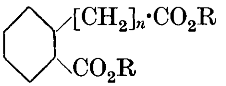
CCCXLI.—*Conditions of Formation of Rings attached to the* o-, m-, *and* p-*Positions of the Benzene Nucleus. Part III.*

By Alan Francis Titley.

In Part I of this series (J., 1922, **121**, 1562) the scope of the proposed investigation was defined as (i) the determination of the limit of size of rings which can be attached to the ortho-positions of the benzene nucleus, and (ii) an enquiry into the possibility of synthesising such rings in the meta- and para-series.

The synthesis of rings of this second type had been previously claimed by von Braun and his collaborators (*Ber.*, 1912, **45**, 1274; 1918, **51**, 1217, 1225; 1919, **52**, 2015; 1925, **58**, 281), and in one case (von Braun, Karpf, and Garn, *Ber.*, 1920, **53**, 98) a supposed heterocyclic "meta-ring" was converted into a homocyclic ring. It was shown, however, in Part II of this series (J., 1926, 508), that in this particular instance both the supposed heterocyclic and homocyclic "meta-rings" of von Braun were in reality benzene compounds containing simple side-chains in the meta-positions.

In the present communication some further results of the application of the Dieckmann reaction (the standard reaction chosen) to esters of the type



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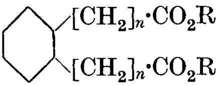

are described, together with some attempts to effect meta- and para-ring closure by the same methods.

Five-membered Ring.—The formation of a five-membered ring by the action of sodium on *o*-phenylenediacetic ester was described in Part I (*loc. cit.*). It is now found that condensation occurs, though less readily, when one of the reacting carbethoxy-groups is directly attached to the benzene nucleus. Thus, sodium reacts with a toluene solution of *ethyl* β-o-*carbethoxyphenylpropionate* (I) at 100°, forming ethyl sodio-1-hydrindone-2-carboxylate (II), about 20% of the ester (I) apparently being saponified. Acidification of the sodium derivative yielded ethyl 1-hydrindone-2-carboxylate (compare Mitchell and Thorpe, J., 1910, **97**, 2273), which was hydrolysed almost quantitatively by acids or alkalis to 1-hydrindone (compare Part I, p. 1563). The phenylhydrazone of this ester, or a mixture of it with dry phenylhydrazine hydrochloride, was converted by concentrated hydrochloric acid into 2 : 3-*indeno*(1 : 2)-*indole* (III),

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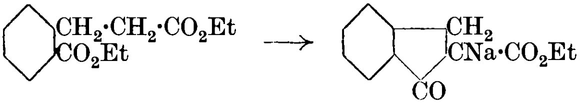
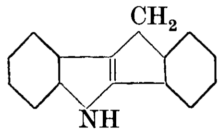
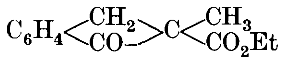


(II.)

(III.)



(IV.)

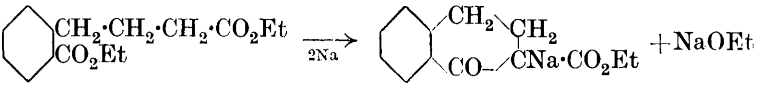
$C_6H_4<\begin{matrix}CH_2\\CO\end{matrix}>C<\begin{matrix}CH_3\\CO_2Et\end{matrix}$ (IV.)

the *N*-methyl compound of which has been described by Armit and Robinson (J., 1922, **121**, 838).

Ethyl 2-methyl-1-hydrindone-2-carboxylate (IV) was readily obtained by the action of methyl iodide on (II) (Mitchell and Thorpe, *loc. cit.*). The introduction of the methyl group into the 1-hydrindone ring appears to decrease the reactivity of the ketonic grouping, since, unlike the 1-methyl-2-hydrindone-1-carboxylic ester, the above ester does not readily form a phenylhydrazone or a semicarbazide. In both esters, however, the stability of the ring is decreased. Thus, on hydrolysis, (IV) yields, in addition to 2-methyl-1-hydrindone (Mitchell and Thorpe, *loc. cit.*), β-o-*carboxyphenyl*iso-*butyric acid.* These results are of some importance in connexion with those obtained in attempting to prepare meta- and para-ring structures.

Six-membered Ring.—The formation of ketotetrahydronaphthalenecarboxylic acids by the dehydration of various γ-phenylbutyric acids has been investigated by Attwood, Stevenson, and Thorpe (J., 1923, **123**, 1755), who have shown that β-substituted phenylbutyric acids, which contain in addition another carboxyl group, readily yield the six-membered ring under the action of sulphuric acid at room temperature. Unsubstituted phenylbutyric acid, however, according to Krollpfeiffer and Schäfer (*Ber.*, 1923, **56**, 620), is not dehydrated at room temperature and only to the extent of 50% at 100°.

