746. *Polyene Acids. Part II.* The Stereochemistry of the β-Methylmuconic Acids.*

By J. A. Elvidge, R. P. Linstead, and Peter Sims.

The preparation, by Pauly *et al.*, of γ-carboxymethyl-β-methyl-Δ^{α}-butenolide (I) from 3-nitro-*p*-cresol and sulphuric acid, and the isomerisation of the derived lactonic ester (II) with sodium alkoxide to a β-methylmuconic half-ester (III) have been re-investigated. The lactonisation of the half-ester (III) and the derived β-methylmuconic acid (IV) to reafford (II) and (I) have been effected. The half-amide (XIII), prepared from (III) and ammonia, also cyclises readily to the lactonic amide (XIV). Partial hydrolysis of methyl β-methylmuconate (V) gives a second half-ester (VIII) which could not be lactonised; nor could the second acid amide (XII). The compounds (I) and (IV) have also been prepared direct by oxidation of *p*-cresol and of homocatechol with peracetic acid. Conversion of (IV) into a high-melting β-methylmuconic acid, also prepared from β-methyladipic acid, occurs with hot alkali.

The evidence bearing on the configuration of these substances is reviewed. It is concluded that the high-melting acid is *trans-trans*, and that Pauly's acid (IV) is *cis-trans*, contrary to Rinkes.

In the course of the work the three positional isomers of dihydro-β-methylmuconic acid were obtained (Δ^{α}, Δ^{β}, Δ^{γ}), and also the two saturated lactonic acids (XV) and (XVIII).

β-Methylmuconic acid is of especial interest as a dicarboxyisoprene. Its stereoisomerism has a significant connection with that of the carotenoids. We have now investigated this compound and the derived unsaturated lactonic acid, by using essentially the methods by which the parent muconic acids were examined (Elvidge, Linstead, Orkin, Sims, Baer, and Pattison, *J.*, 1950, 2228; Elvidge, Linstead, Sims, and Orkin, *ibid.*, p. 2235).

The acid can exist theoretically in four geometrically isomeric forms, *cis-cis*, *cis-trans*, *trans-cis*, and *trans-trans*. Of these, two have been obtained and it is probable, for reasons given later, that the other two will be unstable and difficult to isolate. Positional isomerism

* "The Third Isomeric (*cis-trans*-)Muconic Acid," *J.*, 1950, 2235, is regarded as Part I of this series.

is also possible in that all the mono-derivatives of the acids, such as the half-esters, can exist in two isomeric forms according to whether the *C*-methyl is β- or γ- to the ester group.* We have obtained and oriented isomerides of both types, geometrical and positional.

It will be convenient to deal with the preparation and general chemistry of the β-methylmuconic acids first, and their configuration secondly.

Preparation and Chemistry.—Important earlier work is that of Pauly, who found that 3-nitro-*p*-cresol with sulphuric acid gave (in addition to a nitrogenous compound, m. p. 206—207°) an unsaturated lactonic acid, $C_7H_8O_4$, m. p. 130°, derived from β-methylmuconic acid (Pauly, Gilmour, and Will, *Annalen*, 1914, **403**, 119; Pauly and Will, *ibid.*, 1918, **416**, 1). We have confirmed this preparation. The lactonic acid is converted by methanolic hydrogen chloride or more conveniently by diazomethane into a methyl ester, m. p. 37°. These compounds certainly have the structures (I) and (II) assigned to them by Pauly: the presence of the unsaturated γ-lactone ring followed from the alkaline hydrolysis to β-methyl-lævulic acid, and the position of the double bond from the results of oxidation (*loc. cit.*). The light absorption (see Table) confirms the Δ^{α}-structure (cf. Haynes and Jones, *J.*, 1946, 954), as also does the hydrogenation to a saturated lactone (XVIII).

Pauly and Will (*loc. cit.*) found that the lactonic ester (II) was isomerised by methanolic sodium methoxide to a β-methylmuconic half methyl ester, m. p. 125°, necessarily (δ)-methyl (α)-hydrogen β-methylmuconate (III). On hydrolysis this yielded β-methylmuconic acid, m. p. 170—171° (IV). We find that the m. p. of the acid varies with the rate of heating as with the muconic acids—presumably lactonisation occurs—and this doubtless accounts for the apparent discrepancies in the literature. Both the acid (IV) and the half-ester (III) with diazomethane yield the same methyl ester (V), the properties of which agree with those described by Pauly. This diester was also prepared from the acid (IV) with dilute methanolic hydrogen chloride, and it re-formed the β-methylmuconic acid (IV) on alkaline hydrolysis. The structure of the acid was confirmed by its catalytic hydrogenation to β-methyladipic acid (VI) and reduction by sodium amalgam to the known Δ^{β}-dihydro-β-methylmuconic acid (2-methylbut-2-ene-1 : 4-dicarboxylic acid) (VII). Partial esterification of the β-methylmuconic acid (IV) gave the half-ester (III).

Partial hydrolysis of methyl β-methylmuconate (V) with barium hydroxide gave the second half-ester (VIII), m. p. 170°. This product was reconverted into (V) by diazomethane, hydrolysed to the β-methylmuconic acid (IV) by alkali, and converted into β-methyladipic acid on hydrogenation followed by hydrolysis: its structure is therefore certain. The same half-ester (VIII) was obtained as a by-product from the reaction of the diester (V) with aqueous-methanolic ammonia, a reaction which gave mainly a half-amide ester (IX), m. p. 162°, as described by Pauly and Will (*loc. cit.*). Prolonged reaction of (V) afforded a third product, the diamide (X), which with nitrous acid yielded the parent acid (IV). The orientation of the half-amide ester (IX) was not determined by Pauly but now follows from its conversion with nitrous acid into the second acid ester (VIII). The positionally-isomeric half-amide ester (XI) (m. p. 141°) was obtained by treatment of the half-ester (III) with thionyl chloride (to yield the acid chloride) and then ammonia. Cautious hydrolysis of (XI) then afforded an acid amide (XII), m. p. 210—211°. The second acid amide (XIII) (m. p. 146—147°) was readily obtained by treatment of the half-ester (III) with ammonia. Both half-amides, (XII) and (XIII), with nitrous acid yielded the parent β-methylmuconic acid (IV).

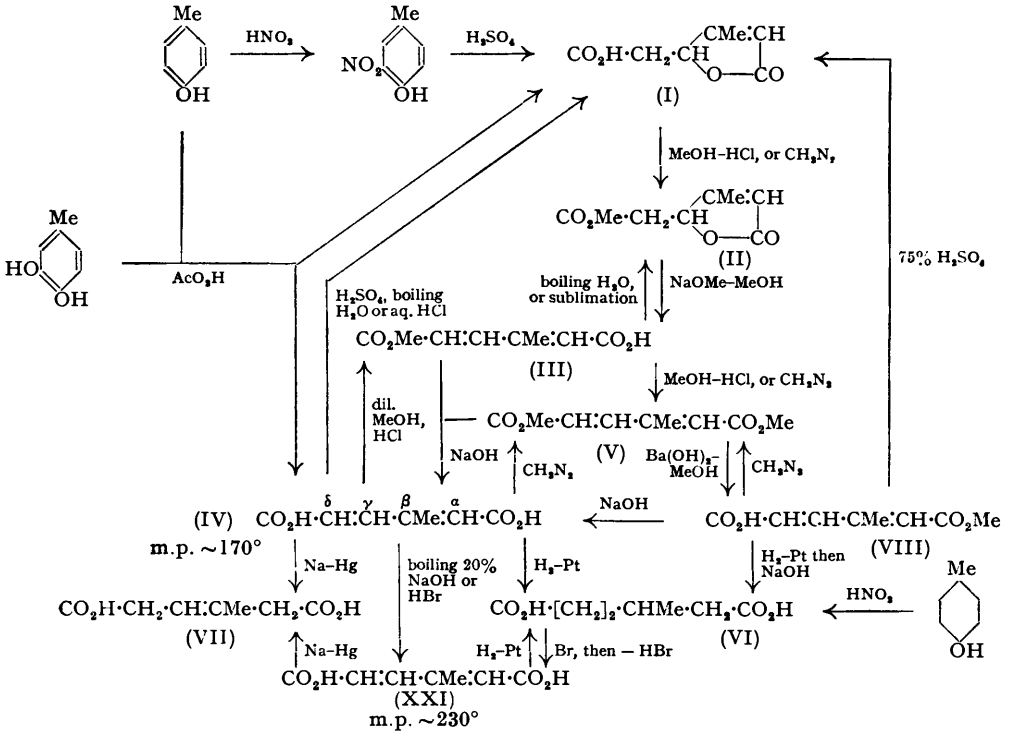
Lactonisation of the β-methylmuconic acid (IV) gave only the original lactonic acid (I) and no isomeride. There was an interesting and significant difference in the behaviour of the two isomeric half-esters, and of the two half-amides, under lactonising conditions. The α-acid δ-ester (III), m. p. 126° (with the *C*-methyl group β to carboxyl), readily changed back to the lactonic ester (II) from which it had been made. On the other hand the isomeride (VIII), m. p. 170°, with the δ-carboxyl group free (*C*-methyl β to carbomethoxyl), was stable to heat and could be sublimed unchanged. However, with 75% sulphuric acid, this stable acid ester (VIII) yielded the lactonic acid (I), evidently because hydrolysis of the ester liberated the α-carboxyl group, already shown to be capable of lactonisation. Again, the half-amide (XIII), m. p. 146°, with a free α-carboxyl group, readily cyclised to the lactonic amide (XIV), whereas

