371. cyclo*Propanes. Part IV.* A New Route to Some* bicyclo[3 : 1 : 0]*Hexene Derivatives.*

By R. W. KIERSTEAD, R. P. LINSTEAD, and B. C. L. WEEDON.

Condensation of *cis*- and *trans*-1 : 4-dibromo*cyclo*pent-2-ene with ethyl sodiomalonate gives ethyl *bicyclo*[3 : 1 : 0]hex-2-ene-6 : 6-dicarboxylate (I ; R = R′ = Et) in 17 and 33% yield respectively. In elucidating the structure of this compound, in which one ester group is sterically hindered, a number of transformations have been effected. Further examples of ready reductive fission of a *cyclo*propane ring are recorded.

HITHERTO only 1 : 4-dibromobut-2-ene has been used as starting material in the route to vinyl*cyclo*propane derivatives described in previous papers in this series. It was of obvious interest to extend the reaction, if possible, to dibromo-*cyclo*pentenes and -*cyclo*hexenes as a new synthesis of the *bicyclo*[3 : 1 : 0]hexane and *bicyclo*[4 : 1 : 0]heptane ring systems present in compounds of the thujane and carane type respectively. With this aim, the condensation of 1 : 4-dibromo*cyclo*pent-2-ene with ethyl malonate has now been studied.

From the reaction of the *trans*-dibromo*cyclo*pentene with ethyl sodiomalonate a dicarboxylic ester, $C_{12}H_{16}O_4$, was obtained in 33% yield. This did not exhibit the characteristic ultra-violet light absorption of a *cyclo*pentadiene and was formulated as (I, R = R′ = Et) by analogy with the corresponding product from dibromobutene (Part I; *J.*, 1952, 3610). Ozonolysis of the diester, followed by oxidative fission of the ozonide and hydrolysis, led to a tetracarboxylic acid (II), isolated as a crystalline monohydrate. Treatment of the diester with cold alkali produced a half-ester in almost quantitative yield; the second ester group was hydrolysed only after prolonged boiling, to a product which, like the half-ester, was obtained crystalline. This difference in ease of hydrolysis of the two ester groups implies that one is subject to considerable steric hindrance, as in ethyl *meso*-2 : 5-dimethyl*cyclo*pentane-1 : 1-dicarboxylate (III) which behaves similarly (Jacobs and Florsheim, *J. Amer. Chem. Soc.*, 1950, **72**, 256). The half-ester was represented as (I; R = H, R′ = Et).

The final product of hydrolysis, while possessing the expected composition, $C_8H_8O_4$, was not the dicarboxylic acid (I; R = R′ = H). Direct titration revealed only one acid group, although, after boiling with excess of alkali, back-titration with mineral acid showed that two equivalents of alkali had been neutralised. Again, treatment with diazomethane gave a mono-, and not a di-, ester. These properties cannot be adequately explained by assuming the presence of a hindered carboxyl group in a structure such as (I; R = R′ = H);

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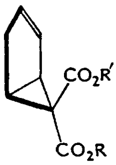
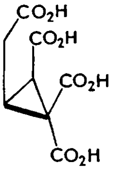
* Part III, preceding paper.

meso-cis-2 : 6-dimethyl*cyclo*hexane-1-carboxylic acid (IV) titrates normally and is esterified on treatment with diazomethane (Jacobs, Reed, and Pacovska, *ibid.*, 1951, **73**, 4505). The final product of hydrolysis of (I; R = R′ = Et) is therefore regarded as the lactonic acid (V; R = H). A γ- rather than a δ-lactone formulation is favoured for steric reasons, and because of the infra-red evidence given below. The alternative lactonic acid structure (VI), which would result from fission of the *cyclo*propane ring by a reaction of the kind reported for *cyclo*propanecarboxylic acid (Perkin, *J.*, 1885, **47**, 801; cf. Fittig and Roeder, *Ber.*, 1883, **16**, 2592), its 2-ethoxy-derivative (Rambaud, *Compt. rend.*, 1949, **229**, 299), and (±)-*cis*- and (±)-*trans*-chrysanthemic acid (Crombie, Harper, and Thompson, *J. Sci. Food Agric.*, 1951, 421), cannot be definitely excluded on the chemical evidence available, but is less consistent with the infra-red spectrum which suggests a *cyclo*propane ring.