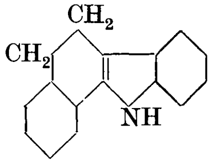
The " internal acetoacetic ester " condensation

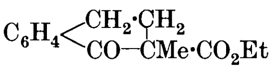


gives a 70% yield in toluene at 100°, and therefore does not take place so readily as either of the two reactions previously described leading to the formation of five-membered rings.

Ethyl 1-keto-1 : 2 : 3 : 4-tetrahydronaphthalene-2-carboxylate (compare Hückel and Goth, *Ber.*, 1924, **57**, 1285) is almost quantitatively converted on hydrolysis with acids or alkalis into 1-keto-1 : 2 : 3 : 4-tetrahydronaphthalene (α-tetralon); it does not give a crystalline phenylhydrazone but, on treatment with phenylhydrazine hydrochloride and hydrochloric acid, it yielded 1 : 2-*indolo*(2 : 3)-3 : 4-*dihydronaphthalene* (V), and its sodio-derivative is methylated by methyl iodide to *ethyl* 1-*keto*-2-*methyl*-1 : 2 : 3 : 4-*tetrahydronaphthalene*-2-*carboxylate* (VI); by acid hydrolysis (VI) is quantitatively converted into 1-*keto*-2-*methyl*-1 : 2 : 3 : 4-*tetrahydronaphthalene*, whilst alkaline hydrolysis yields a mixture of this ketone with γ-o-*carboxyphenyl*-α-*methylbutyric acid*, again pointing to a destabilisation of the saturated ring on the addition of a methyl group.

(V.)

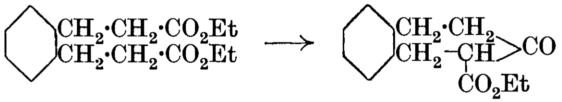




$$C_6H_4{<}\begin{matrix}CH_2\cdot CH_2\\ CO-CMe\cdot CO_2Et\end{matrix}$$

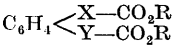
(VI.)

Seven-membered Ring.—*o*-Phenylenedipropionic ester (VII) was found to be only slowly attacked by finely divided sodium in toluene at 100°, being almost entirely saponified; about 2—3%, however, condensed to give (VIII), which was characterised by means of its *phenylhydrazone.* From these results the formation of a seven-

(VII.)  (VIII.)

membered ring by the condensation of two three-membered side-chains in the ortho-position does not appear to be easily brought about. The formation of 1-ketophenheptamethylene from δ-phenylvaleryl chloride by the Friedel–Crafts reaction (Kipping and Hunter, J., 1903, **83**, 246) and the more recent work of von Braun and Bayer (*Ber.*, 1927, **60**, 1257) suggest, however, the probability that ring-closure by means of the Dieckmann reaction on *o*-carboxyphenylvaleric ester might be more readily effected.

m- *and* p-*Ring-closure.*—From the theoretical standpoint there appears to be no valid reason why meta- and para-ring structures should not be capable of a stable existence, but the uncertainty of the benzene structure and the possibility that the rings would not be co-planar render it difficult to predict the most favourable conditions for their formation. The attempts described below to prepare such rings by the methods used for ortho-ring formation led to no conclusive result, but illustrate the difficulties of the problem. The action of sodium at 100° on toluene solutions of the following esters was investigated (R = Me or Et) :

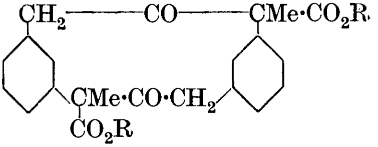


$$C_6H_4<\begin{matrix}X—CO_2R\\Y—CO_2R\end{matrix}$$

meta-Series.	*para*-Series.
(IX) : $X=C_2H_4$; $Y=C_2H_4$.	(X) : $X=C_2H_4$; $Y=C_2H_4$.
(XI) : X= — ; $Y=C_2H_4$.	(XII) : X= — ; $Y=C_2H_4$.
(XIII) : $X=CH_2$; $Y=CH_2$.	(XIV) : $X=CH_2$; $Y=CH_2$.
(XV) : $X=CH_2$; Y= — .	

