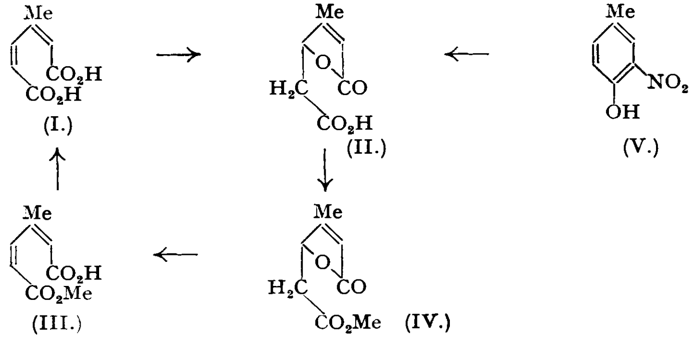
461. *Unsaturated Lactones and Related Substances. Part IV. Lactonic Products derived from Muconic Acid.*

By J. A. Elvidge, R. P. Linstead, B. A. Orkin, Peter Sims, and (in part) Harold Baer and Dexter B. Pattison.

Lactonisation of *cis-cis*-muconic acid with sulphuric acid (*trans-trans*-muconic acid fails to react) gives mainly γ-carboxymethyl-Δ^{α}-butenolide (VI), the structure of which has been proved by hydrolysis to lævulic acid, and oxidation to oxalic and malic acids. Unlike the isomeric γ-carboxymethylidenebutanolide (Part III) by which (VI) is accompanied, the new lactonic acid (VI) is stable to water, acids, and weak bases. Hydrogenation of (VI) proceeds normally to γ-carboxymethylbutanolide (XI), the methyl ester (XII) of which is converted by hot sodium hydrogen carbonate solution into *trans*-Δ^{α}-dihydromuconic acid (XIII). The same acid (XIII) is obtained by hydrolysis of a methyl hydrogen Δ^{α}-dihydromuconate which is formed by isomerisation of (XII) with sodium methoxide in methanol. An isomeric methyl hydrogen Δ^{α}-dihydromuconate has been synthesised from β-carbomethoxypropaldehyde by the Doebner reaction. Various aspects of the literature on derivatives of muconic acids have been revised in the light of the new results.

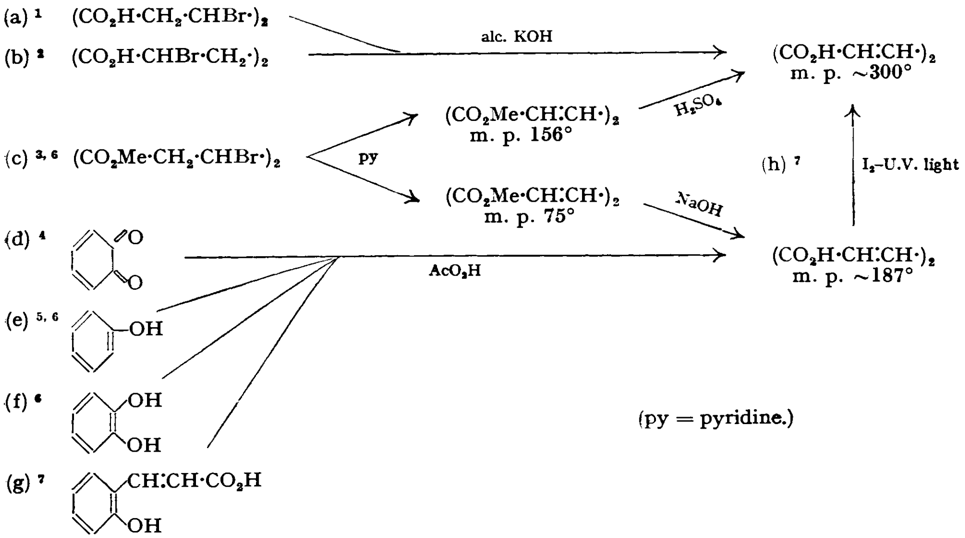
As a by-product of the original lactonisation there is obtained the saturated dicyclic dilactone (XVI).

One of the standard methods of forming γ-lactones is to effect the isomerisation of Δ^{β}- or Δ^{γ}-unsaturated acids by distillation or by treatment with acids. Pauly and Will (*Annalen*, **1918**, **416**, 1) showed that this route could be applied to the lactonisation of β-methylmuconic acid (I) which under a variety of conditions readily gave the unsaturated lactonic acid (II).



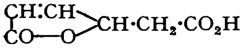
The methylmuconic acid (I) was obtained by hydrolysis of the half methyl ester (III), which in turn had resulted from an interesting reaction, the treatment of the lactonic ester (IV) with sodium methoxide. The lactonic acid (II) and ester (IV) had previously been obtained (Pauly, Gilmour, and Will, *ibid.*, 1914, **403**, 119) by ring fission of 3-nitro-*p*-cresol (V) with sulphuric acid. Pauly and Will (*loc. cit.*) did not concern themselves with the stereochemistry of their methylmuconic acid (I), but it appeared to us that this was probably of primary importance, having a direct bearing upon the ease of isomerisation of (I) to the cyclic form (II). Further investigation of this system is in hand. The present communication is concerned with the simpler case of lactonisation of the unsubstituted muconic acids.

