11. *Studies on the Michael Reaction. Part II. The Nature of the Condensation Product from Ethyl Benzylmalonate and Ethyl Fumarate.*

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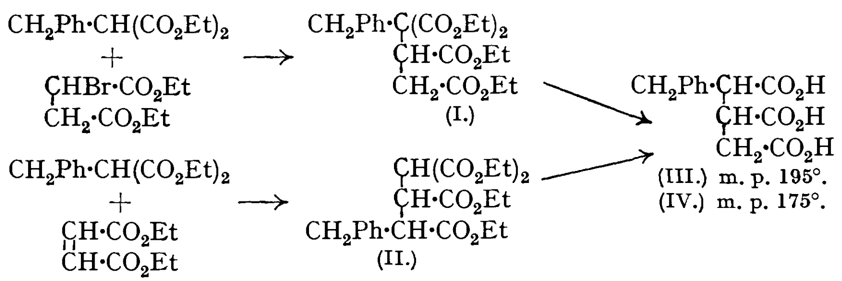
In agreement with Malachowski *et al.* (*Ber.*, 1936, **69**, 1295), the product of this condensation gives rise, on acid hydrolysis, to a mixture of stereoisomeric α-benzyltricarballylic acids which are mutually interconvertible under the conditions of hydrolysis. Nevertheless, the product is structurally different from that obtained by condensation of ethyl benzylmalonate with ethyl α-bromosuccinate, since the proportions of the stereoisomeric acids obtained on hydrolysis differ in the two cases.

THE work here described was carried out in an endeavour to explain the divergences between the results of Malachowski, Bilbel, and Belinski-Tarasowicz (*Ber.*, 1936, **69**, 1295) and those of the earlier workers (Duff and Ingold, J., 1934, 87; Rydon, J., 1935, 420). Whereas both Duff and Ingold and Rydon isolated different, stereoisomeric α-benzyltricarballylic acids (III) and (IV) from the condensation products, (I) and (II), of ethyl benzylmalonate with ethyl α-bromosuccinate and with ethyl fumarate, respectively, Malachowski and his co-workers claimed to have shown that both esters gave the same mixture of stereoisomerides on acid hydrolysis; on these grounds they questioned the difference in structure of the esters (I) and (II).



$$CH_2Ph{\cdot}CH(CO_2Et)_2 + CHBr{\cdot}CO_2Et{\cdot}CH_2{\cdot}CO_2Et \longrightarrow CH_2Ph{\cdot}C(CO_2Et)_2{\cdot}CH(CO_2Et){\cdot}CH_2{\cdot}CO_2Et \text{ (I.)}$$

$$CH_2Ph{\cdot}CH(CO_2Et)_2 + CH(CO_2Et){=}CH{\cdot}CO_2Et \longrightarrow CH(CO_2Et)_2{\cdot}CH(CO_2Et){\cdot}CH(CH_2Ph){\cdot}CO_2Et \text{ (II.)}$$

$$\text{(I.), (II.)} \longrightarrow CH_2Ph{\cdot}CH(CO_2H){\cdot}CH(CO_2H){\cdot}CH_2{\cdot}CO_2H$$

(III.) m. p. 195°.
(IV.) m. p. 175°.

Repetition of the condensations with carefully purified materials gave two esters which differed markedly in physical properties :

	B. p.	$n_D^{17.8°}$.	$d_{4°}^{17.3°}$.	$[R_L]_D$. Found.	$[R_L]_D$. Calc.
Ester (I)	205—207°/1·3 mm.	1·4880	1·1351	107·11	106·81
Ester (II)	198—200°/0·9 mm.	1·4841	1·1287	106·75	106·81

Malachowski and his co-workers found that acid hydrolysis, under certain conditions, brought about interconversion of the stereoisomeric α-benzyltricarballylic acids (III) and

(IV). Accordingly the two esters were hydrolysed under a variety of conditions, and the products submitted to careful fractional crystallisation. With the aid of a melting-point curve obtained with synthetic mixtures of the acids it was possible to make a close estimate of the proportion of the two acids obtained in each experiment.