Certain regularities of behaviour were observed. Thus (IX) and (X) (R = Et) and (XII) (R = Me) were only very slowly acted on by sodium with gradual formation of the sodium salt of the acid. There was no trace of ring-formation or condensation reactions. On the other hand, (XI) (R = Me), (XIII) and (XIV) (R = Me and Et), and (XV) (R = Me) reacted with sodium almost as readily as the corresponding ortho-esters under the same conditions, giving mixtures of sodium salts of the acids with unstable condensation products of varying degrees of molecular complexity, which could not be purified by distillation.

By employing the methyl esters, however, and methylating the resulting sodium compounds with methyl iodide, the products of the reaction could be separated by distillation under greatly reduced pressure. In addition to highly complex condensation products, bimolecular compounds were isolated, presumably of "bridged-ring" structure of the type shown (from XIII).

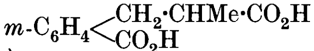


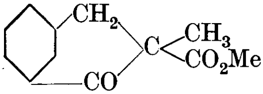
Finally, in each case a lower-boiling product was obtained, consisting mainly of the dimethyl ester, regenerated by the action of the methyl iodide on the disodium salt of the acid which had been produced in the original reaction. The hydrolysis of these low-boiling fractions yielded, in the case of (XIII) and (XIV), not only the simple acids, but also small quantities of the α-methylated acids (XVI) and (XVII), respectively. From (XI), the α-methylated acid (XVIII) was similarly obtained, the position of the methyl group in this instance being settled by synthesising the acid for comparison. On the other hand, no α-methylated acid was obtained in this way from (XV).

(XVI.) 
$m\text{-}C_6H_4{<}\begin{matrix}CHMe\cdot CO_2H\\ CH_2\cdot CO_2H\end{matrix}$

 (XVII.)
$p\text{-}C_6H_4{<}\begin{matrix}CHMe\cdot CO_2H\\ CH_2\cdot CO_2H\end{matrix}$

These two facts appeared to render it doubtful whether the formation of these α-methylated acids could be safely attributed to direct methylation of an α-methylene group, in each open-chain ester, which had been rendered slightly "acid" in character by its position between the phenyl and carbethoxy-groupings. It appeared possible that traces of meta- and para-ring compounds, *e.g.*, of the type (XIX) from (XI), were actually present in the low-boiling fractions, which gave rise to the α-methylated acids, *e.g.*, (XVIII), on hydrolysis. The low-boiling fractions were carefully examined for traces of ketonic substances, but none could be detected. The possibility is nevertheless not entirely excluded because, as previously mentioned, the keto-group in methylated hydrindonecarboxylic esters of the normal type is not very reactive.


$m\text{-}C_6H_4{<}\begin{matrix}CH_2\cdot CHMe\cdot CO_2H\\ CO_2H\end{matrix}$
(XVIII.)

 (XIX.)

The mechanism by which the esters appear to be directly converted in toluene solution into the sodium salts of the corresponding acids is somewhat obscure and is being further investigated.

EXPERIMENTAL.

β-o-*Carboxyphenylpropionic Acid*.—*o*-Aldehydobenzoic acid (25 g.) is condensed with malonic acid (45 g.) in glacial acetic acid (20 g.) in presence of anhydrous sodium acetate (15 g.). The mixture is heated for 8—10 hours at 100°, cooled, and diluted with 150 c.c. of water, whereby monohydrated phthalideacetic acid, m. p. 102—104°, is precipitated in nearly quantitative yield. (Drying in a steam-oven gives the anhydrous acid, m. p. 151°; compare Edwards, J., 1926, 813.) This condensation may also be effected in dry pyridine solution containing a trace of piperidine, the yield being practically the same. The acid is boiled with an excess of 25% sodium hydroxide for about 2 hours, cooled in ice, and acidified with the theoretical quantity of dilute hydrochloric acid; *o*-carboxycinnamic acid then separates as a thick pasty mass, which is filtered and washed with a large volume first of cold and then of boiling water. The crude acid melts at 194°, and after recrystallisation from alcohol forms small prisms, m. p. 197° (Found: C, 62·5; H, 4·2. Calc. for $C_{10}H_8O_4$: C, 62·5; H, 4·2%). Ehrlich (*Monatsh.*, 1888, **9**, 528), Edwards (*loc. cit.*), and Gabriel give m. p. 184°, 182°, and 173—175° respectively, but the acid passes into phthalideacetic acid on melting, for on re-melting it has m. p. 151°.