(I)



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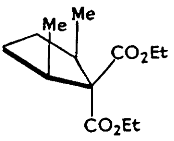

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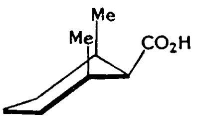

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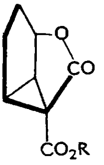

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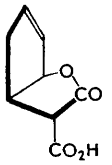

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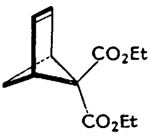


(VII)

The half-ester (I; R = H, R′ = Et), the lactonic acid (V; R = H), and the lactonic ester (V; R = Me) were each shown to contain a five-membered ring by catalytic hydrogenation over platinum. All three absorbed two mols. of hydrogen rapidly to give *cyclo*pentylmalonic acid, either directly or after hydrolysis of the saturated ester. Easy hydrogenolysis of a *cyclo*propane ring when conjugated with a double bond has been noted previously (cf. Parts I and III, *locc. cit.*), but the ease of reduction of the lactonic acid and its ester is remarkable, if these are correctly formulated as (V; R = H) and (V; R = Me). Previously only $\beta\gamma$- and $\gamma\delta$-unsaturated γ-lactones have been found to yield deoxy-acids by a reductive elimination of this type (Jacobs and Scott, *J. Biol. Chem.*, 1930, **87**, 601; Cocker and Hornsby, *J.*, 1947, 1157; Eisner, Elvidge, and Linstead, *J.*, 1950, 2223). The behaviour of the lactonic acid and its ester on hydrogenation thus lends some support to the allylic-type structure (VI) for the former (cf. Carter and Humiston, *J. Biol. Chem.*, 1951, **191**, 727).

At this stage in our investigations, it was clear that the diester from the malonate condensation with dibromo*cyclo*pentene was a *bicyclo*hexene, but none of the chemical or spectral evidence served to distinguish unambiguously between the favoured [3 : 1 : 0]-structure (I; R = R′ = Et), and the also conceivable [2 : 1 : 1]-structure (VII). A decision between these alternatives was, however, made possible by the following observations. Reaction of the diester with ethyl sodiomalonate, under conditions similar to those employed previously with ethyl *cyclo*propane-1 : 1-dicarboxylate and its 2-vinyl derivative (Part II; *J.*, 1952, 3616), gave a mixture of monounsaturated tetraesters. Reduction, followed by hydrolysis and decarboxylation, furnished *trans-cyclo*pentane-1 : 2-diacetic acid, identified by direct comparison with an authentic specimen. Only the *bicyclo*[3 : 1 : 0]hexene structure (I; R = R′ = Et) for the initial diester is compatible with the formation of a 1 : 2-disubstituted *cyclo*pentane. In other Michael reactions with *cyclo*propane esters the initial adduct has been largely cyclised, under the conditions employed, to a 2-keto*cyclo*pentane-1 : 3-dicarboxylate (Part II). Failure of the present tetraester to cyclise to any appreciable extent is attributable to its *trans*-configuration, which is that to be expected from addition of ethyl malonate to (I; R = R′ = Et) by a mechanism involving bimolecular nucleophilic attack of the *cyclo*propane ring.

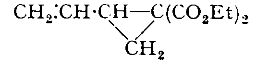
Further support for the structures assigned to some of the compounds described above was provided by light-absorption measurements. In the infra-red region, the spectrum of the diester (I; R = R′ = Et) exhibits a strong band (5·78 μ) characteristic of an ester group, while that of the half-ester (I; R = H, R′ = Et) has strong bands (5·75 and 5·90 μ) which may be attributed to the ester and the carboxyl group. The spectrum of the lactonic acid (V; R = H) shows no ester band, but has two strong peaks (5·88 and 5·60 μ) which are probably due to the carboxyl group and the lactone group. Moreover, the position of the lactone band is more in agreement with that of authentic γ- (5·65 μ) than δ-lactones (5·75 μ). All three spectra have a strong maximum in the region (9·8 μ) believed to be characteristic of *cyclo*propanes (cf. Part I).