The four methods of hydrolysis used were : (a) Seventy hours' refluxing with three volumes of 20% hydrochloric acid. (b) Five hours' refluxing with ten volumes of Malachowski's formic–sulphuric acid mixture [one volume of water, three volumes of concentrated sulphuric acid, nine volumes of formic acid; this mixture is more concentrated than that used by Duff and Ingold and by Rydon; see (d)]. (c) Forty hours' refluxing with Malachowski's mixture. (d) Twenty hours' refluxing with one volume of water, one volume of concentrated sulphuric acid, and three volumes of formic acid.

The results of the fractional crystallisations were :

Method of hydrolysis.	Ester (I).		Ester (II).	
	% (III).	% (IV).	% (III).	% (IV).
(a)	53	47	42	58
(b)	51	49	35	65
(c)	85	15	55	45
(d)	61	39	51	49

These results confirm Malachowski's observation that a stereo-conversion in the sense (IV) ⟶ (III) occurs during the acid hydrolysis; they also show clearly, however, that in every case more of the acid (III) is obtained from the ester (I) than from the ester (II). Both Duff and Ingold (*loc. cit.*) and Rydon (*loc. cit.*) isolated only the acid (III) from the ester (I) and the acid (IV) from the ester (II), using essentially method (d) for hydrolysis; control experiments showed that the solubility relationships are such that, without recourse to careful fractional crystallisation, the mixtures obtained by method (d) do indeed behave in this manner, the product from (I) giving a pure specimen of (III) and the product from (II) a pure specimen of (IV) as the first individual acids to be isolated.

It was, further, found that treatment of the ester (I) with sodium ethoxide gave rise to a product which, on hydrolysis by method (b), yielded 37% of the acid (III) and 63% of (IV); this proportion closely corresponds with that obtained from the ester (II) by this method of hydrolysis and indicates the conversion of (I) into (II) by the sodium ethoxide.

On the basis of these experiments we adhere to the view that the esters (I) and (II) are indeed structurally different, at any rate so far as the principal constituent of each is concerned. Malachowski's statement that the differences shown by the two esters on attempted methylation [(II) can be methylated, whereas (I) cannot (Rydon, *loc. cit.*)] are "nicht grösser als man sie bei Präparaten derselben Substanz von verschiedenem Reinheitsgrad finden könnte" cannot be accepted.

EXPERIMENTAL.

Ethyl Benzylmalonate.—The bulk of the material used was prepared by the method of Leuchs (*Ber.*, 1911, **44**, 1509) and had b. p. 150—152°/4 mm. A specially pure ester was prepared by hydrolysing this to the acid, which was recrystallised from benzene–light petroleum; 20 g. of this acid, m. p. 121°, were refluxed for 24 hours with 75 c.c. of alcohol, 110 c.c. of benzene, and 12 c.c. of concentrated sulphuric acid. The solution was poured into water, and an ethereal extract washed with 10% sodium carbonate solution and water; distillation of the dried extract gave 22 g. (85%) of pure ethyl benzylmalonate, b. p. 140—140·5°/1·5 mm.