The *o*-carboxycinnamic acid is reduced by means of sodium amalgam to *o*-carboxyphenylpropionic acid, m. p. after recrystallisation 167° (Bamberger, *Ber.*, 1890, **23**, 1562, gives m. p. 165°); esterification of the latter acid by saturation of its boiling solution in ethyl alcohol with dry hydrogen chloride gives the *ethyl* ester, b. p. 182—183°/14 mm. (Found : C, 67·0; H, 7·11. $C_{14}H_{18}O_4$ requires C, 67·2; H, 7·20%).

Ethyl 1-*Hydrindone*-2-*carboxylate*.—Metallic sodium (5 g.) is finely granulated by shaking under boiling toluene (100 g.), and a solution of *o*-carboxyphenylpropionic ester (24 g.) in toluene (50 g.) is added. The reaction proceeds smoothly at 100° and is complete in 4—5 hours; the resulting sodium compound (II) dissolves to a considerable extent in the toluene (compare Sidgwick and Brewer, J., 1925, **127**, 2381) and is precipitated on addition of dry ether. On decomposition with dilute acid, 1-hydrindone-2-carboxylic ester separates as an orange oil, b. p. 179—180°/15 mm. (slight decomp.) (Found : C, 70·8; H, 6·0. Calc. : C, 70·6; H, 5·9%) (Mitchell and Thorpe, *loc. cit.*, give b. p. 185°/20 mm.); the phenylhydrazone (Found : C, 73·5; H, 6·35; N, 9·5. Calc. : C, 73·5; H, 6·1; N, 9·5%) has m. p. 103° (Mitchell and Thorpe, *loc. cit.*, give m. p. 101·5°).

Hydrolysis. The ester (5 g.) was mixed with an aqueous solution of 2·5 g. of sodium hydroxide and kept at room temperature for 24 hours; α-hydrindone separated as an oil in almost quantitative yield; b. p. 164—166°/20 mm., m. p. 39°. The phenylhydrazone had m. p. 130° (compare Liebermann, *Ber.*, 1898, **31**, 2081).

2 : 3-*Indeno*(1 : 2)-*indole* (III).—1-Hydrindone-2-carboxylic ester (4 g.), mixed with dry phenylhydrazine hydrochloride (2·8 g.) and

two drops of concentrated hydrochloric acid, is heated first on the water-bath and afterwards at 150° for about 2 minutes; the solid brownish cake is broken up, washed with water, and extracted with hot methyl alcohol. On cooling, small brownish-red plates are deposited, m. p. 251° (Found : N, 6·6. $C_{15}H_{11}N$ requires N, 6·8%).

*Ethyl 2-Methyl-*1*-hydrindone-*2*-carboxylate.*—1-Hydrindone-2-carboxylic ester (10 g.) was converted into the sodium derivative by adding its ethereal solution to sodium previously granulated under toluene. The bright yellow, flocculent mass was collected, washed with a little dry ether, suspended in 100 c.c. of alcohol and boiled with 10 g. of methyl iodide for 3 hours. The ester which separated on addition of water boiled at 166°/14 mm. (Mitchell and Thorpe, *loc. cit.*, give b. p. 181°/20 mm.) and solidified in long prisms, m. p. 31° (Found : C, 71·5; H, 6·5. Calc. for $C_{13}H_{14}O_3$: C, 71·5; H, 6·4%). The ester, on boiling with 20% methyl-alcoholic potash, was hydrolysed to the extent of about 60% to 2-methyl-1-hydrindone, b. p. 125—126°/18 mm. (Found: C, 81·8; H, 6·8. Calc.: C, 82·2; H, 6·8%), and to the extent of about 40% to β-o-*carboxyphenyl*iso*butyric acid*, colourless needles, m. p. 141° (Found : C, 63·4; H, 5·8. $C_{11}H_{12}O_4$ requires C, 63·5; H, 5·8%).

*Ethyl γ-*o*-Carbethoxyphenyl-*n*-butyrate.*—The acid was obtained by the method of Hückel and Goth (*loc. cit.*), and its *ethyl* ester, prepared in the usual manner, had b. p. 188—189°/14 mm. (Found : C, 68·0; H, 7·7. $C_{15}H_{20}O_4$ requires C, 68·2; H, 7·6%).

Ethyl 1-*Keto*-1 : 2 : 3 : 4-*tetrahydronaphthalene-*2*-carboxylate.*—The preceding ester (19 g.) was slowly added to sodium (3·5 g.) dispersed in toluene (100 g.). The reaction was complete after 6—7 hours at 100°. After addition of a little alcohol to decompose traces of unchanged sodium, powdered ice was added, and the mixture made just acid by the addition of 15 c.c. of concentrated hydrochloric acid. The toluene layer was separated, washed with sodium carbonate solution, dried, and the solvent removed under diminished pressure; 10 g. of crude 1-ketotetrahydronaphthalene-2-carboxylic ester (65% yield) were obtained, b. p. 183°/15 mm., m. p. 33° (Hückel and Goth give m. p. 34°). From the aqueous layer and sodium carbonate washings 3—4 g. of *o*-carboxyphenylbutyric acid were obtained on evaporation.