	$\lambda_{max.}$, Å	$\varepsilon_{max.}$		$\lambda_{max.}$, Å	$\varepsilon_{max.}$
Diester (VIII) [1]	<2100	>5,000	Butadiene [2]	2170 *	20,900
Diester (I; R = R′ = Et)	2250	1,120	*cyclo*Pentadiene [3]	2440 *	2,500
Half-ester (I; R = H, R′ = Et)	2260	1,960			
Lactonic acid (V; R = H)	<2200	—	* In hexane.		
Lactonic ester (V; R = Me)	<2200	—			

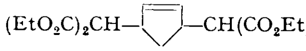
[1] Kierstead, Linstead, and Weedon, *J.*, 1952, 3610. [2] Scheibe and Pummerer, *Ber.*, 1927, **60**, 2164. [3] Pickett, Paddock, and Sackter, *J. Amer. Chem. Soc.*, 1941, **63**, 1073.

Ultra-violet light absorption data are summarised in the Table. Both the diester (I; R = R′ = Et) and the half-ester (I; R = H, R′ = Et) possess a maximum at 2250—2260 Å. which is absent with the vinyl*cyclo*propanedicarboxylate (VIII). However, conjugation between the vinyl group and the *cyclo*propane ring in (VIII), which has maximal absorption below 2100 Å, is clearly shown by molecular-refractivity measurements (Part I). It is suggested that the maximum observed with both (I; R = R′ = Et) and (I; R = H, R′ = Et) is also due to electronic interaction between the double bond and the three-membered ring. The bathochromic and hypsochromic shifts of $\lambda_{max.}$ which have resulted from incorporating the vinyl*cyclo*propane chromophore in a *cyclo*pentane system are in keeping with the well-known difference in ultra-violet light absorption properties between *cyclo*pentadiene and acyclic dienes. In agreement with this interpretation, neither the lactonic acid (V; R = H) nor its ester (V; R = Me) shows maximal absorption in the 2250-Å region.

By distillation of the high-boiling residues from the preparation of (I; R = R′ = Et) two fractions were isolated These were a mixture of diesters, formed by substitution of one bromine atom in dibromo*cyclo*pentene by a malonate residue and solvolysis of the other, and a mixture of tetraesters. From the latter, by hydrogenation, hydrolysis, and decarboxylation, a crystalline *cyclo*pentanediacetic acid was obtained which differed from both the *cis*- and the *trans*-1 : 2-isomer (Linstead and Meade, *J.*, 1934, 935; Barrett and Linstead, *J.*, 1935, 436) and gave no ketone when heated with baryta. It is presumably the *trans*-1 : 3-diacetic acid derived from the tetraester (IX) in the initial mixture.



(VIII)



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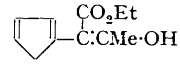

(X)

In view of the evidence given above, which we regard as conclusive, for the formation of a bicyclic product on condensation of ethyl sodiomalonate with *trans*-1 : 4-dibromo*cyclo*pent-2-ene, it is of interest that the reaction of the *cis*-isomer with ethyl sodioacetoacetate was claimed by Reid and Yost (*J. Amer. Chem. Soc.*, 1950, **72**, 1807) to yield (70%) the *cyclo*pentadiene derivative (X). In support of this structure it was stated that the product had a permanent pale yellow colour, was strongly enolic (ferric chloride colour reaction), and on catalytic reduction absorbed 1·9 mol. of hydrogen, giving (90%) ethyl *cyclo*pentylacetoacetate. The latter argument cannot now be regarded as decisive, and the reaction will therefore be re-investigated. We find that in the malonate condensation the *cis*-dibromide gives the same diester (I; R = R′ = Et) as the *trans*-isomer, but only in about half the yield. This result may of course be due, in part, to contamination of the so-called *cis*-dibromide, which is a liquid, with the *trans*-isomer (cf. Owen and Smith, *J.*, 1952, 4035).

EXPERIMENTAL

Alcohol was dried as outlined in Part I (*loc. cit.*). Light-absorptions were determined in alcohol.