Two forms of muconic acid $(CO_2H{\cdot}CH{:}CH{\cdot})_2$ have been described, with melting points of approximately 300° and 187°. Methods of synthesising them are shown below :

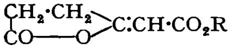


The configuration of the higher-melting form of muconic acid was shown to be *trans-trans* by Behrend (*Ber.*, 1916, **49**, 999) and Behrend and Heyer (*Annalen*, 1919, **418**, 294). They found that on permanganate oxidation *rac.*-tartaric acid was formed—*meso*-tartaric acid was specifically sought but could not be detected—and that on oxidation with sodium chlorate and osmium tetroxide mucic acid was produced, together with a small quantity of *rac.*-idosaccharic acid. The configuration of the lower-melting form of muconic acid as *cis-cis* was considered by Böeseken and Kerkhoven (*loc. cit.*) to have been demonstrated conclusively by its formation from *o*-benzoquinone [route (d)]. In addition, Böeseken and Kerkhoven showed that the tartaric acid formed on permanganate oxidation of this muconic acid was solely the *meso*-form.

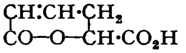
Our attempts to lactonise *trans-trans*-muconic acid [prepared by route (b) and characterised as the methyl ester] were unsuccessful. Under mild conditions sulphuric acid or a mixture of acetic acid and hydrogen chloride did not affect the acid, and under more vigorous conditions it appeared to be largely destroyed. On the other hand, *cis-cis*-muconic acid [prepared by route (e), and characterised by formation of the methyl ester, catalytic hydrogenation to adipic acid, and inversion to *trans-trans*-muconic acid] lactonised readily with sulphuric acid to yield as main product an isomeric monobasic acid (VI) of m. p. 111°, which with diazomethane afforded a methyl ester (X), m. p. 31°. From a similar esterification of the crude product of


$\begin{matrix}\text{CH:CH}\\ \text{CO—O}\end{matrix}\!>\!\text{CH}{\cdot}\text{CH}_2{\cdot}\text{CO}_2\text{H}$

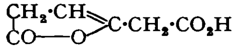
(VI.)


$\begin{matrix}\text{CH}_2{\cdot}\text{CH}_2\\ \text{CO——O}\end{matrix}\!>\!\text{C:CH}{\cdot}\text{CO}_2\text{R}$

(VII.)


$\begin{matrix}\text{CH:CH}{\cdot}\text{CH}_2\\ \text{CO—O—CH}{\cdot}\text{CO}_2\text{H}\end{matrix}$

(VIII.)


$\begin{matrix}\text{CH}_2{\cdot}\text{CH}\\ \text{CO——O}\end{matrix}\!\gg\!\text{C}{\cdot}\text{CH}_2{\cdot}\text{CO}_2\text{H}$

(IX.)

lactonisation, besides (X), an isomeric methyl ester, m. p. 109°, was isolated in small quantity. The latter ester was identified with γ-carbomethoxymethylenebutanolide (VII; R = Me) obtained by lactonising β-ketoadipic acid (Eisner, Elvidge, and Linstead, *J.*, 1950, 2223). It

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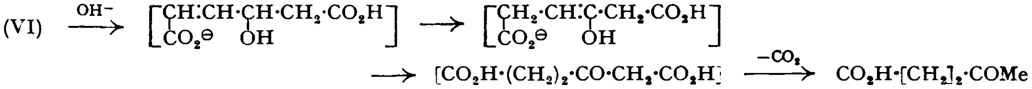
[1] Rupe, *Annalen*, 1890, **256**, 1. [2] Ingold, *J.*, 1921, **119**, 951. [3] Farmer, *ibid.*, 1923, **123**, 2531. [4] Böeseken and Sloof, *Proc. Acad. Sci. Amsterdam*, 1929, **32**, 1043. [5] Böeseken and Engelberts, *ibid.*, 1931, **34**, 1292; Böeseken, *ibid.*, 1932, **35**, 750. [6] Böeseken and Kerkhoven, *Rec. Trav. chim.*, 1932, **51**, 964. [7] Grundmann, *Ber.*, 1936, **69**, 1755.

is possible that the lactonic acid (VI) has been obtained before though not in a pure state (see Beilstein, 4th Edn., **18**, 396).

That the new lactonic acid had a five-membered ring (VI), and not a six-membered ring such as (VIII), was shown by its hydrolysis with hot aqueous sodium hydroxide to lævulic acid, isolated as the semicarbazone. The hydrolysis very probably proceeds as follows :



$$\text{(VI)} \xrightarrow{OH^-} \left[\begin{matrix}\text{CH:CH}\cdot\text{CH}\cdot\text{CH}_2\cdot\text{CO}_2\text{H} \\ \text{CO}_2^{\ominus} \quad \text{OH}\end{matrix}\right] \longrightarrow \left[\begin{matrix}\text{CH}_2\cdot\text{CH:C}\cdot\text{CH}_2\cdot\text{CO}_2\text{H} \\ \text{CO}_2^{\ominus} \quad \text{OH}\end{matrix}\right] \longrightarrow [\text{CO}_2\text{H}\cdot(\text{CH}_2)_2\cdot\text{CO}\cdot\text{CH}_2\cdot\text{CO}_2\text{H}] \xrightarrow{-CO_2} \text{CO}_2\text{H}\cdot[\text{CH}_2]_2\cdot\text{COMe}$$

Alternatively, an alkali-induced migration of the double bond in (VI) might have occurred before hydrolytic opening of the lactone ring, but this seems less likely because the methyl ester of (VI) undergoes no change with triethylamine, even on prolonged treatment.