When warmed to 150° with the calculated quantity of phenylhydrazine hydrochloride and a little concentrated hydrochloric acid, the foregoing ester yields 1 : 2-*indolo*(2 : 3)-3 : 4-*dihydronaphthalene* (V), dark reddish plates, m. p. 161° (Found : N, 6·3. $C_{16}H_{13}N$ requires N, 6·4%).

Ethyl 1-*Keto*-2-*methyl*-1 : 2 : 3 : 4-*tetrahydronaphthalene*-2-*carboxylate* (VI).—An alcoholic solution of 11 g. of the ketonic ester is added to 1·2 g. of sodium, previously dissolved in 20 c.c. of ethyl alcohol. After the addition of 15 g. of methyl iodide, the mixture is boiled for 2—3 hours, evaporated to a small bulk, and poured into water. The *methyl* compound separates as a colourless oil with a terpene-like odour; b. p. 183—184°/18 mm. (Found: C, 72·0; H, 6·9. $C_{14}H_{16}O_3$ requires C, 72·4; H, 6·9%). On steam distillation with 20% sulphuric acid, this is converted into 1-*keto*-2-*methyltetrahydronaphthalene*, b. p. 143°/20 mm. (Found: C, 82·0; H, 7·6. $C_{11}H_{12}O$ requires C, 82·5; H, 7·5%), whereas alkaline hydrolysis with 10% methyl-alcoholic potash gives a mixture of the above ketone with γ-o-*carboxyphenyl*-α-*methylbutyric acid*, prisms, m. p. 173° (Found: C, 64·9; H, 6·6. $C_{12}H_{14}O_4$ requires C, 64·9; H, 6·3%). The decrease in stability of the saturated ring on the addition of the methyl group is very strikingly exemplified in this instance, since the unmethylated ester is hydrolysed to *o*-carboxyphenylbutyric acid only by sodium and boiling *cyclo*hexanol, and then to an extent of not more than 20%.

Ethyl o-*Phenylenedipropionate* (VII).—The acid was prepared by the method of Perkin (J., 1888, **53**, 18); after purification by means of the diethyl ester, it had m. p. 168° (Perkin found m. p. 160—162°, " not very sharply "). The *ethyl* ester had b. p. 200—202°/12 mm. (Found: C, 69·0; H, 7·8. $C_{16}H_{22}O_4$ requires C, 69·1; H, 7·9%).

Action of sodium on the ethyl ester. To sodium (1·8 g.), dispersed in toluene (60 g.), was added *o*-phenylenedipropionic ester (11·5 g.) dissolved in toluene (15 g.), and the mixture heated on the water-bath. After 9 hours, the toluene was filled with a deposit of brown sodium compounds and no unchanged metallic sodium could be detected. The sodium derivatives were filtered off rapidly, washed with dry ether, and decomposed with dilute hydrochloric acid. The brown, flocculent, oily material which separated was extracted with ether, and the ethereal solution thoroughly washed with sodium carbonate solution; on acidification of these sodium carbonate washings, a large quantity of a brownish powder was precipitated, which, after recrystallisation from dilute alcohol, formed microscopic prisms, m. p. 167—168°, and was found on analysis to be *o*-phenylenedipropionic acid; this acid (9 g.) constituted the main product of the reaction. From the ethereal solution was obtained about 0·5 g. of a brownish oil of b. p. approx. 190°/15 mm., which gave an immediate purple colour with ferric chloride. The amount was not sufficient for purification but, on warming with phenylhydrazine at 100° and then adding alcohol, a crystalline *phenylhydrazone* was obtained which formed straw-yellow needles, m. p. 198° (decomp.), from hot alcohol (Found: C, 74·6; H, 6·8; N, 8·55. $C_{20}H_{22}O_2N_2$ requires C, 74·5; H, 6·8; N, 8·7%).

This phenylhydrazone is thus almost certainly derived from *ethyl 3-ketophenheptamethylene-2-carboxylate* (VIII).