* These compounds have all been named as derivatives of β-methylmuconic acid: thus, *e.g.*, $CO_2Me{\cdot}CH{:}\underset{trans}{CH}{\cdot}CMe{:}\underset{cis}{CH}{\cdot}CO_2H$ is named (δ)-methyl (α)-hydrogen β-methyl-*cis-trans*-muconate; $CO_2Me{\cdot}CH{:}\underset{trans}{CH}{\cdot}CMe{:}\underset{cis}{CH}{\cdot}CO{\cdot}NH_2$ is β-methyl-*cis-trans*-muconic (α)-amide (δ)-methyl ester. The terms *cis* and *trans* are always given in positional order, *i.e.* the first cited refers to the lower-numbered double bond.

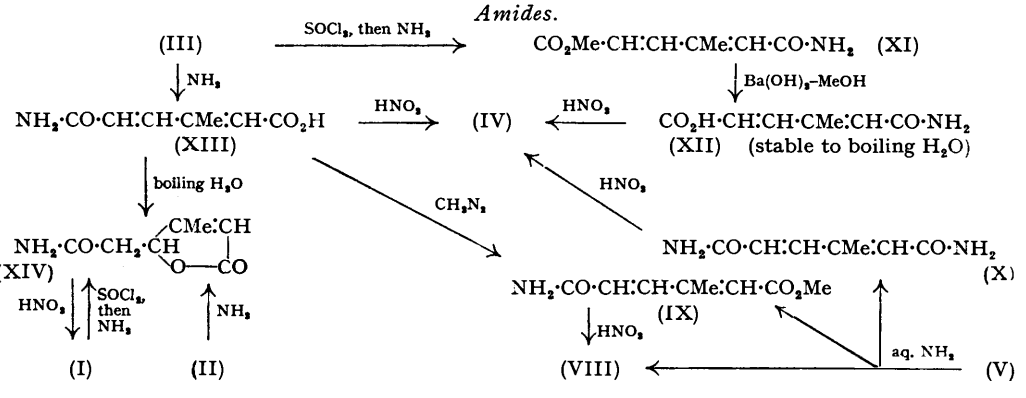
the isomeric half-amide (XII) (δ-carboxyl free) was unchanged. There is a simple stereochemical explanation for these facts which is discussed later.

The structure of the lactonic amide product (XIV) followed from the absorption spectrum, its conversion into the lactonic acid (I) by nitrous acid, and its synthesis, (*a*) from the lactonic acid with thionyl chloride and then ammonia, and (*b*) from the lactonic ester (II) with ammonia.

Lactones, acids, and esters.

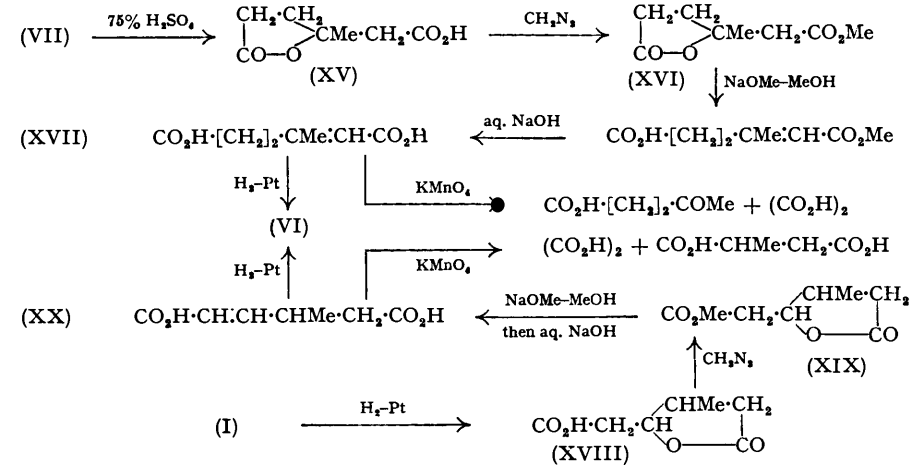


Amides.



It seemed of interest, also, to study the lactonisation of the available Δ^{β}-dihydro-β-methylmuconic acid (VII). This with 75% sulphuric acid readily afforded a lactonic acid product which appeared to be homogeneous. This acid is assigned the structure (XV) on the following evidence : fission of its ester (XVI) with sodium methoxide, and hydrolysis of the monounsaturated acid ester so produced, yielded a dihydro-β-methylmuconic acid (XVII) (reduced catalytically to β-methyladipic acid), which, since it gave oxalic and lævulic acids on oxidation, had the double bond in the αβ-position.

Dihydro-products.



Light-absorption data.

Compound		$\lambda_{max.}$, Å	ε	Solvent
R = OH		2260 *	3,900	EtOH
R = NH_2			5,880 at 2260 Å	EtOH
COR″·CH:CH·CMe:CH·COR′				
R′ = R″ = OH	*cis-trans*	2570 *	17,600	0·1M-NaOH
		2650	19,000	
	trans-trans	2590 *	20,100	0·1M-NaOH
		2650	22,400	
R′ = R″ = OMe	*cis-trans*	2580 *	21,000	EtOH
		2650	22,100	
	trans-trans	2590	26,700	EtOH
		2660	28,400	
R′ = R″ = NH_2	*cis-trans*	2270	11,200	EtOH
		2510 *	22,400	
		2580 *	24,600	
		2650	26,600	
	trans-trans	2260	11,200	EtOH
		2580 *	27,000	
		2650	30,600	
R′ = OH, R″ = OMe	*cis-trans*	2579 *	26,900	EtOH
		2650	28,000	
		2740 *	19,700	
R′ = OMe, R″ = OH	*cis-trans*	2570 *	22,100	EtOH
		2650	25,200	
R′ = OH, R″ = NH_2	*cis-trans*	2280	11,600	EtOH
		2510	14,700	
		2570 *	16,300	
		2640	18,000	
		2770	14,700	
R′ = NH_2, R″ = OH	*cis-trans*	2270	7,890	EtOH
		2500	24,800	
		2580	27,800	
		2640	27,800	
R′ = OMe, R″ = NH_2	*cis-trans*	2580 *	24,200	EtOH
		2650	25,800	
R′ = NH_2, R″ = OMe	*cis-trans*	2570 *	21,200	EtOH
		2650	24,400	
		2720 *	16,900	

* Inflection.

This Δ^{α}-acid (XVII) was identical (mixed m. p.) with an acid prepared for another purpose by Linstead, Lunt, and Weedon (forthcoming publication); this latter acid was obtained by the Reformatsky reaction of ethyl lævulate with ethyl bromoacetate, splitting the lactonic ester product [the ethyl ester corresponding with (XVI)] with sodium ethoxide, and hydrolysing the resultant half-ester with aqueous alkali.

The second saturated lactonic acid (XVIII) was prepared by catalytic reduction of Pauly's lactone (I). Treatment of the methyl ester (XIX) with sodium methoxide and then aqueous alkali gave the third dihydro-β-methylmuconic acid (XX) with the double bond in the γδ-position. This was shown by its oxidation to oxalic and methylsuccinic acids.

The next preparative method for β-methylmuconic acid to be examined was the peracetic acid oxidation of suitable phenols. Böeseken, Metz, and Pluim (*Rec. Trav. chim.*, 1935, **54**, 345) had obtained from *p*-cresol a β-methylmuconic acid, m. p. 188·5°, in 20% yield, together with an acid, m. p. 124°, which they regarded as probably lactonic. We have obtained similar yields of these products (the m. p. of the former varies with the rate of heating, as already mentioned), and identified them with the compounds made by Pauly's method, having the structures (IV) and (I), respectively. Similar oxidation of homocatechol gave a little of the same β-methylmuconic acid (IV) and mainly the related lactonic acid (I).