The exocyclic position of the double bond is established for the isomeric unsaturated lactonic acid and its ester of m. p. 109° (VII; R = Me). The new lactonic acid (m. p. 111°) and its ester (m. p. 31°) must therefore have the double bond in the lactone ring in either the αβ- or the βγ-position (VI and IX). Oxidation shows the αβ-position to be correct.

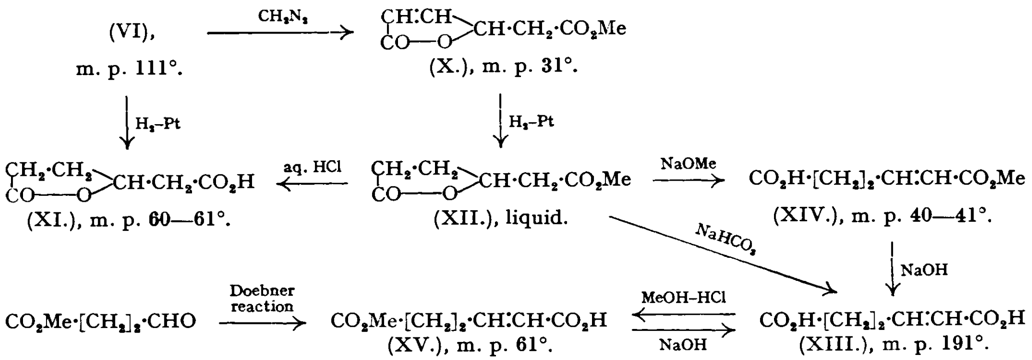
With potassium permanganate in the cold the butenolide afforded oxalic acid, together with a small quantity of malic acid. Succinic and malonic acids were not detected. An acid with structure (IX) should yield malonic acid under these conditions, whilst (VII; R = H) has already been shown (Part III) to yield succinic and oxalic acids. The light-absorption properties—high-intensity absorption only at the extreme end of the usual ultra-violet range—were also in agreement with the structure (VI) (cf. Ruzicka, Plattner, and Heusser, *Helv. Chim. Acta*, 1942, **25**, 435; 1944, **27**, 186; Haynes and Jones, *J.*, 1946, 954).

γ-Carboxymethyl-Δ^{α}-butenolide (VI) proved in general to be less reactive than the isomeric γ-carboxymethylenebutanolide (VII; R = H). Thus it was recovered unchanged after treatment with water, aqueous mineral acid, ammonia, or methanol containing a trace of hydrogen chloride. Neither did the lactonic ester (X) react with aniline. In the Légal test, under controlled conditions (pH 11), the butenolide (X) gave a less intense colour than (VII; R = Me). If these reactions are compared with those of simple Δ^{α}- and Δ^{β}-unsaturated lactones (see, *e.g.*, Kuehl, Linstead, and Orkin, *J.*, 1950, 2213) it will be seen that they fall into line with the Δ^{α}-structure for (VI).

On catalytic hydrogenation the butenolide (VI) absorbed only 1 mol. of hydrogen and gave an acid of m. p. 60—61°, analysis of which agreed with that for the saturated lactone (XI). Again, this result agrees with the Δ^{α}-structure (VI) since Jacobs and Scott (*J. Biol. Chem.*, 1930, **87**, 601) have shown that Δ^{α}-unsaturated γ-lactones are reduced to the corresponding saturated lactones whilst lactones derived from enolised keto-acids are abnormally hydrogenated to deoxy-acids.

Although the hydrogenation results were, thus, quite normal, yet they gave rise to certain subsidiary problems. The hydrogenation product, m. p. 60—61°, did not correspond with the compound which Leuchs and Möbis (*Ber.*, 1909, **42**, 1228) claimed to be the γ-lactone (XI) of β′-hydroxyadipic acid and which melted at 197—198° (201—202°, corr.). Moreover, a preparation due to Farmer (*J.*, 1923, **123**, 3324) was described as a colourless syrup. Furthermore, Farmer suggested that the acid which had been obtained by Leuchs and Möbis "was actually the isomeric Δ^{β}-dihydromuconic acid" (*trans*-Δ^{β}-dihydromuconic acid has m. p. 197°). Direct titration of our hydrogenation product (m. p. 60—61°) with alkali confirmed that it was indeed a monobasic acid. When, however, it was allowed to stand with an excess of alkali a further equivalent was consumed, evidently owing to the opening of the lactone ring. Hydrogenation of the methyl ester (X) of the original unsaturated lactonic acid gave the corresponding saturated lactonic ester (XII), a liquid which was hydrolysed with hot aqueous hydrochloric acid to the crystalline acid of m. p. 60—61°. Hydrolysis of the liquid ester (XII) with aqueous sodium hydrogen carbonate, on the other hand, gave an abnormal reaction : the lactone ring was opened and an isomeric mono-unsaturated dibasic acid of m. p. 191° was formed. This compound gave adipic acid on reduction and hence was a dihydromuconic acid. Direct comparison showed it to be the known *trans*-Δ^{α}-dihydromuconic acid (XIII) (Farmer and Hughes, *J.*, 1934, 1929, 1938; cf. Carrière, *Ann. Chim.*, 1922, **17**, 38). These results, which are summarised in the annexed scheme, prove that the hydrogenation product of (VI), m. p. 60—61°, is the γ-lactone (XI) of β′-hydroxyadipic acid.