Condensation of 1 : 4-*Dibromo*cyclo*pent-2-ene with Ethyl Sodiomalonate.*—A solution of *trans*-1 : 4-dibromo*cyclo*pent-2-ene (60 g.; m. p. 45—46°) in alcohol (200 c.c.) was added during ½ hr. to a well-stirred, warm (70°) solution of ethyl sodiomalonate (from 85 g. of ethyl malonate and 12·2 g. of sodium) in alcohol (200 c.c.). The mixture was heated (*ca.* 90°) for 45 min. and then cooled and poured into water. The product was isolated with ether and distilled. The portion with b. p. <110°/0·15 mm. was fractionated through a Stedman column (2 × 15 cm.) fitted with a total reflux, partial take-off head and gave : (i) *Ethyl* bicyclo[3 : 1 : 0]*hex-2-ene-*6 : 6-*dicarboxylate* (I; R = R′ = Et) (19·1 g.), b. p. 85—88°/0·15 mm., n_{D}^{22} 1·4678 (Found : C, 63·85; H, 7·25. $C_{12}H_{16}O_4$ requires C, 64·25; H, 7·2%). (ii) A mixture of dicarbethoxymethylethoxy*cyclo*pentenes (10·1 g., 14%), b. p. 94°/0·1 mm., n_{D}^{22} 1·4518 (Found : C, 62·5; H, 8·35. Calc. for $C_{14}H_{22}O_5$: C, 62·2; H, 8·2%). Hydrolysis of the mixture of esters (2·14 g.) under reflux with potassium hydroxide (1·75 g.) in water (5 c.c.) and alcohol (2 c.c.) gave an acidic product which solidified partially. Crystallisation of the solid from benzene gave a *dicarboxylic acid* (728 mg., 43%) as plates, m. p. 110° (decomp.) (Found : C, 55·8; H, 6·7%; equiv., 107. $C_{10}H_{14}O_5$ requires C, 56·05; H, 6·6%; equiv., 107).

An ethereal solution of the high-boiling residue (19 g.), from the preliminary distillation, was washed thoroughly with aqueous potassium hydroxide (2% w/v). Acidification of the alkaline extract with dilute (1 : 1) hydrochloric acid, and extraction of the oil thus liberated with ether yielded an enolic fraction (5·5 g.) which gave a wine-red colour with ferric chloride but was not examined further. The enol-free ethereal solution was washed with water, dried (Na_2SO_4), and evaporated. Distillation gave a mixture of tetraesters (10·0 g., 10%), b. p. 120° (bath-temp.)/10^{-5} mm., n_{D}^{23} 1·4617 (Found: C, 59·4; H, 7·4. Calc. for $C_{19}H_{28}O_8$: C, 59·35; H, 7·35%). This was converted into *trans-cyclo*propane-1 : 3-diacetic acid as described below.

Condensation of *cis*-1 : 4-dibromo*cyclo*pent-2-ene (55·4 g.), n_{D}^{24} 1·5796, prepared by Blomquist and Mayes' method (*J. Org. Chem.*, 1945, **10**, 136; cf. Owen and Smith, *loc. cit.*), with ethyl sodiomalonate, in the manner described above for the *trans*-isomer, also gave ethyl *bicyclo*-[3 : 1 : 0]hex-2-ene-6 : 6-dicarboxylate (9·1 g., 17%), b. p. 90—93°/0·5 mm., n_{D}^{29} 1·4660.

In one experiment in which the ethyl sodiomalonate solution was added slowly to a boiling alcoholic solution of *trans*-1 : 4-dibromo*cyclo*pent-2-ene, none of the *bicyclo*hexene derivative was obtained. The main product, a *substance* separated with difficulty from recovered ethyl malonate by fractional distillation, was formed by ethanolysis of the dibromide and had b. p. 73—74°/14 mm., 177°/754 mm., n_{D}^{25} 1·4430 (Found : C, 69·0; H, 10·2. $C_9H_{16}O_2$ requires C, 69·2; H, 10·3%).

4-*Carboxymethyl*cyclo*propane*-1 : 1 : 2-*tricarboxylic Acid* (II).—A slow stream of ozonised oxygen (*ca.* 3% of O_3) was bubbled through a solution of ethyl *bicyclo*[3 : 1 : 0]hex-2-ene-6 : 6-dicarboxylate (2·0 g.) in acetic acid ("AnalaR," 15 c.c.) for 6 hr. Hydrogen peroxide (30 c.c.; 20-vol.) was then added, and the mixture was kept at 20° overnight and evaporated under reduced pressure to 5 c.c. A solution of potassium hydroxide (6·0 g.) in water (6·0 c.c.) was added, and the mixture was heated on a steam-bath for 2 hr., then cooled, extracted with ether, acidified, saturated with ammonium sulphate, and again extracted with ether (constant extractor for 2 days). Evaporation of the final ethereal extract gave a viscous oil which solidified on trituration with benzene and ether. Crystallisation from ether–light petroleum (b. p. 40—60°) gave the *tetra-acid* as a monohydrate (210 mg., 10%), m. p. 93° (Found : C, 38·05; H, 4·35. $C_8H_{10}O_9$ requires C, 38·4; H, 4·05%).