We then examined the bromination and alkali dehydrobromination of β-methyladipic acid (VI). This yielded a second β-methylmuconic acid, m. p. 230° (XXI), with a dimethyl ester, m. p. 56°, and a diamide, m. p. 231°; these derivatives reafforded the parent acid on hydrolysis with alkali and nitrous acid, respectively. The structure was established by catalytic hydrogenation to β-methyladipic acid and amalgam reduction to Δ^{β}-dihydro-β-methylmuconic acid (VII). There can be little doubt that the acid (XXI) is identical with the high-melting acid [m. p. 235° (decomp.)] made by Stephen and Weizmann (*J.*, 1913, **103**, 269) by dehydrobromination of αα′-dibromo-β-methyladipic ester with trimethylamine and with the material (m. p. 232°) made by Kuhn and Grundmann (*Ber.*, 1936, **69**, 1757; 1937, **70**, 1894) *via* the condensation of ββ-dimethyl- and β-ethyl-acrylic esters with oxalic ester.

Von Braun, Leistner, and Münch (*Ber.*, 1926, **59**, 1950), using diethylamine for the dehydrobromination of dibromo-β-methyladipic acid, isolated a small quantity of a β-methylmuconic acid, m. p. 173°; this was most probably identical with Pauly's acid. The formation side by side of two stereoisomeric muconic acids by an analogous dehydrobromination has been observed by Farmer (*J.*, 1923, **123**, 2531).

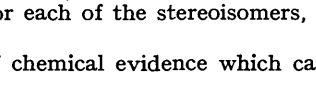
The β-methylmuconic acid, m. p. ~230°, is quite unchanged by sulphuric acid and by the conditions which convert the isomeric acid (IV), m. p. ~170°, into the lactonic acid (I).

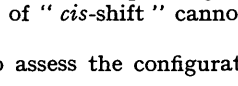
Finally, the interconversion of the β-methylmuconic acids, (IV) and (XXI), was examined. When the acid, m. p. 170°, was heated for some hours with 20% aqueous sodium hydroxide it was converted into the acid of m. p. 230°, as described by Rinkes (*Rec. Trav. chim.*, 1929, **48**, 1093). Hot concentrated hydrobromic acid also effected the same change, as reported by Pauly and Will (*loc. cit.*). The high-melting product of these changes was identical with the acid prepared from β-methyladipic acid, and the identity was confirmed by comparison of the dimethyl esters. Somewhat surprisingly, the low-melting acid showed no detectable change when its solutions were irradiated in the presence of traces of iodine. The high-melting acid was quite unchanged after similar treatment, and also after prolonged heating with alkali.

Configuration.—Light absorption provides no guide to configuration among muconic acids. The positions of the main absorption bands are practically the same for each isomer, there being no shift to shorter wave-lengths in the *cis*-forms. This would agree with the postulate that the absorbing systems have rather similar dimensions, corresponding with an *s-trans*-configuration for each of the stereoisomers, but the lack of " *cis*-shift " cannot be entirely so explained.

The lines of chemical evidence which can be used to assess the configuration of isomeric muconic acids are :

(1) *Ease of lactonisation.* A carboxyl group disposed *cis*- to the acrylic residue will lactonise readily, the *trans*-isomeride with difficulty if at all.





The determining factor in the reaction $A \longrightarrow B$ is the approach of the α-carboxyl to the γ-carbon atom, and this is affected by the geometry of the double bond αβ to carboxyl but not

by that of the γδ-double bond, or by that of the βγ-single bond (whether *s-cis* or *s-trans*). This applies to half-esters as well as to diacids.

(2) *Fission of unsaturated lactones.* The product of ring opening $B \longrightarrow A$, where R = alkyl, which is brought about by alkoxides, will be expected to have, initially, a *cis-trans*-configuration. The αβ-double bond must be *cis* in the lactone, and since it plays no part in the reaction, should remain *cis* in the product, unless other factors mentioned below [in (4)] operate. It has been shown that ring-opening of γ-dicarbethoxymethylenebutenolide under these conditions gives an undoubtedly *cis*-product (Eisner, Elvidge, and Linstead, *J.*, 1951, 1501). The γδ-double bond, which is formed in the reaction $B \longrightarrow A$, is considered to be *trans* by general analogy with such homogeneous elimination reactions and more particularly by analogy with related ester fissions now under study (cf. Elvidge, Linstead, Sims, and Orkin, *loc. cit.*).

(3) *Dehydrohalogenation.* In the same way we should expect double bonds formed by dehydrobromination of αα′-dibromoadipic acids to be predominantly *trans*.

(4) *Stability and interconversion.* The relative stabilities of the various isomerides, and the conditions required for their interconversion, will be some guide to configuration. The stabilities of substituted muconic acids will be affected by alkyl substitution and will therefore differ among the various homologous series. The most stable steric forms will be those in which there is the least intramolecular interference between substituent groups.

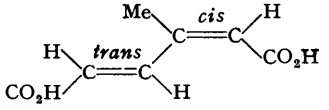
(5) *Fission of aromatic rings.* When a muconic acid is formed by fission of an aromatic ring under mild conditions, the carbon atoms will be expected to appear initially in a coiled phase with the bonds arranged *cis*, *s-cis*, *cis*. The central single bond will then most probably change to *s-trans*; whether the configuration about the double bonds will change will depend upon the conditions of reaction and the inherent stability of the *cis-cis*-isomer [as indicated under (4)].

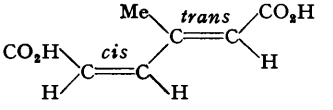
Additional considerations. These last points will also apply to unsaturated products derived by fission of lactones and other ring-compounds. Thus it is conceivable that the diene obtained from a reaction such as $B \longrightarrow A$ would not persist in its nascent *cis-trans*-form but would at once invert to the *trans-trans*-isomer. This could well be expected if the γ-carbon carried a bulky substituent. Reaction conditions alone might in some cases provoke inversion; the fission of a Δ^{α}-unsaturated lactone to a *trans*-product by aniline was observed by Eisner, Elvidge, and Linstead (*loc. cit.*). Likewise, a diene product isolated from the opening of a muconic anhydride (in which the butadiene bonds are necessarily arranged *cis*, *s-cis*, and *cis*) would not automatically have the *cis-cis*-configuration. The important case of β-methylmuconic anhydride, which gives rise to *cis-trans*-products, we discuss in the next paper.

No one of the foregoing criteria is sufficient by itself for the assignment of geometrical configuration to a muconic acid. Taken together, however, they provide powerful evidence, and, when applied to the β-methylmuconic acids and their derivatives, lead to the following conclusions :

(1) The acid (XXI), m. p. 230°, cannot be lactonised : hence it evidently has no *cis*-double bond. The acid (IV), m. p. 170°, readily forms a lactone; hence it has at least one *cis*-arrangement. As a second lactone (the *C*-methyl positional isomer) is not formed, it appears that the two double bonds are dissimilar, *i.e. cis* and *trans*. This conclusion is supported by the behaviour of the two half-esters and the two half-amides : the half-ester and half-amide which lactonise evidently have a *cis*-double bond adjacent to the free carboxyl group. As the other half-ester and half-amide fail to lactonise, the free carboxyl group is evidently in the unfavourable *trans*-position. The acid, m. p. 170°, is therefore *cis-trans*.

(2) The Δ^{α}-lactonic ester (II) with sodium alkoxide yields an acid ester of the acid, m. p. 170°. The *C*-methyl group is known to be on the β-carbon of the lactone ring so that the orientation of the half-ester product (and thence of the derived amide, etc.) is in no doubt. The *C*-methyl group will appear at one end of a *cis*-double bond in the β-methylmuconic product and hence the acid, m. p. 170°, is *cis-trans* (*C*) and not *trans-cis* (*D*).

(*C*) 



(*D*)

(3) As the acid, m. p. 230°, is formed from dehydrobromination reactions it should be *trans-trans*; Kuhn's method of preparation would also be expected to give a *trans*-product.

(4) To form an estimate of the relative stabilities of the various isomerides, scale models, based on covalent atomic radii, have been constructed. In accordance with current theory

concerning conjugated systems, the models have been given a planar arrangement. Interference between the various groups can then be observed in the following way :

$$\underset{\delta}{CO_2H\cdot CH}{:}\underset{\gamma}{CH}\cdot\underset{\beta}{CMe}{:}\underset{\alpha}{CH}\cdot CO_2H$$

Steric form αβ	γδ	βγ	Atoms or groups which interfere with one another (possible minor effects are shown in brackets)
cis	*cis*	*s-cis*	α-carboxyl and δ-carboxyl
cis	*cis*	*s-trans*	β-methyl and δ-carboxyl
trans	*cis*	*s-cis*	[α-hydrogen and δ-carboxyl]
trans	*cis*	*s-trans*	β-methyl and δ-carboxyl, [β-methyl and α-carboxyl]
cis	*trans*	*s-cis*	[α-carboxyl and δ-hydrogen]
cis	*trans*	*s-trans*	none
trans	*trans*	*s-cis*	none
trans	*trans*	*s-trans*	[α-carboxyl and β-methyl]

The conclusion is drawn that β-methyl-*cis-trans*- and -*trans-trans*-muconic acid (and their esters, etc.) will be stable, and the other isomerides unstable. The fact that the several preparative methods lead only to two acids, either the acid, m. p. 170°, or the acid, m. p. 230°, is in agreement, and the conversion of the former into the latter acid is not inconsistent with it.

