381. *The Action of Sodium Ethoxide on Itaconic, Citraconic, and Mesaconic Esters.*

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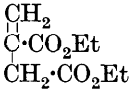
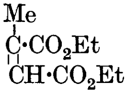
Although the experiments of Hope (J., 1912, **101**, 895) and Ingold, Shoppee, and Thorpe (J., 1926, 1477) on the condensation of ethyl sodiomalonate with ethyl citraconate or itaconate prove, as the latter authors suggest, that tautomeric change in the esters is responsible for the results obtained, the formation of a condensation



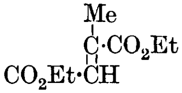
$$\begin{array}{l} CH_2 \\ \| \\ C\cdot CO_2Et \\ | \\ CH_2\cdot CO_2Et \end{array}$$

(I.)



$$\begin{array}{l} Me \\ | \\ C\cdot CO_2Et \\ \| \\ CH\cdot CO_2Et \end{array}$$

(II.)



$$\begin{array}{r} Me \\ | \\ C\cdot CO_2Et \\ \| \\ CO_2Et\cdot CH \end{array}$$

(III.)

product cannot be taken as a strict measure of the equilibrium established, since this is largely influenced by other factors such as the solubility of the resulting sodio-derivatives. We have therefore undertaken a study of the equilibration of ethyl itaconate (I) and its αβ-isomerides, ethyl citraconate and mesaconate (II and III), under Kon and Linstead's standard conditions (J., 1929, 1269).

Preliminary tests showed that the pure esters suffer a rapid addition of the elements of ethyl alcohol on treatment with sodium ethoxide, with the formation of Hope's ethoxy-ester (ethyl ω-ethoxymethylsuccinate). A quantitative technique for the estimation of this together with the three unsaturated esters, the latter based on Linstead and Mann's work on the acids (J., 1931, 726), has been developed, and its accuracy tested on mixtures of known composition; results accurate to 2% are obtained (Table I).

TABLE I.

No.	Ester.	Time, mins.	Composition, %. Citra.	Mesa.	Ita.	Ethoxy.	Error, %.
1	Citraconic	5	6	26	9	55	− 4
2	,,	30	11	17	—	71	− 1
3	,,	180	12	14	—	76	+ 2
4	,,	420	14	10	—	68	− 8
5	,,	2880	4	7	—	80	− 9
6	Itaconic	5	7	18	8	63	− 4
7	,,	30	16	14	—	74	+ 4
8	,,	180	14	7	—	77	− 2
9	Mesaconic	5	7	33	12	37	−11
9a	,,	5	8	39	11	41	− 1
10	,,	30	7	12	—	72	− 9
11	,,	180	14	12	—	74	0
12	Ethoxy	240	6	10	—	80	− 4

The addition of alcohol amounts to some 50% at the end of 5 minutes and reaches a maximum of about 80%, but some unsaturated ester is always recovered. Treatment of the ethoxy-ester with sodium ethoxide leads to a similar mixture and the addition of alcohol to these esters is therefore reversible. In all but the shortest experiments, the unsaturated ester consists of the two αβ-forms only (citraconic and mesaconic ester), but a definite, though small, amount of ethyl itaconate is isolated in the 5-min. experiments (Nos. 1, 6, 9, and 9a).

The addition of alcohol is so great that the mobility and equilibrium in this system can hardly be profitably discussed. The mobility must be of a very high order, because equilibration appears to be complete in the 5-min. experiments, but the constant removal of one of the reaction products in the form of ethoxy-ester must, by disturbing the equilibrium, lead to increased mobility.

The isolation of ethyl itaconate in the experiments of short duration, no matter what initial material is employed, shows that an equilibrium between the unsaturated esters is actually established and that the three-carbon change is more rapid than the addition of alcohol. The proportion of unsaturated esters present in these equilibrium mixtures is roughly 77% αβ and 23% βγ (the true value is probably even nearer the αβ side, because the ethoxy-acid has a slight but appreciable affinity for bromine, 0·9%). On the other hand, the equilibrium value can be regarded as giving a maximum for the αβ content, because the effect of addition, by artificially removing the βγ-form, tends to increase the amount of αβ-form produced.

In the experiments with ethyl citraconate, the proportion of this ester decreases rapidly at first and then rises again, when most of the ethyl itaconate present has been removed as ethoxy-ester, whereas the reverse is true of ethyl mesaconate. Since Linstead and Mann (*loc. cit.*) have shown that the interconversion of the corresponding acids takes place through the intermediate production of itaconic acid, it seems likely that the above observation can be explained in a similar way and that the change of configuration proceeds by way of the more rapid tautomeric change.