With sodium methoxide in methanol, the saturated lactonic ester (XII) was readily isomerised to a monobasic unsaturated acid of m. p. 40—41°. The new product gave *trans*-Δ^{α}-dihydromuconic acid (XIII) on hydrolysis, and succinic acid on oxidation, and was therefore the hitherto undescribed methyl hydrogen *trans*-Δ^{α}-dihydromuconate (XIV). A methyl hydrogen *trans*-Δ^{α}-dihydromuconate with m. p. 60° had previously been obtained by Farmer and Hughes (*J.*, 1934, 304, 1929, 1938) by partial esterification of the acid (XIII). Farmer and Hughes assigned the structure (XV) to their half-ester by analogy with the investigations of partial esterification by Sudborough and his collaborators (*J.*, 1911, **99**, 2307 etc.), and Eccott and Linstead (*J.*, 1929, 2153), who showed that carboxyl groups next to a double bond resisted esterification.

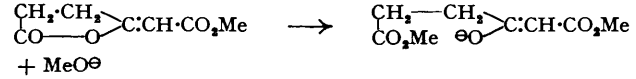


To clarify the structural position we have subjected β-carbomethoxypropaldehyde to the Doebner condensation with malonic acid. This yields a half ester of *trans*-Δ^{α}-dihydromuconic acid, m. p. 61°, undoubtedly identical with Farmer's product. Its structure is fully proved by the method of preparation and by the following facts : (*a*) on hydrogenation and hydrolysis it gives adipic acid; (*b*) on permanganate oxidation it yields methyl hydrogen succinate. Carrière (*loc. cit.*, p. 111) carried out a similar synthesis of Δ^{α}-dihydromuconic acid from succinaldehydic acid. Incidentally, he reports m. p. 208—210° for the product, which is higher than any recorded by other workers. Melting points in this series of compounds vary substantially with the rate of heating : our preparations of this Δ^{α}-acid melted at 190—191° with slow heating, and, in agreement with Farmer and Hughes (*loc. cit.*), never as high as Carrière's figure.

The rearrangement with alkali of the saturated lactonic ester (XII) to unsaturated open-chain material (XIII, XIV) presents an interesting difference from the normal tendency of lactones to yield open-chain hydroxy-compounds under similar conditions. When, however, the special structural peculiarities of these materials are considered, the reaction is seen to be not unexpected. Indeed, we have observed a similar isomerisation of the *unsaturated* lactonic ester (X) to a methyl hydrogen muconate. (This is described in a separate paper because it raises certain interesting stereochemical points.) Moreover, Pauly *et al.* (*loc. cit.*) have made related observations in the β-methylmuconic series.

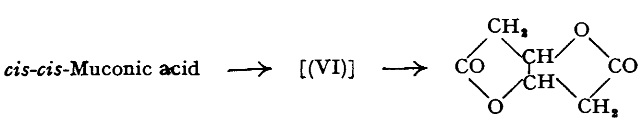
The reason for these reactions is clear : Lactonic esters such as (XII) are compounds in which an acylated hydroxyl is situated in the β-position to an electron-attracting group (carbalkoxyl). On treatment with alkaline reagents β-acyloxy-compounds of this type can undergo either normal hydrolysis (to the parent hydroxy-compounds) or *elimination* of the acyl group with the formation of an αβ-double bond. This reaction, which is now under study in these laboratories, will be further discussed in a later paper. But it is clear that the formation of double bonds by the alkaline rearrangement of lactones of this type is only a special case of a general process.

We must direct attention to the fact that the lactonic ester with the exocyclic double bond (VII; R = Me) is *not* isomerised to a methyl hydrogen muconate by means of alkoxide, being converted instead into the diester of β-ketoadipic acid (Eisner, Elvidge, and Linstead, *loc. cit.*). This is a highly interesting difference, which we attribute to the ability of (VII; R = Me) to add methoxide to form the stable enolate ion of the β-keto-ester :



This is not possible with either the isomeric unsaturated lactonic ester (X) or the saturated lactonic ester (XII). On this basis we should expect the ester of the unknown Δ^{β}-lactone (IX) to react with alkoxide in the same way as (VII; R = Me).

The evidence presented above shows that the crude product of the lactonisation of *cis-cis*-muconic acid contains both the two conjugated Δ^{α}- and Δ^{γ}-unsaturated lactones (VI) and (VII; R = H). We have no evidence that the third isomeride, the Δ^{β}-lactone (IX), is present, and in this respect the muconic acid system resembles the unsaturated diphenyl lactones investigated by Thiele and Straus (*Annalen*, 1901, **319**, 216). We have, however, found that an isomeric non-acidic material (XVI) is present as a by-product :



(XVI.)

The residues from a number of preparations on repeated crystallisation gave a compound $C_6H_6O_4$, of m. p. 128—129°. This depressed the m. p. of (VI), and was insoluble in hydrogen carbonate solution though soluble in aqueous alkali. The new compound was best prepared by prolonged treatment of *cis-cis*-muconic acid with sulphuric acid at room temperature, and could also be obtained by refluxing *cis-cis*-muconic acid with 50% sulphuric acid or by fusion of the acid, but the yields were low. It did not react with cold water, or with diazomethane under the usual conditions. Although it has not yet been examined in detail, there seems little doubt that it is the interesting dicyclic dilactone (XVI). This is in keeping with the fact that it sublimes slowly at 100° under reduced pressure. Dicyclic dilactones of similar structure (for example, the dilactone of β-acetylglutaric acid) have similar high melting points. Presumably the dilactone (XVI) has a *cis*-fusion of the rings.