(5) The preparations from aromatic material are at first sight anomalous because they give rise to the acid, m. p. 170°, for which the *cis-trans*-configuration has been deduced. It is true that in the unsubstituted series it is possible to obtain the *cis-cis*-form by peracid oxidation of phenol, but the margin of stability of the product is slight and its conversion into the *cis-trans*-isomeride can be brought about even by very brief treatment with boiling water (Elvidge, Linstead, Sims, and Orkin, *loc. cit.*). Scale models show that the additional methyl group in β-methylmuconic acid gives rise to interference in the *s-trans*-form of the *cis-cis*-isomer and a lower stability than in *cis-cis*-muconic acid is to be expected. (There is of course serious interference in the *s-cis*-form.) We are, therefore, not disposed to regard the isolation of the acid (IV), m. p. 170°, from the oxidations of *p*-cresol and homocatechol as a very sound pointer to its steric configuration. The same remark applies to the isolation of the acid, m. p. 170°, from the reaction of β-methylmuconic anhydride with water, which we discuss in the next paper.

Supporting evidence for the *cis-trans*-formulation for the acid, m. p. 170°, is provided by the fact that it is easily lactonised to give *only one* lactonic acid (*A* ⟶ *B*). If it had the *cis-cis*-structure it ought to give two products—one lactonised on to the methylated β-carbon atom, the other on to the unmethylated γ-carbon atom. Moreover, both acid esters [(III) and (VIII)] and both acid amides [(XII) and (XIII)] should lactonise readily. Lactonisation involving the δ-carboxyl group, in the sense *E* ⟶ *F*, which is not observed, might be expected for two reasons.

(*E*) $CO_2H\cdot CH{:}\overset{cis}{CH}\cdot CMe{:}\overset{cis}{CH}\cdot COR$

$$\begin{matrix}CO{-}O \\ | \\ CH{=}CH\end{matrix}\!\!>\!CMe\cdot CH_2\cdot COR$$ (*F*)

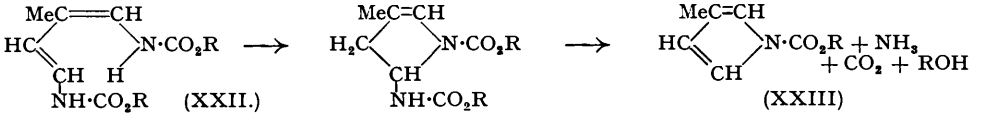
(where R = OH, OMe, NH_2)

First, the δ-carboxy-function of the β-methylmuconic system is more reactive than the α, irrespective of the geometrical configuration. This is shown by the facts that the acid (IV) is partially esterified to the (δ)-ester (α)-acid (III), that the diester (V) is partially hydrolysed to the (δ)-acid (α)-ester (VIII), that (V) reacts with ammonia to yield the (δ)-amide (α)-ester (IX), and that, as shown by Rinkes (*loc. cit.*), the higher-melting β-methylmuconic acid and its dimethyl ester, respectively, undergo partial esterification and partial hydrolysis in this same general sense.

Secondly, the lactonisation *E* ⟶ *F* might be favoured by the *C*-methyl group. Lactonisation of pyroterebic and related acids is known to be assisted very greatly by the methyl substituents (Linstead, *J.*, 1932, 115; Linstead and Rydon, *ibid.*, 1933, 580) and the same has now been shown of Δ^{β}-dihydro-β-methylmuconic acid (VII), which yields only the lactone (XV), cyclisation having proceeded on to the methylated carbon.

Rinkes (*Rec. Trav. chim.*, 1929, **48**, 603), in addition to invoking the synthesis from aromatic material, adduced a second line of evidence in favour of a *cis-cis*-configuration for the acid, m. p. 170°. The derived diamide (X), on Hofmann degradation, yielded an isoprene diurethane (XXII) which in dilute sulphuric acid readily cyclised to 3-methylpyrrole-1-carboxylic ester (XXIII). In our view, however, these reactions are consistent with a *cis-trans*-structure. Scale models show that a *cis-trans*-isoprene urethane when in the *s-cis*-form (and cyclisation of

the *cis-cis*-isomer would also require intermediation of an *s-cis*-form) can cyclise readily by addition of the α-imino-group to the γδ-double bond : subsequent elimination of a urethane residue would then lead to the pyrrole (XXIII).



We therefore regard the two β-methylmuconic acids as having the following configurations :

	αβ	*γδ*
Acid, m. p. ~170° (IV)	*cis*	*trans*
Acid, m. p. ~230° (XXI)	*trans*	*trans*

The importance of this in relation to the configuration of the carotenoids is discussed in the following paper.

Experimental.

(M. p.s marked with an asterisk were taken from a bath at 165°, with the temperature rising 8°/minute. Other m. p.s were determined normally.)

γ-Carboxymethyl-β-methyl-Δ^α-butenolide (I) *and its Methyl Ester* (II).—3-Nitro-*p*-cresol (Schultz, *Ber.*, 1907, **40**, 4324) (200 g.) was treated with concentrated sulphuric acid (600 g.) according to the directions of Pauly, Gilmour, and Will (*loc. cit.*) to yield, besides a nitrogen-containing by-product (12 g.; needles, m. p. 206—206·5°, from ethanol), the lactonic acid (I) (170 g., 83%) which separated from ethanol–light petroleum (b. p. 40—60°), or from ethyl acetate, as prisms, m. p. 129—130° (Found : C, 53·8; H, 5·4. Calc. for $C_7H_8O_4$: C, 53·9; H, 5·2%).

Esterification of the acid (45 g.) with methanol (400 c.c.) containing 0·3% of hydrogen chloride gave the lactonic ester (II) (31 g., 63%), b. p. 180°/15 mm., m. p. 34—35° (needles), as described by Pauly, Gilmour, and Will (*loc. cit.*). An identical product (mixed m. p.) was obtained by brief treatment of the lactonic acid with excess of ethereal diazomethane and evaporation of the solution.

(δ)-Methyl (α)-Hydrogen β-Methyl-cis-trans-*muconate* (III).—The preceding lactonic ester (30 g.) was dissolved in methanolic sodium methoxide (from 4·6 g. of sodium and 60 c.c. of methanol), and the solution then concentrated under reduced pressure to two-thirds bulk and poured into cold 10% aqueous sulphuric acid (100 c.c.). The precipitated (δ)-methyl (α)-hydrogen β-methyl-*cis-trans*-muconate (III) (25 g., 83%) crystallised from benzene as needles, m. p. 126—127° (Found : C, 56·45; H, 6·0. Calc. for $C_8H_{10}O_4$: C, 56·5; H, 5·9%). Pauly and Will (*loc. cit.*) record m. p. 127° for a similarly obtained product.

β-Methyl-cis-trans-*muconic Acid* (IV).—(δ)-Methyl (α)-hydrogen β-methyl-*cis-trans*-muconate (5 g.) was kept with 10% aqueous sodium hydroxide (25 c.c.) for 30 minutes at room temperature and the solution then acidified (Congo-red) with concentrated hydrochloric acid. The precipitated β-methyl-*cis-trans*-muconic acid (4·08 g., 90%) crystallised from ethanol as micro-needles, m. p. *ca.* 170° or 178—179° * (Found : C, 53·5; H, 5·3%; equiv., 77·2. Calc. for $C_7H_8O_4$: C, 53·8; H, 5·2%; equiv., 78). Pauly and Will (*loc. cit.*) give m. p. 170—171° (with gas evolution).

Variation of the M. P. of β-Methyl-cis-trans-*muconic Acid with Rate of Heating.*—

Initial temp. of bath.	Temp. rise.	M. p.
room temp.	8°/min.	172—173°
165°	8	178—179
165	15	190—191
165	1·5	167—167·5

Reduction.—(*a*) The preceding acid (500 mg.) in ethanol (10 c.c.) was hydrogenated in the presence of Adams's catalyst (50 mg.) (Hydrogen uptake : 170 c.c. at 25°/750 mm. Calc. for 2 double bonds : 161 c.c.) to yield β-methyladipic acid (0·4 g.; from nitric acid), m. p. and mixed m. p. 96—98°.

(*b*) Reduction of the acid (100 mg.) in 10% aqueous sodium hydroxide (6 c.c.) with 2·5% sodium amalgam (2·5 g.) for 30 minutes at room temperature gave, after filtration, acidification, and extraction with ether (3 × 10 c.c.), *trans*-Δ^β-dihydro-β-methylmuconic acid (VII) which crystallised from water as needles, m. p. 139—140°. Pauly and Will (*loc. cit.*) record m. p. 140—141°.