Ethyl Hydrogen bicyclo[3 : 1 : 0]*Hex-2-ene-*6 : 6-*dicarboxylate* (I; R = H, R′ = Et).—Ethyl *bicyclo*[3 : 1 : 0]hex-2-ene-6 : 6-dicarboxylate (2·36 g.) was shaken with a solution of potassium hydroxide (2·36 g.) in water (2·5 c.c.). The resulting brown solution was extracted with ether and then acidified with cold concentrated hydrochloric acid and saturated with ammonium sulphate. Thorough extraction with ether and evaporation of the extract gave the *half-ester* (1·92 g.), which crystallised from benzene–light petroleum (b. p. 40—60°) in rhombohedra, m. p. 68° (Found : C, 61·45; H, 6·35%; equiv., 195. $C_{10}H_{12}O_4$ requires C, 61·2; H, 6·15%; equiv., 196).

Samples of the diester prepared from both *cis*- and *trans*-1 : 4-dibromo*cyclo*pent-2-ene were hydrolysed in the above manner and gave the same half-ester, m. p. and mixed m. p. 68°.

γ-*Lactone of* 2-*Hydroxy*bicyclo[3 : 1 : 0]*hexane-*6 : 6-*dicarboxylic Acid* (V; R = H).—A solution of the preceding half-ester (490 mg.) and potassium hydroxide (1·0 g.) in water (5 c.c.) and alcohol (2—3 c.c.) was heated under reflux for 30 hr. Isolation of the product as in the preceding experiment gave the *lactonic acid*, which crystallised from benzene (charcoal) in plates (300 mg., 72%), m. p. 100° (Found : C, 57·45; H, 4·85%; equiv., 167 by direct titration, 84 by heating on steam-bath for ½ hr. with excess of alkali and back-titration. $C_8H_8O_4$ requires C, 57·15; H, 4·8%; equiv., 168 for $1CO_2H$, 84 for $2CO_2H$).

Treatment of the lactonic acid (1·08 g.) with diazomethane gave the *methyl* ester (0·93 g.), b. p. 103°/0·15 mm., n_{D}^{21} 1·4670 (Found : C, 59·4; H, 5·75. $C_9H_{10}O_4$ requires C, 59·35; H, 5·55%).

cyclo*Pentylmalonic Acid.*—(i) A solution of the half ester (I; R = H, R′ = Et) (442 mg.) in ethyl acetate (10 c.c.) was shaken in hydrogen in the presence of Adams' catalyst until absorption was complete (103 c.c. at 18°/749 mm., equiv. to 1·9 double bonds). Removal of catalyst and solvent gave an oil which was heated under reflux with a solution of potassium hydroxide (520 mg.) in water (2 c.c.) for 2 hr. Isolation of the acidic product in the usual way gave a solid (350 mg.), m. p. 145—155°, which was crystallised from benzene–ether–light petroleum (b. p. 40—60°), giving *cyclo*pentylmalonic acid (204 mg., 53%), m. p. 163° (decomp.), undepressed on admixture with an authentic specimen [Neunhoeffer, *J. pr. Chem.*, 1932, **133**, 95, gives m. p. 163° (decomp.)].

(ii) The lactonic acid (V; R = H) (300 mg.) in ethyl acetate (10 c.c.) was hydrogenated in the above manner (hydrogen absorbed, 94 c.c. at 19°/774 mm., equiv. to 2·2 double bonds). Removal of catalyst and solvent gave *cyclo*pentylmalonic acid, which crystallised from chloroform in prisms (153 mg., 50%), m. p. and mixed m. p., 162° (decomp.).