Action of Sodium on m- *and* p-*Phenylenediacetic Esters.*

These esters are conveniently obtained from the corresponding nitriles (see Part II, *loc. cit.*) by simultaneous hydrolysis and esterification by means of the appropriate alcohol saturated with dry hydrogen chloride. *Methyl* m-*phenylenediacetate* has b. p. 185—187°/15 mm. (Found: C, 64·9; H, 6·3. $C_{12}H_{14}O_4$ requires C, 64·8; H, 6·3%). *Ethyl* m-*phenylenediacetate* has b. p. 188—189°/12 mm. (Found: C, 66·8; H, 7·3. $C_{14}H_{18}O_4$ requires C, 67·2; H, 7·2%). *Methyl* p-*phenylenediacetate* has b. p. 189—190°/15 mm. (Found: C, 64·6; H, 6·2%). *Ethyl* p-*phenylenediacetate* has m. p. 59° (Found: C, 66·9; H, 7·1%).

Ethyl *m*-phenylenediacetate (48 g.) was slowly added to metallic sodium (10 g.) finely granulated under toluene (150 g.). On warming on the water-bath, a vigorous reaction set in which was complete in about 20 minutes. The mass of brown sodium compounds was filtered off quickly, washed with a large volume of dry ether, and dried in a vacuum. An iodoform test showed that considerable quantities of sodium ethoxide were present. The sodium compounds were decomposed with the theoretical quantity of ice-cold dilute hydrochloric acid and the viscous yellow product was extracted with ether. Free *m*-phenylenediacetic acid was removed by shaking with dilute sodium carbonate, and the ethereal solution dried and distilled. The syrup so obtained, on removal of the last traces of ether in a vacuum, set to a solid sticky mass, which softened and melted at 30—40° and decomposed vigorously above 100° (Found: C, 70·8; H, 6·3. $C_{12}H_{12}O_3$ requires C, 70·6; H, 5·9%). This *compound* showed no tendency to crystallise on standing for 9 months or on cooling to —40°, whilst attempts at distillation under pressures as low as 0·3 mm. led to complete decomposition, with formation of a horny, shellac-like mass. The alcoholic solution gave a deep purple colour with ferric chloride and a deep green copper salt with copper acetate, indicating the presence of a keto-enol structure, but no crystalline compound with phenylhydrazine could be isolated. Hydrolysis with alcoholic potash gave rise to yellowish, insoluble resins.

Almost precisely similar results were obtained with ethyl *p*-phenylenediacetate, but the syrupy product obtained combined fairly readily with phenylhydrazine, yielding an amorphous, red, glassy mass. This was extracted with boiling methyl alcohol, and the solution poured into a large volume of dry ether. A small quantity of microscopic yellow needles was obtained which softened at 190°

and melted at 194—195° (Found: C, 73·6; H, 6·3; N, 9·5. $C_{18}H_{18}O_2N_2$ requires C, 73·5; H, 6·1; N, 9·5%). As this *phenylhydrazone* was obtained in very small yield and its molecular weight was not determined, it cannot be regarded as positive evidence of the formation of a *p*-β-hydrindonecarboxylic ester.

The action of sodium on the two dimethyl esters was carried out in a similar manner. The sodium compounds were mixed with dry methyl alcohol and a slight excess of methyl iodide and boiled for 12 hours. The solution was then poured into water, and the methylated product extracted with ether, dried, and distilled under 1 mm. pressure. Starting with methyl *m*-phenylenediacetate, three main fractions were obtained: (*a*) b. p. 131—135°, (*b*) b. p. 217—222°, (*c*) 270° and upwards; (*c*) was not further investigated, as it appeared to be of a high degree of molecular complexity. The *compound* constituting the middle fraction (*b*) probably has the bridged-ring structure (p. 2575) (Found: C, 70·2; H, 6·3; *M*, cryoscopic in acetic acid, 418. $C_{24}H_{24}O_6$ requires C, 70·6; H, 5·9%; *M*, 408); on hydrolysis with 2—3% methyl-alcoholic potash it gives about a 40% yield of a colourless, amorphous powder, which is insoluble in sodium carbonate but dissolves in warm dilute sodium hydroxide. This *substance*, which appears to be a lactone or acid anhydride, sinters at 340° and melts fairly sharply at 345—346° (Found: C, 72·5; H, 5·1. $C_{22}H_{18}O_5$ requires C, 72·9; H, 5·0%).

The low-boiling fraction (*a*) redistilled at 182—190°/15 mm. and could not be further separated by fractionation. After hydrolysis with dilute methyl-alcoholic potash, the crude acid obtained was extracted with cold chloroform until the insoluble residue melted sharply at 169° (pure *m*-phenylenediacetic acid). The soluble portion was fractionally recrystallised from water to remove traces of the above acid from the more soluble *phenylene*-1-*acetic*-3-α-*propionic acid* (XVI), m. p. 132° (Found: C, 63·6; H, 6·0. $C_{11}H_{12}O_4$ requires C, 63·5; H, 5·8%).