Methyl β-Methyl-cis-trans-*muconate* (V).—The half-ester (III) (10 g.) was kept for 24 hours with methanol (50 c.c.) containing 5% of dry hydrogen chloride. Evaporation of the solution under reduced pressure left methyl β-methyl-*cis-trans*-muconate (V) (9·7 g., 90%) which crystallised from aqueous methanol or light petroleum (b. p. 40—60°) as needles, m. p. 38—38·5° (Found : C, 58·8; H, 6·6. Calc. for $C_9H_{12}O_4$: C, 58·7; H, 6·6%). Pauly and Will (*loc. cit.*) give m. p. 38·5°.

Brief treatment of the half-ester (III) (0·1 g.) with ethereal diazomethane and evaporation of the solution gave the diester (0·1 g.), m. p. and mixed m. p. 37·5—38°.

The diester (m. p. and mixed m. p. 38—38·5°) was also prepared from β-methyl-*cis-trans*-muconic acid with ethereal diazomethane, and with 5% methanolic hydrogen chloride (10 parts by weight) for 48 hours at room temperature.

Hydrolysis of the diester (1·2 g.) in methanol with 10% aqueous sodium hydroxide (5·5 c.c.) for 1 hour at room temperature reafforded β-methyl-*cis-trans*-muconic acid (0·81 g., 80%) which separated from ethanol as micro-needles, m. p. and mixed m. p. 178—179°.*

Partial Esterification of β-Methyl-cis-trans-*muconic Acid*: *Formation of the Half-ester* (III).—A suspension of β-methyl-*cis-trans*-muconic acid (1·5 g.) in methanol (15 c.c.) containing 0·5% of dry hydrogen chloride was kept for 48 hours in the dark. Unchanged acid was filtered off, the filtrate evaporated under reduced pressure, and the residue extracted with boiling benzene (2 × 25 c.c.). Evaporation of the benzene afforded an oil which was extracted with saturated aqueous sodium hydrogen carbonate (5 c.c.). Th eaqueous extract was washed with ether (2 × 10 c.c.), acidified (Congo-red) with concentrated hydrochloric acid, and cooled in ice. (δ)-Methyl (α)-hydrogen β-methyl-*cis-trans*-muconate (0·23 g., 14%) separated; from benzene it formed needles, m. p. and mixed m. p. 126—127°.

Treatment of the product (0·1 g.) with ethereal diazomethane gave methyl β-methyl-*cis-trans*-muconate (needles from aqueous methanol), m. p. and mixed m. p. 37·5—38°.

Partial Hydrolysis of the Diester: *Formation of (α)-Methyl (δ-)Hydrogen β-Methyl*-cis-trans-*muconate* (VIII).—Methyl β-methyl-*cis-trans*-muconate (1·2 g.) was kept overnight with methanolic barium hydroxide (15·3 c.c.; 0·46N). The precipitate was dissolved in water, and the solution acidified. (α)-*Methyl* (δ)-*hydrogen* β-*methyl*-cis-trans-*muconate* (VIII) (0·9 g., 81%) crystallised from aqueous methanol as needles, m. p. 170° (Found: C, 56·6; H, 6·2%; equiv., 170. $C_8H_{10}O_4$ requires C, 56·5; H, 5·9%; equiv., 170·2).

Treatment of this half-ester with ethereal diazomethane reafforded methyl β-methyl-*cis-trans*-muconate, m. p. and mixed m. p. 37—38°.

Treatment of the half-ester (200 mg.) with boiling sodium hydroxide solution (5 c.c.; 2N) for 30 minutes, and acidification, afforded β-methyl-*cis-trans*-muconic acid (110 mg.), m. p. and mixed m. p. 180—182°.*

Reduction of the half-ester (350 mg.) in ethanol (15 c.c.) with hydrogen and Adams's catalyst (hydrogen uptake: 55·0 c.c. at 21°/755 mm. Calc. for 2 double bonds: 49·2 c.c.) and hydrolysis of the oily product with boiling 10% sodium hydroxide (2 c.c.) for 30 minutes gave, on acidification, evaporation, and extraction with ethanol, β-methyladipic acid (200 mg.), m. p. and mixed m. p. 94—96°.

Amides derived from β-Methyl-cis-trans-*muconic Acid*.—(a) *The ester amide* (IX). Methyl β-methyl-*cis-trans*-muconate (V) (6 g.) was kept with methanol–aqueous ammonia (sp. gr. 0·88) mixture (150 c.c.; 1 : 1) for 4 days at 0°. The filtrate from unchanged ester was concentrated under reduced pressure to 20 c.c. (solid appeared), cooled, and filtered. Acidification of the filtrate gave (α)-methyl (δ)-hydrogen β-methyl-*cis-trans*-muconate (VIII) (0·5 g.), m. p. and mixed m. p. 167—168°. The solid was crystallised from ethanol yielding prisms, m. p. 162—163°, of β-methyl-*cis-trans*-muconic (α)-methyl ester (δ)-amide (IX) (4 g., 73%) (Found: C, 57·0; H, 6·7; N, 8·5. Calc. for $C_8H_{11}O_3N$: C, 56·8; H, 6·55; N, 8·3%). Pauly and Will (*loc. cit.*) record m. p. 161—162°

To the ester amide (IX) (1 g.) in 4% aqueous hydrochloric acid solution (60 c.c.) at room temperature, 10% sodium nitrite solution (10 c.c.) was added during 2 hours, with occasional shaking. The mixture was kept at 0° for 16 hours, and the solid then treated with aqueous sodium hydrogen carbonate. The insoluble material was unchanged ester amide (IX), m. p. and mixed m. p. 162—163°. Acidification of the alkaline extract gave (α)-methyl (δ)-hydrogen β-methyl-*cis-trans*-muconate (VIII) (100 mg., 10%) which crystallised from aqueous methanol as needles, m. p. and mixed m. p. 170°.

(b) *The diamide* (X). When methyl β-methyl-*cis-trans*-muconate (V) (4 g.) was kept with a methanol–aqueous ammonia (sp. gr. 0·88) mixture (50 c.c.; 1 : 1) for 10 days at room temperature, and the solution then evaporated under reduced pressure, β-methyl-*cis-trans*-muconamide (X) (3·3 g., 83%) was obtained, which crystallised from water as massive needles, m. p. 215—216° (Found: N, 18·2. Calc. for $C_7H_{10}O_2N_2$: N, 18·2%). Pauly and Will (*loc. cit.*) give m. p. 213—214°.

The finely powdered diamide (0·5 g.) was suspended in 10% aqueous hydrochloric acid (10 c.c.), and 20% sodium nitrite solution (4 c.c.) added during 4 hours, with occasional shaking. Crystallisation of the resulting solid from ethanol afforded micro-needles of β-methyl-*cis-trans*-muconic acid (0·35 g., 70%), m. p. and mixed m. p. 178—179°,* which with ethereal diazomethane gave methyl β-methyl-*cis-trans*-muconate (needles from aqueous methanol), m. p. and mixed m. p. 38·5°.

(c) *The amide ester* (XI). (δ)-Methyl (α)-hydrogen β-methyl-*cis-trans*-muconate (III) (0·8 g.; m. p. 127°) was heated under reflux with thionyl chloride (5 c.c.) for 15 minutes. Excess of reagent was removed under reduced pressure, and the residue added slowly to ammonia solution (2 c.c.; sp. gr. 0·88) at 0°. The precipitate (0·55 g., 69%) was washed with water and crystallised from ethanol yielding prisms, m. p. 141°, of β-*methyl*-cis-trans-*muconic* (α)-*amide* (δ)-*methyl ester* (XI) (Found: C, 56·7; H, 6·7; N, 8·4. $C_8H_{11}O_3N$ requires C, 56·8; H, 6·55; N, 8·3%).

(d) *The amide acid* (XII). Treatment of the foregoing amide ester (XI) (0·3 g.) with methanolic barium hydroxide (4 c.c.; 0·79N) for 30 minutes at room temperature, dilution with water (4 c.c.), and acidification (hydrochloric acid), afforded β-*methyl*-cis-trans-*muconic* (α)-*amide* (δ)-*acid* (XII) (0·15 g., 52%) which crystallised from water as needles, m. p. 210—211° (Found: C, 54·05; H, 6·0; N, 9·3. $C_7H_9O_3N$ requires C, 54·2; H, 5·85; N, 9·0%).

To this amide acid (0·2 g.), suspended in water (5 c.c.) containing a few drops of concentrated hydrochloric acid, 10% aqueous sodium nitrite (2 c.c.) was added during 6 hours with occasional shaking. The resulting crude β-methyl-*cis-trans*-muconic acid (0·125 g., 62%), m. p. 168—172° *, was treated with diazomethane in ether, and the product crystallised from aqueous methanol giving methyl β-methyl-*cis-trans*-muconate (V) as needles, m. p. and mixed m. p. 37—38°.