(iii) The lactonic ester (V; R = Me) (179 mg.) was hydrogenated in ethyl acetate (5 c.c.) (hydrogen absorbed, 46 c.c. at 22°/758 mm., equiv. to 1·95 double bonds). Removal of catalyst and solvent, hydrolysis of the residue, and isolation of the product as in (i), gave *cyclo*pentylmalonic acid, which crystallised from chloroform in prisms (100 mg., 60%), m. p. and mixed m. p. 162° (decomp.).

Addition of Ethyl Sodiomalonate to Ethyl bicyclo[3 : 1 : 0]*Hex*-2-*ene*-6 : 6-*dicarboxylate* (cf. Part II).—A solution of the diester (I; R = R′ = Et) (7·0 g.) and ethyl sodiomalonate (from 5·0 g. of ethyl malonate and 0·72 g. of sodium) in alcohol (50 c.c.) was heated under reflux for 11 hr. and then cooled and poured into dilute sulphuric acid. The product was extracted with ether, and the extract washed with aqueous potassium hydroxide (2% w/v), dried, and evaporated. Distillation of the residue (7 g.) gave recovered *bicyclo*hexenedicarboxylate (4·3 g.) and a mixture of tetraesters (1·6 g.), b. p. 120° (bath-temp)/10^{-5} mm., n_D^{25} 1·4558—1·4601 (Found: C, 59·6; H, 7·45. Calc. for $C_{19}H_{28}O_8$: C, 59·35; H, 7·35%). From the alkaline extract a negligible quantity of an enolic product was obtained on acidification.

trans-cyclo*Pentane*-1 : 2-*diacetic Acid.*—A solution of the preceding mixture of tetraesters (251 mg.) in ethyl acetate (5 c.c.) was shaken in hydrogen in the presence of Adams' catalyst until absorption was complete (17 c.c. at 23°/765 mm., equiv. to 1·05 double bonds). The catalyst and solvent were removed. Concentrated hydrochloric acid (1 c.c.) was added to the residue, and the mixture heated under reflux for 17 hr. On cooling, a solid separated. Recrystallisation from water gave *trans-cyclo*pentane-1 : 2-diacetic acid (50 mg.), as cubes, m. p. 129·5—131·5° (Found: C, 58·3; H, 7·85. Calc. for $C_9H_{14}O_4$: C, 58·05; H, 7·6%). The m. p. was undepressed on admixture with an authentic specimen, m. p. 130·5—132° (Linstead and Meade, *J.*, 1934, 935; Barrett and Linstead, *J.*, 1935, 436).

trans-cyclo*Pentane*-1 : 3-*diacetic Acid.*—A solution of the mixture of tetraesters (9·9 g.) from the condensation of *trans*-1 : 4-dibromo*cyclo*pent-2-ene with ethyl sodiomalonate, and sodium ethoxide (from 0·59 g. of sodium) in alcohol (50 c.c.) was heated under reflux for 18 hr. and then cooled and poured into dilute sulphuric acid. The product was extracted with ether, and the extract washed with aqueous potassium hydroxide (2% w/v), dried, and evaporated. Distillation of the residue gave an oil (4·9 g.), b. p. 120° (bath-temp.)/10^{-5} mm., n_D^{22} 1·4588, which was hydrogenated (Adams' catalyst) in ethyl acetate (15 c.c.), giving a mixture of saturated tetraesters (2·6 g.), b. p. 140° (bath-temp.)/10^{-4} mm., n_D^{33} 1·4520 (Found: C, 59·4; H, 8·0. Calc. for $C_{19}H_{30}O_8$: C, 59·05; H, 7·8%). This was hydrolysed under reflux with concentrated hydrochloric acid (7·5 c.c.) and gave a solid (531 mg.), m. p. 133—138°. Recrystallisation from water (charcoal) yielded trans-cyclo*pentane*-1 : 3-*diacetic acid* (355 mg.), m. p. 135·5—137·5° (Found: C, 58·3; H, 7·75%; equiv., 93. $C_9H_{14}O_4$ requires: C, 58·05; H, 7·6%; equiv., 94). The dicarboxylic acid (180 mg.) was recovered unchanged after 1 hr.'s heating with baryta (5 mg.) at 280—290°.

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Department of Organic Chemistry,
Imperial College of Science and Technology,
London, S.W.7.

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