The conclusion of Ingold, Shoppee, and Thorpe (*loc. cit.*), from theoretical considerations, that the equilibrium in the citraconic–itaconic system favours the βγ-form (compare Shoppee, J., 1930, 968) should be qualified : it is correct to say that the presence of the β-carbethoxyl group confers additional stability on the βγ-form in this system as compared with the vinylacetic–crotonic system, in which the equilibrium may be supposed to be completely on the side of the αβ-form (no observations are available regarding the esters, but the above inference nevertheless appears to be justified).

The structure of the ethoxy-ester has been established by Ingold, Shoppee, and Thorpe (*loc. cit.*) by its conversion, through the corresponding acid, into paraconic acid; the acid, therefore, has the constitution (IV). The analogous methoxy-acid was obtained by Hope (*loc. cit.*) by the same method as the acid (IV) and should therefore have a similar structure : it melts, however, 10° lower than an acid of that formula synthesised by Simonsen (J., 1915, **107**, 783). As Hope's acid might have the alternative formula (V), the ethoxy-acid (IV) was prepared by a modification of Simonsen's method ; it was identical with the ethoxy-acid prepared by Hope's method.

$CH_2(OEt)\cdot CH(CO_2H)\cdot CH_2\cdot CO_2H$ (IV.)

$CHMe(CO_2H)\cdot CH(OEt)\cdot CO_2H$ (V.)

In view of the great mobility of the esters of the itaconic group, it appeared possible that they could be alkylated; all attempts to do so with ethyl iodide and potassium in toluene or potassium ethoxide in ether failed, however, and no evidence could be obtained of their ability to form sodio- or potassio-derivatives.

We have also made numerous attempts to equilibrate the three isomeric esters under conditions precluding addition of alcohol. Heat alone does not cause interconversion, apart from polymerisation of ethyl itaconate; alcoholic sulphuric acid and alcoholic hydrochloric acid are also without effect.

EXPERIMENTAL.

Materials.—Itaconic, citraconic, and mesaconic acids were prepared as described in " Organic Syntheses " (Vol. **11**, pp. 70, 28, 74) and converted into the ethyl esters by the procedure of Kon and Watson (this vol., p. 1): itaconate, b. p. 117·5°/19 mm., $d_{4^\circ}^{20\cdot0^\circ}$ 1·0467, $n_D^{20\cdot0^\circ}$ 1·4377, $[R_L]_D$ 46·65; citraconate, b. p. 122°/21 mm., $d_{4^\circ}^{20\cdot0^\circ}$ 1·0491, $n_D^{20\cdot0^\circ}$ 1·4442, $[R_L]_D$ 47·14; mesaconate, b. p. 118°/20 mm., $d_{4^\circ}^{20\cdot0^\circ}$ 1·0453, $n_D^{20\cdot0^\circ}$ 1·4488, $[R_L]_D$ 47·74.

Trial expts. showed that itaconic acid could also be esterified without isomerisation by Hope's method (*loc. cit.*) (50% yield) or by the Fischer and Speier method (64% yield): the latter method was adopted for the prep. of the esters in quantity; it gave yields of about 85% when applied to citraconic and mesaconic acids. The purity of the esters was checked by their physical properties, by analysis, and by hydrolysis to the acids (see below).

Ethyl ω-ethoxymethylsuccinate, prepared by Hope's method (*loc. cit.*) and repeatedly fractionated, was obtained in 30% yield, b. p. 137—138°/16 mm., $d_{4^\circ}^{20\cdot0^\circ}$ 1·0274, $n_D^{20\cdot0^\circ}$ 1·4269, $[R_L]_D$ 57·97 (calc., 57·95) (Found: C, 56·7; H, 8·4. Calc.: C, 56·9; H, 8·6%). The ester, on hydrolysis by the standard method described below, gave the acid, which had the correct mol. wt. without purification (Found: *M*, dibasic, 175·1. Calc., 176·1) and crystallised from Et_2O–petroleum in thick needles, m. p. 86° (Found: C, 48·1; H, 6·9. Calc.: C, 47·8; H, 6·8%); it had a Br addition of 0·9% under the standard conditions employed.

Analytical Methods.—It was not found possible to apply iodometric or bromometric methods of analysis to the esters themselves. The esters could, however, be hydrolysed without change, and the resulting mixture of acids analysed by a slight modification of the method used by Linstead and Mann (*loc. cit.*).