Condensation of Ethyl Benzylmalonate with Ethyl Bromosuccinate.—125 G. of ethyl benzylmalonate were added to sodium ethoxide (from 11·5 g. of sodium and 160 c.c. of absolute alcohol). 127 G. of ethyl α-bromosuccinate (b. p. 136—138°/17 mm.) were then added to the cooled mixture, and the product refluxed overnight. The product was poured into water, acidified with dilute sulphuric acid, and extracted with ether. Distillation of the dried extract, after washing with 10% sodium carbonate solution and water, yielded 113 g. of a fraction, b. p. 218—224°/3 mm. Redistillation gave 105 g. of ethyl δ-phenyl-*n*-butane-αβγγ-tetracarboxylate (I), b. p. 214—216°/2 mm., as a pale yellow oil with a slight green fluorescence. A very pure specimen obtained similarly from ethyl benzylmalonate prepared from the acid had b. p. 205—207°/1·3 mm., $n_{\mathrm{D}}^{17\cdot3^\circ}$ 1·4880, $d_{4^\circ}^{17\cdot3^\circ}$ 1·1351, $[R_L]_{\mathrm{D}}$ 107·11 (calc., 106·81) (Malachowski, Bilbel, and Belinski-Tarasowicz, *loc. cit.*, give b. p. 206—208°/1·5 mm., $n_{\mathrm{D}}^{20^\circ}$ 1·4862, $d_{4^\circ}^{20^\circ}$ 1·1338).

Hydrolysis. Hydrolysis was carried out by refluxing with the appropriate reagent for a definite time; the product crystallising on cooling was then recrystallised once from 20% hydrochloric acid (except when this was used for the hydrolysis) in order to remove sulphuric acid. The crude acid so obtained was systematically fractionally crystallised from glacial acetic acid, the minimum amount of solvent being used in the first crystallisation and thereafter 3 parts by weight. The composition of fractions too small for further crystallisation was determined by reference to a melting-point curve constructed from the following data on synthetic mixtures of the two α-benzyltricarballylic acids, m. p. 195° (III) and m. p. 175° (IV) :

% (III)	0	10	20	27	40	50	60	67·5	75	80	100
M. p.	175°	169°	166°	165°	166°	167·5°	169°	171°	173°	174·5°	195°

Four hydrolyses were carried out: (a) 5·5 G. with 30 c.c. of 20% hydrochloric acid; 67 hours. Crude product : 3·08 g. (90%), m. p. 167—171°. Recrystallisation gave 1·00 g. of (IV), m. p. 175°, 1·00 g. of an acid, m. p. 188—190°, 97·5% of (III), and 0·30 g. of an acid, m. p. 170—174°, 78·5% of (III). Hence, based on recrystallised material, the product contained 53% of (III) and 47% of (IV); recovery, 75%.

(b) 5 G. with 50 c.c. of Malachowski's mixture (see p. 43); 5 hours. Crude product : 2·70 g. (86%), m. p. 155—159°. This gave 0·80 g. of (IV), m. p. 174—175°; 0·60 g., m. p. 189—192°, 99% of (III); 0·30 g., m. p. 167—169°, 58% of (III); 0·20 g., m. p. 180—183°, 93% of (III). Hence, 51% of (III) and 49% of (IV); recovery, 70%.

(c) 5·4 G., as (b); 37 hours. Crude product : 3·20 g. (92%), m. p. 160—168°. This gave 1·30 g., m. p. 188—191°, 98% of (III); 0·30 g., m. p. 172—176°, 83% of (III); 0·45 g., m. p. 166—170°, 63% of (III); 0·15 g., m. p. 164—167°, 47% of (III). Hence 85% of (III) and 15% of (IV); recovery, 69%.

(d) 5·3 G. with 5 c.c. of water, 5 c.c. of sulphuric acid, and 15 c.c. of formic acid; 20 hours. Crude product : 3·00 g. (90%), m. p. 150—160°. This gave 1·10 g., m. p. 190—192°, 99% of (III); 0·40 g., m. p. 173—174°, 1% of (III); 0·10 g., m. p. 181—185°, 94% of (III); 0·40 g., m. p. 168—170°, 9% of (III). Hence 61% of (III) and 39% of (IV); recovery, 67%.