The action of sodium on methyl *p*-phenylenediacetate gave similar results. The middle fraction had b. p. 225—228°/1 mm. (Found: C, 70·3; H, 6·2. $C_{24}H_{24}O_6$ requires C, 70·6; H, 5·9%). On hydrolysis, the low-boiling fraction (188—192°/16 mm.) gave a mixture of *p*-phenylenediacetic acid, m. p. 244°, and *phenylene*-1-*acetic*-4-α-*propionic acid* (XVII), m. p. 189° (Found: C, 63·3; H, 5·9. $C_{11}H_{12}O_4$ requires C, 63·5; H, 5·8%).

Action of Sodium on m- *and* p-*Carboxyphenylpropionic Esters.*

Preparation of Esters.—*m*-Carboxyphenylpropionic acid was prepared by condensing *iso*phthalaldehydic acid (Davies, Perkin, and Clayton, J., 1922, **121**, 2215) with malonic acid in glacial acetic acid or pyridine to obtain *m*-carboxycinnamic acid, needles, m. p. 275° (corr.) (Simonis, *Ber.*, 1912, **45**, 1584, gives m. p. 264°) (Found : C, 62·5; H, 4·3. Calc. : C, 62·5; H, 4·2%), and reducing this with sodium amalgam and sodium carbonate solution to m-*carboxyphenylpropionic acid*, plates, m. p. 177° (Found : C, 61·6; H, 5·25. $C_{10}H_{10}O_4$ requires C, 61·8; H, 5·2%). The *methyl* ester, prepared from this in the usual way, had b. p. 184—185°/15 mm. (Found : C, 64·9; H, 6·5. $C_{12}H_{14}O_4$ requires C, 64·9; H, 6·3%).

p-Carboxyphenylpropionic acid was prepared by two methods. (1) *p*-Toluoyl chloride (1 mol.) treated at 185—190° with bromine (2 atoms) gave a mixture of ω-bromo-*p*-toluoyl chloride, b. p. 155—156°/20 mm., and ω-*bromo*-p-*toluoyl bromide*, b. p. 170—171°/20 mm., m. p. 56° (Found : Br, 57·8. $C_8H_6OBr_2$ requires Br, 57·5%), together with some high-boiling material which was not distilled but appeared to consist of a mixture of ωω-dibromo-*p*-toluoyl chloride and bromide, since, on mixing with alcohol it yielded *ethyl* ωω-*dibromo*-p-*toluate*, hexagonal prisms, m. p. 103° (Found : C, 36·8; H, 3·08. $C_{10}H_{10}O_2Br_2$ requires C, 37·2; H, 3·10%). *Ethyl* ω-*bromo*-p-*toluate*, prepared from the mixture of monobromo-acid chloride and bromide, has b. p. 165°/18 mm. and crystallises in needles, m. p. 35—36° (Found : Br, 32·7. $C_{10}H_{11}O_2Br$ requires Br, 32·9%); when condensed with chloromalonic ester, it gives a fair yield of *ethyl chloro*-p-*carbethoxybenzylmalonate*, b. p. 235°/20 mm., m. p. 54—55° (Found : Cl, 9·95. $C_{17}H_{21}O_6Cl$ requires Cl, 9·81%), which, on reduction with zinc dust and acetic acid, yields *ethyl* p-*carbethoxybenzylmalonate*, b. p. 218—219°/15 mm. (Found : C, 62·8; H, 6·6. $C_{17}H_{22}O_6$ requires C, 63·2; H, 6·8%). On hydrolysis this is converted into p-*carboxybenzylmalonic acid*, a microcrystalline powder, m. p. 186—188° (Found : C, 55·5; H, 4·6. $C_{11}H_{10}O_6$ requires C, 55·4; H, 4·3%). The dicarboxylic acid does not lose carbon dioxide readily, but on heating to 240° it is converted into *p*-carboxyphenylpropionic acid, m. p. 294° (Found : C, 62·0; H, 5·2. Calc. : C, 61·8; H, 5·2%). The yields in the last stages of this synthesis are not good.