EXPERIMENTAL.

trans-trans-Muconic acid was obtained as a chalk-like solid, m. p. 297—300°, in 29% yield from adipic acid by Ingold's procedure (*J.*, 1921, **119**, 951). Farmer (*J.*, 1932, 2531) recorded m. p. 289° (decomp.) and 300—305°, depending on the rate of heating.

Methyl trans-trans-*Muconate.*—The acid (24·8 g.) was refluxed for 80 hours with a 3% solution of hydrogen chloride in methanol (216 c.c.), and methyl *trans-trans*-muconate isolated by evaporation of the solution and crystallisation from benzene : yield, 22·5 g. ; m. p. 156—157°. Esterification of the acid with ethereal diazomethane gave an identical product, and was a considerably more convenient procedure. Farmer (*loc. cit.*) reported m. p. 156° for the ester.

cis-cis-*Muconic Acid.*—The method of Böeseken and Engelberts (*loc. cit.*) was modified (cf. Grundmann, *loc. cit.*) as follows. Approximately 13% peracetic acid (755 g.) was obtained by adding a mixture of acetic anhydride (642 g.) and sulphuric acid (5 c.c.) during 9·5 hours to stirred, cooled (4—9°) 30% hydrogen peroxide (150 g.) and, after a further 3 hours, distilling the product under reduced pressure (10—15 mm.) from a bath at 30—35° into an ice-cooled receiver. The content of peracetic acid was determined by adding an excess of potassium iodide to an aliquot portion and titrating the liberated iodine. A solution of pure phenol (22·8 g.) in 13·5% peracetic acid (435 g.) was kept for 15 days in the dark. The precipitate (12 g.) was dissolved in 10% aqueons sodium hydrogen carbonate, and the solution washed with ether and stirred with charcoal. After filtration, *cis-cis*-muconic acid was precipitated with hydrochloric acid, and had m. p. 184° (Found : equiv., 71·5. Calc. for $C_6H_6O_4$: equiv., 71).

Hydrogenation.—*cis-cis*-Muconic acid (100 mg.) in ethanol was hydrogenated at room temperature and pressure in the presence of Adams's catalyst to yield adipic acid, m. p. and mixed m. p. 149—151° (hydrogen uptake : 38 c.c. at 26°/750 mm. Calc. for 2 double bonds : 35 c.c.).

Methyl cis-cis-*Muconate.*—A solution of *cis-cis*-muconic acid (0·5 g.) in methanol (60 c.c.) containing 0·5% of hydrogen chloride was kept at 5° in the dark for 48 hours. The solvent was removed under reduced pressure, and the residue washed with 10% aqueous sodium hydrogen carbonate, dried *in vacuo*, and crystallised from hexane. Methyl *cis-cis*-muconate (0·45 g.) formed massive needles, m. p. 73—73·5°. An identical product was more conveniently obtained by esterification with ethereal diazomethane. Farmer (*loc. cit.*) reported m. p. 75°, and Böeseken and Kerkhoven (*loc. cit.*) m. p. 73—74° for a methyl muconate. As we shall show in a subsequent paper, there is some doubt as to the configuration of their material.

Inversion of cis-cis- *to* trans-trans-*Muconic Acid* (cf. Grundmann, *loc. cit.*).—A solution of *cis-cis*-muconic acid (134 mg.) in alcohol (13·5 c.c.) containing a trace of iodine was irradiated with a 100-watt lamp. The precipitate, which did not further increase on continued irradiation of the solution in a quartz flask with ultra-violet light, was collected (25 mg.) and had m. p. 301° alone or in admixture with *trans-trans*-muconic acid.

Lactonisation Experiments.—(*a*) 1-G. portions of *trans-trans*-muconic acid were treated with sulphuric acid as detailed below, and the solutions were poured on crushed ice. The precipitated solid had m. p. *ca.* 300° undepressed in admixture with starting material : no other product was detected.

	H_2SO_4. Vol., c.c.	H_2SO_4. Concn., %.	Temp.	Time, hrs.	Recovery of muconic acid, %.
(i)	30	95	23— 25°	24	100
(ii)	4·5	95	120—125	0·5	82
(iii)	5	95	160—165	1	0
(iv)	50	86	23— 25°	24	100
(v)	28	86	140—165	4	70

(*b*) *trans-trans*-Muconic acid (1 g.) was recovered unchanged (m. p. and mixed m. p. 300°) in >80% yield after being heated for 7 hours in a sealed tube at 100° with acetic acid (25 c.c.) saturated with hydrogen chloride, or after being refluxed with the same reagent (70 c.c.) for 24 hours.