Action of sodium ethoxide. 15·5 G. of the ester (I) were added to sodium ethoxide (from 0·75 g. of sodium and 12 c.c. of absolute alcohol), and the mixture refluxed for 48 hours. The product was poured into water and extracted with ether, and the extract washed with 10% sodium carbonate solution and water, dried, and distilled. Three fractions were collected at 3 mm. : (1) b. p. 140—160°, 3·0 g.; (2) b. p. 160—215°, 1·3 g.; (3) b. p. 215—220°, 2·1 g. Fraction (1) was identified as ethyl benzylmalonate by hydrolysis to the acid (mixed m. p.). Fraction (3) was boiled with 20 c.c. of Malachowski's mixture for 5 hours and gave 0·9 g. of a crude acid, m. p. 156—158°. Fractional crystallisation gave 0·2 g., m. p. 184—186°, 95% of (III), and 0·5 g., m. p. 166—168°, 13% of (III). Hence, 37% of (III) and 63% of (IV); recovery, 78%.

Condensation of Ethyl Fumarate and Ethyl Benzylmalonate.—43 G. of ethyl fumarate and 56 g. of ethyl benzylmalonate were added to sodium ethoxide prepared from absolute alcohol (70 c.c.) and sodium (5·6 g.). After being left at room temperature for 14 days, the red solution was poured into water, acidified, and extracted with ether. The extract was washed with 10% sodium carbonate solution and water, dried, and distilled. Refractionation of the product (54 g.), b. p. 200—224°/3·5 mm., yielded 42 g. (42%) of the pure condensation product (II), b. p. 216—218°/2·5 mm., as a practically colourless oil with a very slight green fluorescence. A specimen, prepared similarly from ethyl benzylmalonate made from the specially purified acid, had b. p. 198—200°/0·9 mm., $n_{\mathrm{D}}^{17\cdot3^\circ}$ 1·4841, $d_{4^\circ}^{17\cdot3^\circ}$ 1·1287, $[R_L]_{\mathrm{D}}$ 106·75 (calc., 106·81) (Malachowski *et al.*, *loc. cit.*, give b. p. 208—210°/1·5 mm., $n_{\mathrm{D}}^{20^\circ}$ 1·4851, $d_{4^\circ}^{20^\circ}$ 1·1283).

Hydrolysis. Four experiments were carried out: (a) 5·4 G. with 30 c.c. of 20% hydrochloric acid; 72 hours. Crude product : 3·15 g. (92%), m. p. 169—171°. This gave 0·90 g. of (IV), m. p. 175°; 0·50 g., m. p. 188—191°, 98% of (III); 0·30 g., m. p. 168—170°, 8·5% of (III); 0·80 g., m. p. 168—171°, 67% of (III). Hence 42% of (III) and 58% of (IV); recovery, 79%.

(b) 5·9 G. with 50 c.c. of Malachowski's mixture; 5 hours. Crude product : 3·05 g. (82%), m. p. 152—156°. This gave 0·80 g. of (IV), m. p. 175°; 0·50 g., m. p. 187—189°, 96% of

(III); 0·50 g., m. p. 169—172°, 5% of (III); 0·40 g., m. p. 168—171°, 68% of (III). Hence, 35% of (III) and 65% of (IV); recovery, 72%.

(c) As (b); 40 hours. Crude product: 2·70 g. (85%), m. p. 151—153°. This gave 0·90 g. of (III), m. p. 193—194°; 0·50 g. of (IV), m. p. 175°; 0·40 g., m. p. 164—166°, 21% of (III). Hence, 55% of (III) and 45% of (IV); recovery, 67%.

(d) 5 G. with 5 c.c. of water, 5 c.c. of sulphuric acid, and 15 c.c. of formic acid; 20 hours. Crude product: 2·60 g. (82%), m. p. 152—157°. This gave 0·50 g. of (IV), m. p. 175°; 0·20 g., m. p. 166—169°, 58% of (III); 0·30 g., m. p. 168—172°, 71% of (III); 0·50 g., m. p. 167—171°, 66% of (III); 0·25 g., m. p. 186—188°, 96% of (III). Hence, 51% of (III) and 49% of (IV); recovery, 68%.

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