(2) The condensation of terephthalaldehydic acid with malonic acid gave a good yield of *p*-carboxycinnamic acid, a highly insoluble powder which, after subliming a little from 350° upwards, melts at 358° (decomp.) (Löw, *Annalen*, 1885, **231**, 367, gave no m. p.) (Found : C, 62·7; H, 4·3. Calc. : C, 62·5; H, 4·2%). The acid cannot be purified by recrystallisation, and this is best effected by converting it into the *ethyl* ester, which crystallises from dilute alcohol in prisms, m. p. 52° (Found : C, 67·5; H, 6·5. $C_{14}H_{16}O_4$ requires C, 67·8; H, 6·5%). On reduction of *p*-carboxycinnamic

acid with sodium amalgam and sodium carbonate, *p*-carboxyphenylpropionic acid, m. p. 294° (compare above) is obtained (Moses, *Ber.*, 1900, **33**, 2626, gave m. p. 280°). The *methyl* ester crystallises from chloroform in prisms, m. p. 33° (Found: C, 64·6; H, 6·47. $C_{12}H_{14}O_4$ requires C, 64·9; H, 6·3%).

Methyl *m*-carboxyphenylpropionate (27 g.), dissolved in toluene (20 g.), was added to sodium (5·6 g.) dispersed in toluene (60 g.), and the mixture heated for 12 hours on the water-bath. The sodium compounds were filtered off rapidly, washed with ether, suspended in 100 g. of dry methyl alcohol and, after the addition of 40 g. of methyl iodide, boiled for 3 hours. On distilling the product under 1 mm. pressure, two fractions were obtained at about 140°/1 mm. and 275°/1 mm. The low-boiling fraction redistilled at 183—187°/15 mm. and weighed 7·2 g. (Found: C, 66·0; H, 6·5%); 7 g. were hydrolysed in a sealed tube at 100° with 15 g. of 10% methyl-alcoholic potash, and on addition of water a clear brown solution was obtained, there being no evidence of ketone formation. The acidified solution was extracted with ether and yielded 6 g. of acid; two treatments of this crude product with 30 g. of cold chloroform extracted 1·55 g. and the residue then had m. p. 177°, thus being pure *m*-carboxyphenylpropionic acid. The chloroform-soluble acid was recrystallised several times from chloroform and finally from water to constant m. p. 137—138° (corr.) (Found: C, 63·6; H, 5·8. $C_{11}H_{12}O_4$ requires C, 63·5; H, 5·8%). It was proved to be β-m-*carboxyphenyl*iso*butyric acid* (XVIII) by the following synthesis.

m-Toluoyl chloride was chlorinated at 160—165°, until the gain in weight was equivalent to one atom of chlorine. This gave a 90% yield of ω-*chloro*-m-*toluoyl chloride*, b. p. 149—150°/20 mm. (Found: Cl, 37·2. $C_8H_6OCl_2$ requires Cl, 37·6%), which on mixing with alcohol yielded *ethyl* ω-*chloro*-m-*toluate*, b. p. 168—169°/25 mm. (Found: C, 60·2; H, 5·7; Cl, 17·6. $C_{10}H_{11}O_2Cl$ requires C, 60·4; H, 5·5; Cl, 17·9%). This chloro-ester condensed with sodiomethylmalonic ester to give *ethyl* m-*carbethoxybenzylmethylmalonate*, which distilled without decomposition at 234°/24 mm. (Found: C, 63·8; H, 7·0. $C_{18}H_{24}O_6$ requires C, 64·3; H, 7·1%). The corresponding *acid*, obtained on hydrolysis, is a microcrystalline powder fairly soluble in water, m. p. 182—183° (decomp.). On heating to 185° until no more carbon dioxide is evolved, it is converted into β-*m*-carboxyphenyl*iso*butyric acid. The crude product had m. p. 136—137°, but after conversion to the *methyl* ester, b. p. 182°/18 mm., distilling, and re-hydrolysing, it crystallised from water in small prisms, m. p. 138—139° (Found: C, 63·7; H, 5·9%). The mixed m. p. of this acid with that obtained above was 138°.

m- *and* p-*Phenylenedipropionic Esters.*—The respective acids were obtained by the method of Kipping (J., 1888, **53**, 21). *Ethyl* m-*phenylenedipropionate* has b. p. 197—198°/15 mm. (Found : C, 68·8; H, 7·95. $C_{16}H_{22}O_4$ requires C, 69·1; H, 7·9%). *Ethyl* p-*phenylenedipropionate* crystallises in plates, m. p. 69° (Found : C, 68·9; H, 7·8%).

My thanks are due to the Ramsay Memorial Trustees for a Fellowship, during the tenure of which the greater part of this work was carried out, and to Professor W. H. Perkin for his advice.

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[*Received, April 4th,* 1928.]