(*c*) *γ-Carboxymethyl-*Δ^{α}*-butenolide* (VI).—*cis-cis*-Muconic acid (15 g.) was suspended in a cold mixture of sulphuric acid (60 c.c.) and water (20 c.c.), and after 24 hours the solution was poured on crushed ice (200 g.). The bulk of the acid was neutralised by addition of concentrated aqueous ammonia, and the solution (just acid to Congo-red) extracted with ether for 48 hours. Evaporation of the ether gave *γ-carboxymethyl-*Δ^{α}*-butenolide* (1 : 3-*lactone* of 3-hydroxybut-1-ene-1 : 4-dicarboxylic acid) which crystallised from benzene–ethanol as large prisms, m. p. 110·5—111·5° (12 g., 80%) (Found : C, 51·1 ; H, 4·5% ; hydrolysis-equiv., 71. $C_6H_6O_4$ requires C, 50·7 ; H, 4·25% ; equiv., 71). Light absorption in dry dioxan : end absorption only, $\varepsilon = 1420$ at 2260 A. [*cf.* the isomeric lactonic acid (Part III)]. Its *methyl* ester (X) was prepared by treating the recrystallised lactonic acid (VI) (8 g.) with an excess of ethereal diazomethane ; the solution was distilled, finally under reduced pressure, to yield an oil, b. p. 154°/12 mm., which rapidly solidified. Crystallisation was effected by cooling an ether solution with solid carbon dioxide ; the ester formed a fine white powder, m. p. 30·5—31° (Found : C, 54·0 ; H, 5·3% ; hydrolysis-equiv., 78·1. $C_7H_8O_4$ requires C, 53·9 ; H, 5·1% ; equiv., 78).

γ-Carbomethoxymethylenebutanolide (*γ-Carbomethoxymethylene-γ-butyrolactone*) (VII ; R = Me).—Crude lactonic acid (12·7 g. ; direct from cyclisation of *cis-cis*-muconic acid) was treated with an excess of ethereal diazomethane, and the solution filtered and distilled, eventually under reduced pressure. After a small forerun, the main fraction was collected at 126—134°/1 mm. as a mixture (10·2 g.) of liquid and solid. The latter was collected and washed with ether ; yield, 0·9 g. After crystallisation from ether–light petroleum (b. p. 40—60°) the material had m. p. 108—109° (Found : hydrolysis-equiv., 77·4. Calc. for $C_7H_8O_4$: equiv., 78) and was identical with γ-carbomethoxymethylenebutanolide, m. p. 110° (Eisner, Elvidge, and Linstead, *J.*, 1950, 2223).

Colour Reactions of the Lactonic Esters and Acids.—The procedures have been outlined previously (Kuehl, Linstead, and Orkin, *J.*, 1950, 2213).

Légal reaction :	pH 11.	pH 13.
γ-Carbomethoxymethyl-Δ^{α}-butenolide (X)	Light pink, fading slowly	Red, fading to yellow
γ-Carbomethoxymethylenebutanolide (VII ; R = Me)	Darker pink	Darker red
Tollens's reagent :		
γ-Carboxymethyl-Δ^{α}-butenolide (VI)	Instantaneous ppt. of silver	
(X)	,, ,, ,,	
γ-Carboxymethylenebutanolide (VII ; R=H)	Negative	
(VII ; R = Me)	,,	
Ammoniacal silver nitrate :		
(VI)	Slight ppt. of silver after 2 hours	
(X)	,, ,, ,,	
(VII ; R=H)	Negative	
(VII ; R = Me)	,,	
2 : 6-Dichlorophenolindophenol :	pH 11.	pH 13.
(X)	Fades to green	Fades rapidly to greenish-yellow
(VII ; R = Me)	Fades very slowly (4 hours) to green	Reddish-brown after 4 hours

The last red colour denoted that the solution had become acid, owing to opening of the lactone ring.

Alkaline Hydrolysis of γ-Carboxymethyl-Δ^{α}*-butenolide.*—A solution of the lactonic acid (0·1 g.) in 10% sodium hydroxide (5 c.c.) was refluxed for 20 minutes, then acidified with hydrochloric acid, clarified, and treated with semicarbazide hydrochloride (0·15 g.) in water (7 c.c.) containing sodium acetate (0·3 g.). Overnight, crystals of lævulic acid semicarbazone separated (35 mg.), m. p. and mixed m. p. 184°.

Oxidation of γ-Carboxymethyl-Δ^{α}*-butenolide.*—A solution of the lactonic acid (1·5 g.) and sodium carbonate (0·56 g.) in water (10 c.c.) was cooled in ice and stirred whilst potassium permanganate (3·35 g., 3 atoms of O) in water (500 c.c.) was added during 10 hours. Manganese dioxide was filtered off, and the filtrate made acid to Congo-red with hydrochloric acid and extracted with ether for 40 hours. Evaporation of the ether gave a residue which was dissolved in hot water (10 c.c.) and treated with a slight excess of 10% calcium chloride solution. The precipitate was collected, washed with boiling water, then treated with hydrochloric acid. By extraction with ether for 40 hours colourless crystals (450 mg., 47%) were obtained which had m. p. 100° alone and in admixture with oxalic acid dihydrate. The aqueous solution from the first ether-extraction was evaporated to 10 c.c., neutralised to litmus with ammonia, and treated hot with a small excess of 10% aqueous lead acetate. The precipitate was washed with boiling water, then decomposed in water with hydrogen sulphide, and the filtrate evaporated to dryness to yield a white solid (100 mg., 7%) which had m. p. 124—126° undepressed by malic acid (m. p. 130°).