(e) *The acid amide* (XIII). After (δ)-methyl (α)-hydrogen β-methyl-*cis-trans*-muconate (III) (2 g.) had been kept with aqueous ammonia (10 c.c.; sp. gr. 0·88) for 2 days, the excess of ammonia was

removed under reduced pressure and the solution acidified (hydrochloric acid). *β-Methyl*-cis-trans-*muconic* (α)-*acid* (δ)-*amide* (XIII) (0·9 g., 49%) crystallised slowly, and was recrystallised from methanol giving needles, m. p. 146—147° (Found: C, 54·5; H, 6·1; N, 8·7. $C_7H_9O_3N$ requires C, 54·2; H, 5·85; N, 9·0%).

Reaction of this acid amide (200 mg.), suspended in ether, with an excess of ethereal diazomethane afforded the methyl ester amide (IX) which formed prisms, m. p. 159—160°, from ethanol. A mixture with authentic material had m. p. 162—163°.

Treatment of the acid amide (XIII) (200 mg.), as a fine suspension in water (2 c.c.) containing concentrated hydrochloric acid (several drops), with 10% aqueous sodium nitrite (2 c.c.) during 6 hours at room temperature gave a sparingly soluble acid (90 mg., 45%), m. p. 172—174° * undepressed by β-methyl-*cis-trans*-muconic acid. Reaction of the crude product with ethereal diazomethane, and crystallisation from aqueous methanol yielded methyl β-methyl-*cis-trans*-muconate as needles, m. p. and mixed m. p. 37°.

Lactonisation Experiments.—(a) *Cyclisation of β-methyl*-cis-trans-*muconic acid.* (i) The acid (1 g.) was kept with 75% sulphuric acid (2 c.c.) overnight, and the solution added to crushed ice (40 g.), and extracted with ether for 48 hours. On evaporation of the ether, γ-carboxymethyl-β-methyl-Δ^{α}-butenolide (I) (0·73 g., 73%) was obtained, which crystallised from ethanol–benzene as prisms, m. p. and mixed m. p. 129—130°. (ii) After β-methyl-*cis-trans*-muconic acid (2 g.) had been heated under reflux with water (20 c.c.) containing concentrated hydrochloric acid (several drops) for 12 hours, γ-carboxymethyl-β-methyl-Δ^{α}-butenolide (1·8 g., 90%) was similarly isolated (m. p. and mixed m. p. 127—128°). (iii) By heating β-methyl-*cis-trans*-muconic acid (2 g.) with water (20 c.c.) under reflux for 24 hours, and extracting the solution with ether for 48 hours, the lactonic acid (I) (1·7 g., 85%) was again obtained (m. p. and mixed m. p. 127—128°).

(b) *Lactonisation of* (δ)-*methyl* (α)-*hydrogen β-methyl*-cis-trans-*muconate.* (i) The half-ester (III) (1 g.) was heated under reflux with water (20 c.c.) for 2 hours, and the solution cooled and extracted with ether (2 × 20 c.c.). After being washed with saturated aqueous sodium hydrogen carbonate (20 c.c.), the ether was evaporated and γ-carbomethoxymethyl-β-methyl-Δ^{α}-butenolide (II) (0·9 g., 90%) obtained as an oil, b. p. 175—176°/12 mm. (ii) Distillation of (δ)-methyl (α)-hydrogen β-methyl-*cis-trans*-muconate (III) (2 g.) under reduced pressure also afforded the lactonic ester (II), b. p. 170—173°/12 mm., m. p. and mixed m. p. 34—35°, in 65% yield. Some dark gum remained in the distilling flask.

(c) *Attempts to lactonise* (α)-*methyl* (δ)-*hydrogen β-methyl*-cis-trans-*muconate.* (i) After the half-ester (VIII) (100 mg.) had been heated with water (10 c.c.) under reflux for 48 hours, 90% was recovered directly as long needles (90 mg.), m. p. and mixed m. p. 170—171°. The remainder (10 mg.), m. p. and mixed m. p. 168—169°, was recovered by evaporation of the filtrate. (ii) The half-ester (VIII) (1 g.) when heated at 220°/15 mm. slowly sublimed as prismatic needles (0·7 g., 70%), m. p. 165—167°, and m. p. 165—168° when mixed with the starting material. (iii) The half-ester (VIII) (0·7 g.) was heated at 220° for 2 hours and the pressure then reduced to 15 mm. A sublimate of needles appeared (0·35 g., 50%) which when recrystallised from hot water had m. p. 169—170°, alone and in admixture with the starting material. A brown-coloured resin remained in the distilling flask. (iv) A mixture of the half-ester (VIII) (0·5 g.) and 75% sulphuric acid (10 c.c.) was kept for 24 hours, then poured on ice (45 g.), and the solution extracted with ether for 24 hours to yield γ-carboxymethyl-β-methyl-Δ^{α}-butenolide (0·2 g., 43%) which separated from ethanol–light petroleum (b. p. 40—60°) as prisms, m. p. and mixed m. p. 127—129°.

(d) *Behaviour of the two acid amides.* (i) β-Methyl-*cis-trans*-muconic (α)-acid (δ)-amide (XIII) (0·5 g.) was heated under reflux with water (10 c.c.) for 2 hours, and the solution evaporated to dryness. From ethanol, the amide of γ-carboxymethyl-β-methyl-Δ^{α}-butenolide (XIV) (0·45 g., 90%) formed needles, m. p. 150—151° undepressed by authentic material (described below). (ii) The (α)-amide (δ)-acid (XII) (50 mg.) was recovered unchanged after being heated under reflux with water (5 c.c.) for 3 hours. The only changed material obtained by heating the (α)-amide (δ)-acid (XII) at above the m. p. was a resinous substance.

The Amide of γ-Carboxymethyl-β-methyl-Δ^{α}*-butenolide.*—(i) γ-Carboxymethyl-β-methyl-Δ^{α}-butenolide (I) (5 g.) was heated under reflux with thionyl chloride (20 c.c.). After 30 minutes, excess of the reagent was removed under reduced pressure, and the residue, in dry ether (50 c.c.), was added during 20 minutes, with stirring, to ether (250 c.c.) through which dry ammonia gas was being passed. The solid was dissolved in water (100 c.c.), and the solution extracted with ether for 48 hours to yield the *amide* of γ-carboxymethyl-β-methyl-Δ^{α}-butenolide (XIV) (4·3 g., 96%) which crystallised from ethanol as needles, m. p. 151° (Found: C, 54·3; H, 5·9; N, 9·1. $C_7H_9O_3N$ requires C, 54·2; H, 5·85; N, 9·0%). (ii) A solution of the lactonic ester (II) (1 g.) in methanol–ammonia (sp. gr. 0·88) (10 c.c.; 1 : 1) was kept for 2 days, then evaporated under reduced pressure. From ethanol, the lactonic amide (XIV) formed needles (0·8 g., 80%), m. p. and mixed m. p. 145—148°.

Treatment of the lactonic amide (1 g.) in 10% hydrochloric acid (10 c.c.) with 10% sodium nitrite solution (8 c.c.), added during 6 hours at room temperature, afforded (after constant ether-extraction for 48 hours) γ-carboxymethyl-β-methyl-Δ^{α}-butenolide (I) which crystallised from ethanol as needles (0·25 g., 25%), m. p. and mixed m. p. 126—127°.

Dihydro-β-methylmuconic Acids and Related Lactones.—*trans*-Δ^{β}-Dihydro-β-methylmuconic acid (2-methyl-*trans*-but-2-ene-1 : 4-dicarboxylic acid) (VII) was obtained in 87% yield by amalgam reduction of (δ)-methyl (α)-hydrogen β-methyl-*cis-trans*-muconate (III) (13 g.) in sodium hydroxide solution (80 c.c.; 0·1N), according to Pauly and Will's directions (*loc. cit.*); the dihydro-acid separated from water a needles, m. p. 140—141° (Found: C, 53·25; H, 6·55. Calc. for $C_7H_{10}O_4$: C, 53·1; H, 6·4%).

Reduction of the Δ^{β}-dihydro-acid (450 mg.) with hydrogen and Adams's catalyst (hydrogen uptake: 72·0 c.c. at 18°/755 mm. Calc. for 1 double bond: 68·5 c.c.) afforded β-methyladipic acid, m. p. 95—96° and mixed m. p. 95—97°.

