tube with a solution of hydrogen bromide in acetic acid for 2 hours. The product was evaporated on the steam-bath and left in a vacuum desiccator over potassium hydroxide. A white crystalline solid remained, m. p. 60°. Owing to the extremely small amount available it was not possible to recrystallise this and confirm its identity with 1-bromo-1-*cyclo*hexylacetic acid (m. p. 90°). The fact that a solid acid and not a liquid lactone was obtained, however, indicates that the ethoxyl group in the original ester is in the β-position to the carbethoxyl group.

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