Reactivity of γ-Carboxymethyl-Δ^{α}-butenolide.—(i) The lactonic acid was unaffected by being kept at room temperature with water or dilute acids, and was recovered unchanged (m. p. and mixed m. p. 109—110°) after being refluxed for 2·5 hours with dry methanol containing a trace of hydrogen chloride. (ii) The lactonic acid (500 mg.) was dissolved in 0·1N-potassium hydroxide (70·4 c.c., 2 equivs.), and after 18 hours at room temperature the yellowish solution was acidified to Congo-red with dilute sulphuric acid and extracted with ether for 16 hours. The solid obtained by evaporation of the ether was separated from oil and crystallised from anethole to give prisms, m. p. 110° undepressed by the lactonic acid (VI). The oil was treated with semicarbazide hydrochloride (0·2 g.), sodium acetate (0·2 g.), and water (2 c.c.), and the white crystals which formed were recrystallised from ethanol; they then had m. p. 184° undepressed by lævulic acid semicarbazone. (iii) The lactonic acid methyl ester (X) (0·8 g.) and aniline (0·6 g.) were dissolved together in a minimum of ethanol. After 3 days at room temperature the solvent was evaporated to leave a residue which failed to crystallise. By distillation, aniline (0·5 g., 83%), b. p. 180—182°, was recovered.

Hydrogenation of γ-Carboxymethyl-Δ^{α}-butenolide: The γ-Lactone of β′-Hydroxyadipic Acid.—The unsaturated lactonic acid (VI) (0·65 g.) in acetic acid (25 c.c.) was hydrogenated at room temperature and pressure in the presence of Adams's catalyst (36 mg.). Hydrogen uptake (Found: 122 c.c. at 25°/760 mm. Calc. for 1 double bond: 112 c.c.) was complete in 10 minutes. The catalyst was removed, and the filtrate evaporated to yield an oil which slowly solidified. From benzene or ether–hexane, the *γ-lactone* (XI) of β′-hydroxyadipic acid slowly crystallised, m. p. 60—61° (Found: C, 50·5; H, 5·5. $C_6H_8O_4$ requires C, 50·0; H, 5·6%). On rapid titration of this compound (72·4 mg.) in water (5 c.c.) to the phenolphthalein end-point 4·96 c.c. of 0·105N-sodium hydroxide were consumed ($C_5H_7O_2{\cdot}CO_2H$ requires 4·55 c.c.); an excess of alkali was then added, the solution heated on the steam-bath for 5 minutes and back-titrated with standard acid (Found: hydrolysis-equiv., 71·5. $C_6H_8O_4$ requires equiv., 72).

Methyl ester (XII). The unsaturated lactonic ester (X) (3·43 g.) in 95% alcohol (45 c.c.) was hydrogenated at room temperature and pressure in the presence of Adams's catalyst (69 mg.). The uptake of hydrogen (570 c.c. at 27°/758 mm. Calc. for 1 double bond: 596 c.c.) was complete in 30 minutes. After filtration, the solution was distilled, finally under reduced pressure, to give the *methyl* ester (XII) as a colourless liquid, b. p. 125°/2 mm. (Found: C, 52·6; H, 6·5. $C_7H_{10}O_4$ requires C, 53·15; H, 6·3%).

Hydrolysis of the Methyl Ester (XII).—(a) *With acid.* The ester (1·5 g.) was heated under reflux with 10% hydrochloric acid (25 c.c.) for 4 hours, and the solution concentrated to small bulk in a vacuum-desiccator. The residue solidified on treatment with ether. Crystallisation from benzene afforded (XI), m. p. and mixed m. p. 60—61°.

(b) *With alkali.* A solution of the ester (0·5 g.) in alcohol was refluxed for 3 hours with 10% aqueous sodium hydrogen carbonate (10 c.c.). Acidification of the cooled solution with 10% hydrochloric acid precipitated a solid (0·39 g.) which, recrystallised from hot water, had m. p. 190—191° alone and when mixed with an authentic specimen of *trans*-Δ^{α}-dihydromuconic acid (XIII) (see below) (Found: C, 50·1; H, 6·1%; equiv., 72·8. Calc. for $C_6H_8O_4$: C, 50·0; H, 5·6%; equiv., 72). Hydrogenation of this product (117 mg.) in 95% alcohol (25 c.c.) in the presence of platinum-black gave adipic acid, m. p. and mixed m. p. 146—148° (Hydrogen uptake: 20 c.c. at 27°/757 mm. Calc. for 1 double bond: 20 c.c.).

The Action of Sodium Methoxide on γ-Carbomethoxymethylbutanolide (XII).—The ester (0·8 g.) was treated for 20 minutes at room temperature with anhydrous methanolic sodium methoxide (2·2 c.c.; 2·28N.). The solvent was evaporated, the residue taken up in water (10 c.c.), and the solution acidified with 10% hydrochloric acid. An oil separated which was isolated with ether; crystallisation then occurred. From ether–light petroleum (b. p. 40—60°) slender needles (650 mg.), m. p. 40—41°, of *methyl 5-carboxy-*trans*-pent-2-enoate** (XIV) separated (Found: C, 53·6; H, 6·3%; equiv., 158; hydrolysis-equiv., 78·3. $C_7H_{10}O_4$ requires C, 53·15; H, 6·3%; equivs., 158, 79). The solution from the saponification of this ester (115 mg.) was acidified and concentrated *in vacuo*. *trans*-Δ^{α}-Dihydromuconic acid separated (90 mg.), m. p. 188—190° and mixed m. p. 189—191°.