γ-Carboxymethyl-γ-methylbutanolide (XV). *trans*-Δ$^{\beta}$-Dihydro-β-methylmuconic acid (VII) (5·5 g.) was kept with 75% sulphuric acid (60 c.c.) at room temperature for 48 hours. The solution was poured on crushed ice (200 g.) and extracted with ether for 48 hours to yield *γ-carboxymethyl-γ-methylbutanolide* (XV) (4·2 g., 76%) which slowly crystallised, and then formed needles, m. p. 60—63°, from ether–light petroleum (b. p. 40—60°) (Found : C, 53·5; H, 6·4%; equiv., 156·2; hydrolysis-equiv., 78·8. $C_7H_{10}O_4$ requires C, 53·1; H, 6·4%; equivs., 158·1, 79·05)

γ-Carbomethoxymethyl-γ-methylbutanolide (XVI). This *lactone*, b. p. 142°/10 mm., n_D^{15} 1·4573 (Found : C, 55·6; H, 6·9. $C_8H_{12}O_4$ requires C, 55·8; H, 7·0%) was obtained in 73% yield from the preceding lactonic acid (2·5 g.) and ethereal diazomethane

trans-Δ$^{\alpha}$-*Dihydro-β-methylmuconic Acid* (2-*Methyl*-trans-*but*-1-*ene*-1 : 4-*dicarboxylic Acid*) (XVII).—(a) *Preparation.* To the preceding lactonic ester (XVI) (1·6 g.) in methanol (2 c.c.), methanolic sodium methoxide (2·7 c.c.; equivalent to 0·214 g. of sodium) was added, and after 20 minutes the solution was evaporated under reduced pressure and the residue taken up in water (10 c.c.). The solution was acidified (hydrochloric acid) and the resulting mixture extracted with ether (3 × 10 c.c.). Back extraction of the latter with saturated aqueous sodium hydrogen carbonate (2 × 20 c.c.), acidification of the ether-washed aqueous extract, and isolation with ether afforded an oil, presumed to be mainly methyl hydrogen *trans*-Δ$^{\alpha}$-dihydro-β-methylmuconate (1·3 g.) (Found : equiv., 171·2. $C_8H_{12}O_4$ requires equiv., 172·2). Hydrolysis of this half-ester (1 g.) by heating it under reflux with 10% aqueous sodium hydroxide (8 c.c.) for 15 minutes, acidifying the solution and cooling it to 0° for several hours, yielded a crude acid (0·85 g.), m. p. 125—151°. Fractional crystallisation from water and from ethyl acetate–benzene gave trans-Δ$^{\alpha}$-*dihydro-β-methylmuconic acid* (2-*methyl*-trans-*but*-1-*ene*-1 : 4-*dicarboxylic acid*) (XVII) (0·29 g., 31%) as needles, m. p. 158—161° (Found : C, 53·4; H, 6·5. $C_7H_{10}O_4$ requires C, 53·1; H, 6·4%). Hydrolysis of the half-ester (160 mg.) by treatment with 10% aqueous sodium hydroxide (1 c.c.) for 30 minutes at room temperature, and acidification of the solution, gave a similar crude product. Repeated crystallisation (as before) then afforded the Δ$^{\alpha}$-acid, m. p. and mixed m. p. 158—161°.

The acid prepared by Linstead, Lunt, and Weedon, as mentioned earlier, had m. p. 157—160° and a mixture with the preceding Δ$^{\alpha}$-acid had m. p. 158—161°.

(b) *Reduction.* The Δ$^{\alpha}$-acid (XVII) (158 mg.) in ethanol (10 c.c.) was hydrogenated in the presence of Adams's catalyst (hydrogen uptake : 24·5 c.c. at 20°/768 mm. Calc. for 1 double bond : 24·4 c.c.) to yield β-methyladipic acid, m. p. and mixed m. p. 94—95°.

(c) *Oxidation.* To an ice-cold solution of the Δ$^{\alpha}$-acid (300 mg.) in saturated aqueous sodium hydrogen carbonate (10 c.c.), 2% potassium permanganate solution (30·8 c.c.; 3 atoms of O) was added, with stirring, during 2 hours. The manganese dioxide was filtered off and washed with hot water (10 c.c.), and the combined filtrate acidified (hydrochloric acid) and ether-extracted for 24 hours. Evaporation of the ether afforded a mixture of a solid with an oily acid. When crystallised from water, the solid acid (98 mg., 41%) had m. p. 99—100°, undepressed by oxalic acid dihydrate. From the oil (160 mg., 72%) a 2 : 4-dinitrophenylhydrazone and a semicarbazone were prepared, which had m. p.s 204—205° and 184°, respectively, not depressed by the corresponding derivatives of lævulic acid.

γ-Carboxymethyl-β-methylbutanolide (XVIII). The unsaturated lactonic acid (I) (3 g.) in ethanol (20 c.c.) was reduced with hydrogen and Adams's catalyst (hydrogen uptake : 496 c.c. at 20°/755 mm. Calc. for 1 double bond : 483 c.c.) to yield *γ-carboxymethyl-β-methylbutanolide* (2·7 g., 93%) which crystallised from ether–light petroleum (b. p. 40—60°) as stout prisms, m. p. 90—91° (Found : C, 53·4; H, 6·4%; equiv., 157·5; hydrolysis-equiv., 78·6. $C_7H_{10}O_4$ requires C, 53·1; H, 6·4%; equivs., 158·1, 79·05).

γ-Carbomethoxymethyl-β-methylbutanolide (XIX), obtained in 74% yield by treating the preceding lactonic acid (XVIII) (2·7 g.) with ethereal diazomethane, had b. p. 154°/10 mm., n_D^{15} 1·4576 (Found : C, 55·6; H, 7·0. $C_8H_{12}O_4$ requires C, 55·8; H, 7·0%).

trans-Δ$^{\gamma}$-*Dihydro-β-methylmuconic Acid* (3-*Methyl*-trans-*but*-1-*ene*-1 : 4-*dicarboxylic Acid*) (XX).—(a) *Preparation.* The preceding saturated lactonic ester (XIX) (0·4 g.) in methanol (1 c.c.) was treated with methanolic sodium methoxide (1 c.c.; equivalent to 0·08 g. of sodium). After 20 minutes, the solution was diluted with water (12 c.c.), acidified (hydrochloric acid), and extracted with ether (3 × 10 c.c.) to yield an oil which was heated under reflux with 10% aqueous sodium hydroxide (3 c.c.) for 30 minutes. The hydrolysate was acidified (hydrochloric acid) and cooled to 0°. trans-Δ$^{\gamma}$-*Dihydro-β-methylmuconic acid* (3-*methyl*-trans-*but*-1-*ene*-1 : 4-*dicarboxylic acid*) (XX) (0·21 g., 54%) crystallised from water as needles, m. p. 129° (Found : C, 53·3; H, 6·6. $C_7H_{10}O_4$ requires C, 53·1; H, 6·4%).

(b) *Reduction.* Hydrogenation of the Δ$^{\gamma}$-acid (210 mg.) in methanol (10 c.c.) in the presence of Adams's catalyst (hydrogen uptake : 36 c.c. at 20°/764 mm. Calc. for 1 double bond : 33 c.c.) yielded β-methyladipic acid (200 mg.), m. p. and mixed m. p. 95—97°.

(c) *Oxidation.* 2% Aqueous potassium permanganate (37 c.c.; 4 atoms of O) was added during 2 hours to a stirred solution of *trans*-Δ$^{\gamma}$-dihydro-β-methylmuconic acid (270 mg.) in saturated aqueous sodium hydrogen carbonate (5 c.c.). The filtrate from the manganese dioxide was acidified and extracted with ether for 12 hours. Evaporation of the ether gave a sticky solid which was extracted with hot benzene (3 × 10 c.c.). On concentration of the benzene extract, methylsuccinic acid (150 mg., 67%) crystallised as needles, m. p. 106—107° and mixed m. p. 106—108°. The residue from the benzene extraction was taken up in hot water. On concentration and cooling, oxalic acid dihydrate (70 mg., 29%) was obtained, m. p. and mixed m. p. 100—101°.

Peracetic Acid Oxidation of p-*Cresol* (cf. Böeseken, Metz, and Pluim, *loc. cit.*).—A solution of *p*-cresol (35 g.) in 13% peracetic acid (600 g.) was kept for 14 days in the dark, and the crystalline precipitate (3 g., 6%) recrystallised from ethanol to yield β-methyl-*cis-trans*-muconic acid as micro-needles, m. p. and mixed m. p. 178—179° * (Found : C, 53·8; H, 5·2. Calc. for $C_7H_8O_4$: C, 53·9; H, 5·2%). The

product was further characterised by reaction with ethereal diazomethane to give methyl β-methyl-*cis-trans*-muconate (needles from aqueous methanol), m. p. and mixed m. p. 38—38·5°.

The acetic acid filtrate was concentrated to a small bulk under reduced pressure, whereupon γ-carboxymethyl-β-methyl-Δ^{α}-butenolide (I) (29 g., 56%) separated; recrystallised from ethanol–benzene, the lactonic acid had m. p. and mixed m. p. 129—130° (Found: C, 53·9; H, 5·3. Calc. for $C_7H_8O_4$: C, 53·9; H, 5·2%). Esterification of the lactonic acid (14 g.) with boiling 0·3% methanolic hydrogen chloride (50 c.c.) for 2 hours gave γ-carbomethoxymethyl-β-methyl-Δ^{α}-butenolide (II) (11 g., 73%), b. p. 179°/11 mm., m. p. and mixed m. p. 35°.