In a preliminary expt., the pure esters were treated with a 10% excess of 2*N*-NaOH diluted with an equal vol. of abs. EtOH and kept at room temp. for 24 hrs.; hydrolysis was then complete. The EtOH was removed under reduced press., the calc. amount of 2*N*-H_2SO_4 added, and the liberated acids extracted with Et_2O. The extract was dried, evaporated to a small vol., quantitatively transferred to a tared wide-mouthed flask, and evaporated to dryness, first on the steam-bath and finally in a vac. desiccator. The pure esters gave the following results:

Ester.	Wt., g.	Acid rec., g.	Wt., calc.	M. p. of acid.
Itaconic	2·28	1·56	1·59	163°
Citraconic	1·85	1·20	1·29	87
Mesaconic	3·76	2·51	2·63	202
Ethoxy	3·26	2·42	2·47	80

In carrying out the actual analyses, the hydrolysis was conducted as above but the EtOH was not removed, the neutralised liquid being steam-distilled to remove citraconic acid; the residual acids (itaconic and mesaconic) were then extracted as above and estimated bromometrically (compare Linstead and Mann, *loc. cit.*). The analysis of a mixture of all three esters (itaconate 14·4, citraconate 51·3, mesaconate 34·3%) gave the following result: itaconate 15·4, citraconate 44·3, mesaconate 34·8%.

Owing to the considerable error in the amount of citraconic acid found, Linstead and Mann's procedure was modified, the citraconic acid in the steam distillate being neutralised with 15 c.c. of 2*N*-NaOH. The liquid was then evaporated to a small vol., 30 c.c. of *N*-H_2SO_4 added, and the excess of acid titrated with alkali (the addition of excess of acid is necessary owing to the formation of bicarbonate in the course of the concn. of the solution). This method gave accurate results; *e.g.*, 1·17 g. of citraconic acid were dissolved in 2 l. of H_2O and estimated as above, 1·15 g. being found. Apart from this, Linstead and Mann's method was followed exactly; it was found convenient to make a new reference curve for the Br additions.

Estimation of the Ethoxy-acid.—The ethoxy-acid was not volatile in steam and could be estimated by Perkin's modification of the Zeisel method (J., 1903, **83**, 1369). This was carried out on the crude acid mixture isolated after the removal of the citraconic acid, and a titration with *N*/10-$Ba(OH)_2$ was carried out at the same time; it was thus possible to calculate the quantity of the mixed acids necessary to make up an *M*/15-solution of the unsaturated acids for the bromometric estimation, the presence of the ethoxy-acid being neglected. As already mentioned, this tends to give slightly high results for the $\beta\gamma$- (itaconic) acid content of the mixture, as the ethoxy-acid has an addition of 0·9%.

An artificial mixture of all four esters (itaconate 15·8, citraconate 40·9, mesaconate 29·7, ethoxy-ester 13·6%) was analysed as above with the following result: itaconate 16·7, citraconate 40·1, mesaconate 31·1, ethoxy-ester 12·5%.

Equilibrations.—These were carried out as described by Kon and Linstead (*loc. cit.*), and the products isolated in the same way. The principal results are in Table I.

Synthesis of the Ethoxy-acid (IV).—A mixture of 50 g. of ethyl ethane-$\alpha\alpha\beta$-tricarboxylate (Kay and Perkin, J., 1906, **89**, 1640) and 8 g. of "molecular" K in C_6H_6 was kept until the reaction was complete (1 hr.), 40 g. of chloromethyl ethyl ether (" Organic Syntheses," **9**, p. 58; EtOH was used in place of MeOH) were gradually added, and the mixture was kept in the cold overnight. H_2O was then added, and the ester isolated from the C_6H_6 solution. Two fractions, b. p. 169—174°/21 mm. (28 g.), and 174—184°/19 mm. (23 g.), were obtained. A part of the higher fraction, hydrolysed with KOH, gave an acid, m. p. 130—134° (decomp.), which was heated at 140° until the evolution of CO_2 was complete: the residue could not be recrystallised and was evidently a mixture.

The remainder of the high-boiling tricarboxylic ester was again fractionated, the highest-boiling portion (b. p. 167—170°/14 mm.) hydrolysed, the resulting acid heated as above, the crude dicarboxylic acid (2·5 g.) esterified, and two fractions obtained by distillation. The higher-boiling (1·2 g.), b. p. 136—140°/14 mm., gave on hydrolysis an acid, m. p. 81—82° after crystn. from Et_2O–petroleum, mixed m. p. with the pure ethoxy-acid, 84° (Found: C, 47·6; H, 6·8; *M*, dibasic, 175·7. Calc.: C, 47·8; H, 6·8%; *M*, 176·1).

Heat Treatment of the Esters.—Ethyl itaconate was boiled under reflux for 16 hrs.: only a small portion (18%) of the product boiled between 110° and

125°/14 mm.; $n_D^{20\cdot0^\circ}$ 1·4444; the remainder was viscous and high-boiling. After only 2 hrs.' boiling, the distillate (50%) consisted of the unchanged ester. A similar result was obtained when the ester was heated in a sealed tube at 200° for 4 hrs., but the recovery of unsaturated ester, $n_D^{20\cdot0^\circ}$ 1·4396, was better.

Ethyl citraconate, heated in a sealed tube as above or in an atm. of N or CO_2, underwent no change even in 24 hrs. Ethyl itaconate also did not undergo any change except polymerisation. Both gave the pure acids on hydrolysis.

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