Oxidation of the Methyl Hydrogen Dihydromuconate (*Methyl 5-Carboxy-*trans*-pent-2-enoate**) (XIV).—The half-ester (350 mg.) was dissolved in water (5 c.c.) by addition of a small excess of 10% sodium carbonate, and to the solution at 0° 3% aqueous potassium permanganate (30 c.c.) was added dropwise. Excess of permanganate was decomposed with sodium hydrogen sulphite, the manganese dioxide filtered off and washed with hot water (30 c.c.), and the combined filtrate and washings were acidified with 10% hydrochloric acid and extracted with ether for 44 hours. Evaporation of the ether to small bulk afforded a crystalline solid (170 mg., 65%), m. p. 178—180° undepressed by succinic acid. The mother-liquors were acidified with dilute sulphuric acid and diluted with water to 100 c.c. Oxalic acid was detected and determined by titration of a portion (50 c.c.) with 0·055N-potassium permanganate (Consumption: 45·0 c.c. Calc. for 100% yield of oxalic acid: 40·0 c.c.).

[With DEXTER B. PATTISON.]

The Methyl Hydrogen Dihydromuconate (*5-Carbomethoxypent-2-enoic Acid**) (XV).—(a) *Preparation by the Doebner reaction.* A mixture of β-carbomethoxypropaldehyde (15 g.) (Johnson, Linstead, and Whetstone, *J.*, 1950, 2219), malonic acid (15·4 g.), and dry pyridine (16 c.c.) was kept at room temperature for 3 days, then heated on the steam-bath overnight. Water was added, and the solution acidified with

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* Geneva numbering.

hydrochloric acid and extracted (5 times) with ether. The extract was shaken with sodium hydrogen carbonate solution, and the aqueous layer washed with ether, acidified, and extracted with ether. Evaporation of the latter afforded 5-carbomethoxy-*trans*-pent-2-enoic acid * (12·6 g.; 62%) which crystallised from light petroleum (b. p. 60—80°) and then had m. p. 61° (Found: C, 53·3; H, 6·55%; equiv., 157·5. Calc. for $C_7H_{10}O_4$: C, 53·15; H, 6·3%; equiv., 158). Farmer and Hughes (*J.*, 1934, 1929, 1938) gave m. p. 60°.

(b) *Hydrolysis to* trans-Δ^{α}-*dihydromuconic Acid* (XIII). The preceding half-ester was heated under reflux for 15 minutes with aqueous sodium hydroxide (1·5 equivs.), and the solution acidified and extracted with ether. The ether was dried (Na_2SO_4) and evaporated, and the residue of *trans*-Δ^{α}-dihydromuconic acid crystallised from water; it had m. p. 191—193°.

(c) *Oxidation.* A stirred solution of the methyl hydrogen dihydromuconate (XV) (2 g.) in water (300 c.c.) containing sodium hydrogen carbonate (1·1 g.) was treated at 0° during 2 hours with a slight excess of 2% potassium permanganate solution. Excess of permanganate was decomposed with aqueous formaldehyde, and the filtrate from the manganese dioxide acidified with hydrochloric acid and extracted with ether (5 × 100 c.c.). Acidic material present in the ether was purified by passage through aqueous sodium hydrogen carbonate and recrystallisation from carbon disulphide. The methyl hydrogen succinate (0·21 g., 12·5%) formed plates, m. p. and mixed m. p. 56—57°.

(d) *Hydrogenation.* Reduction of the methyl hydrogen dihydromuconate (XV) (2·3 g.) in acetic acid (8 c.c.) with hydrogen and Adams's catalyst (27 mg.) was complete in 15 minutes. The solution was filtered, boiled with concentrated hydrochloric acid, and evaporated, and the residue extracted with ether. The latter was dried (Na_2SO_4) and evaporated to give crystals (1·7 g., 80%), m. p. 150—151° undepressed by adipic acid.

[With HAROLD BAER.]

3 : 7-*Diketo*-2 : 6-*dioxa*bicyclo[3 : 3 : 0]*octane* (*Butanolido-βγ-γ′β′-butanolide*) (XVI).—(i) A solution of *cis-cis*-muconic acid (6 g.) in a mixture of sulphuric acid (30 c.c.) and water (10 c.c.) was kept for 6 weeks, then neutralised (to Congo-red) at 0° with ammonia. Water was added to dissolve the precipitate, and the solution extracted with ether for 24 hours. On cooling the ether, a solid separated (2·4 g.), m. p. 118—121°. Repeated crystallisation from ether or anisole afforded the *diketone*, m. p. 128—129° (Found: C, 50·6; H, 4·2. $C_6H_6O_4$ requires C, 50·7; H, 4·25%), which was insoluble in aqueous sodium hydrogen carbonate. A mixture with γ-carboxymethyl-Δ^{α}-butenolide (m. p. 110°) had m. p. 89—92°. (ii) *cis-cis*-Muconic acid was heated at 200°, then cooled, and the red gel-like mass taken up in alcohol. After filtration and evaporation of the solution, crystallisation slowly occurred. From alcohol (charcoal), by concentration, the cyclic diketone crystallised, having m. p. and mixed m. p. 125—126°. On titration at room temperature the dilactone consumed only 1 equiv. of sodium, hydroxide; at 50°, 2 equivs. were rapidly taken up.

One of us (P. S.) gratefully acknowledges a grant from the Ministry of Education.

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[*Received, May 8th*, 1950.]