Peracetic Acid Oxidation of Homocatechol.—Homocatechol (10 g.) was added slowly, with cooling, to 13% peracetic acid (250 c.c.), and the solution kept for 14 days in the dark. β-Methyl-*cis-trans*-muconic acid (50 mg., 4%) was precipitated, and on crystallisation from ethanol formed micro-needles, m. p. and mixed m. p. 178—179°.* Treatment with ethereal diazomethane yielded methyl β-methyl-*cis-trans*-muconate (needles from aqueous methanol), m. p. and mixed m. p. 38—38·5°. Concentration of the acetic acid filtrate gave γ-carboxymethyl-β-methyl-Δ^{α}-butenolide (I) (7·8 g., 61%), m. p. and mixed m. p. 129—130°.

β-*Methyl*-trans-trans-*muconic Acid.*—(a) *Preparation.* To a mixture of 50% nitric acid (402 g.) and ammonium vanadate (0·2 g.) at 95°, 4-methyl*cyclo*hexanol (100 g.) was added at such a rate that the temperature kept at 55—60°. Next day, β-methyladipic acid (90 g., 65%), m. p. 96—98°, was collected (cf. D.R.P. 473,960; cf. also the preparation of the lower homologue, *Org. Synth.*, Coll. Vol. II, 18). The acid (65 g.) was cautiously treated with thionyl chloride (120 g.), the mixture heated under reflux on the steam-bath to complete the reaction, and excess of thionyl chloride then distilled under reduced pressure. To the crude acid chloride, iodine (a few crystals) was added, and, with continued heating on the steam-bath, dry bromine (150 g.) was run in during 12 hours. After being heated for 2 hours longer, the reaction product was cooled and slowly added to ice-cooled anhydrous ethanol (360 c.c.). The solution was poured into water (500 c.c.), the oil separated, and the aqueous layer extracted with ether (2 × 250 c.c.). The oil and ethereal extracts were combined and washed with 5% aqueous sodium carbonate (250 c.c.), 5% aqueous sodium hydrogen sulphite (250 c.c.), and water (250 c.c.). After the solution had been dried (Na_2SO_4), the ether was distilled, and the crude ethyl αδ-dibromo-β-methyladipate (138 g., 91%) added slowly to a boiling solution of potassium hydroxide (360 g.) in methanol (600 c.c.), which was heated for 1 hour longer and then cooled. The potassium salts were collected, dissolved in water (charcoal), and the solution acidified (Congo-red) with concentrated hydrochloric acid. β-Methyl-*trans-trans*-muconic acid (XXI) (5·5 g., 8·5%) slowly separated, and from hot water crystallised as needles, m. p. 229—231° (Found: C, 54·0; H, 5·2%; equiv., 77·2. Calc. for $C_7H_8O_4$: C, 53·9; H, 5·2%; equiv., 78·0) (cf. the preparation of the lower homologue due to Ingold, *J.*, 1921, **119**, 951).

(b) *Reduction.* The *trans-trans*-acid (500 mg.) with hydrogen and Adams's catalyst (hydrogen uptake: 172·5 c.c. at 25°/754 mm. Calc. for 2 double bonds: 160·5 c.c.) gave β-methyladipic acid, m. p. and mixed m. p. 96—98°.

Reduction of the *trans-trans*-acid (100 mg.) with 2·5% sodium amalgam (as for the *cis-trans*-isomer) gave *trans*-Δ^{β}-dihydro-β-methylmuconic acid, m. p. 139—140°.

(c) *Methyl ester.* The *trans-trans*-acid (1 g.) with ethereal diazomethane yielded methyl β-methyl-*trans-trans*-muconate (1 g.) which crystallised from aqueous methanol, and from light petroleum (b. p. 40—60°), as needles, m. p. 56° (Found: C, 58·9; H, 6·6. Calc. for $C_9H_{12}O_4$: C, 58·7; H, 6·6%).

The ester (0·3 g.) was dissolved in 10% aqueous sodium hydroxide (25 c.c.) with the aid of methanol. After 1 hour at room temperature, the solution was acidified (hydrochloric acid) (Congo-red), and the precipitate crystallised from water. β-Methyl-*trans-trans*-muconic acid (0·18 g., 41%) was obtained, m. p. and mixed m. p. 230°.

(d) *Amide.* The preceding ester (900 mg.) was kept with methanol–aqueous ammonia (sp. gr. 0·88) (15 c.c., 1 : 1) for 7 days. β-*Methyl*-trans-trans-*muconamide* (220 mg., 29%) separated from water as stout needles, m. p. 230—231° (Found: C, 54·5; H, 6·6; N, 17·9. $C_7H_{10}O_2N_2$ requires C, 54·5; H, 6·5; N, 18·2%).

The amide (300 mg.) was suspended in 30% hydrochloric acid (3 c.c.) and treated with 20% aqueous sodium nitrite (1 c.c.) during 3 hours. The solid was recrystallised from hot water yielding β-methyl-*trans-trans*-muconic acid (120 mg., 40%), m. p. and mixed m. p. 230—231°, which with ethereal diazomethane afforded the dimethyl ester, m. p. and mixed m. p. 53—54°.

(e) *Attempted lactonisation.* When the *trans-trans*-acid (0·5 g.) was kept with 80% sulphuric acid (5 c.c.) for 48 hours, the solution poured on crushed ice (10 g.), and the precipitate crystallised from hot water, β-methyl-*trans-trans*-muconic acid (0·45 g., 90%) was recovered, m. p. and mixed m. p. 230°. Extraction of the filtrate with ether for 24 hours yielded only a small quantity of *trans-trans*-acid, m. p. 225—227° undepressed by authentic material.

After being heated under reflux with 10% hydrochloric acid (10 c.c.) for 24 hours, β-methyl-*trans-trans*-muconic acid (0·5 g.) was recovered (0·46 g., 92%), m. p. and mixed m. p. 229—230°.

Isomerisation Experiments.—(a) *Conversion of* β-*methyl*-cis-trans- *into* -trans-trans-*muconic acid.* (i) The *cis-trans*-acid (1 g.) was heated under reflux with 20% sodium hydroxide (10 c.c.) for 4 hours. On acidification of the solution, β-methyl-*trans-trans*-muconic acid (0·7 g., 70%) was obtained, m. p. and mixed m. p. 223—227°, which on reaction with ethereal diazomethane gave fine needles (from aqueous methanol) of methyl β-methyl-*trans-trans*-muconate, m. p. and mixed m. p. 55—56°. (ii) The *cis-trans*-acid (1 g.) was heated at 100° for 3 hours with 48% aqueous hydrogen bromide (10 c.c.), and the solution evaporated under reduced pressure. Recrystallisation of the residue from water gave β-methyl-*trans-trans*-muconic acid (0·45 g., 45%), m. p. and mixed m. p. 228—229°, additionally characterised by

reaction with ethereal diazomethane to yield methyl β-methyl-*trans-trans*-muconate, m. p. and mixed m. p. 55—56°.

(b) *Stereochemical stability of β-methyl*-cis-trans-*muconic acid.* (i) A solution of the *cis-trans*-acid (1 g.) in ethanol (10 c.c.) containing iodine (one small crystal) was exposed to ultra-violet light (from a Hanovia lamp) for 1 hour, then evaporated under reduced pressure. From ethanol, only β-methyl-*cis-trans*-muconic acid was obtained, m. p. and mixed m. p. 178—179° *, which with diazomethane in ether yielded methyl β-methyl-*cis-trans*-muconate, m. p. and mixed m. p. 38°. (ii) The *cis-trans*-acid was recovered after being kept in methanol containing sulphur dioxide and a trace of hydrogen chloride.

(c) *Stereochemical stability* of trans-trans-*β-methylmuconic acid.* (i) The *trans-trans*-acid (1 g.) in ethanol (10 c.c.) containing a trace of iodine underwent no change on being irradiated with ultra-violet light as above. The solution was evaporated and the residue treated with ethereal diazomethane. Methyl β-methyl-*trans-trans*-muconate was obtained, m. p. and mixed m. p. 56°, after being crystallised from aqueous methanol. (ii) The *trans-trans*-acid (1 g.) was heated under reflux with 30% aqueous sodium hydroxide (20 c.c.) for 4 hours, and the solution acidified (hydrochloric acid). β-Methyl-*trans-trans*-muconic acid (0·62 g., 62%) was recovered, m. p. and mixed m. p. 230—231°. The filtrate was heated under reflux for 3 hours (in order to lactonise any *cis-trans*-acid which might have been produced) and the solution extracted with ether for 24 hours. Evaporation of the ether gave a residue, m. p. 221—225° not depressed by β-methyl-*trans-trans*-muconic acid.

We thank Dr. E. A. Braude for the light-absorption data, and the Ministry of Education for a grant (to P. S.).

Imperial College of Science and Technology,
South Kensington, London, S.W.7.

[*Received, July 17th*, 1951.]