182. *Polyene Acids. Part IV.* The Three Geometrical Isomers of αα′-Dimethylmuconic Acid.*

By J. A. Elvidge, R. P. Linstead, and John F. Smith.

Methods described in previous papers of this series have been applied to the hitherto unknown αα′-dimethylmuconic acid which has been prepared in all three possible geometrical forms. Peracetic acid oxidation of *p*-xylenol yields the *cis-cis*-isomer (II), m. p. 210°. This is inverted by boiling alkali to the *trans-trans*-acid (VII), m. p. 322°, and isomerised by sulphuric acid to the lactonic acid (III). Treatment of the derived lactonic methyl ester (IV) with sodium methoxide affords a half methyl ester (V), m. p. 115°, of *cis-trans*-αα′-dimethylmuconic acid (VI) which has m. p. 185°. The high-melting *trans-trans*-acid has also been prepared from αα′-dibromo- and αα′-dihydroxy-αα′-dimethyladipic acids, and by hydrolysis of αα′-dimethylmucononitrile, obtained in poor yield by dehydration of acetonylacetone biscyanohydrin. On catalytic reduction, each of the three stereoisomeric αα′-dimethylmuconic acids affords a mixture of the known *meso*- and racemic forms of αα′-dimethyladipic acid.

αα′-DIMETHYLMUCONIC ACID has not been previously reported in the literature. An examination of scale models indicates that all three of the theoretically possible geometrical isomeric forms (*cis-cis*; *cis-trans*; *trans-trans*) should be capable of existence, as in none of them is there any steric hindrance in the planar *s-trans*-configuration. We have accordingly investigated the acid, partly in extension of the investigation of stereo-isomeric polyene acids reported in earlier papers of this series, and partly as the geometrical forms were of interest for studies of the stereochemistry of hydrogenation. The preparative procedures and the methods for the diagnosis of configuration were extensions of those previously used for the muconic and β-methylmuconic acids (*J.*, 1950, 2235; 1951, 3386).

The cis-cis-*Acid.*—Oxidation of *p*-xylenol (I) with peracetic acid gave, in poor yield, αα′-dimethyl-*cis-cis*-muconic acid (II) with m. p. 208—210°, which was converted by diazomethane into the dimethyl ester, m. p. 70°.

The cis-trans-*Acid.*—With cold 80% sulphuric acid αα′-dimethyl-*cis-cis*-muconic acid (II) was isomerised to the unsaturated lactonic acid (III), m. p. 127°, which afforded a liquid methyl ester (IV). Proof of the structure of the lactone is given below. Treatment of this lactonic methyl ester (IV) with methanolic sodium methoxide afforded, as had been expected, an open-chain isomeride, the diene acid ester (V), hydrolysis of which

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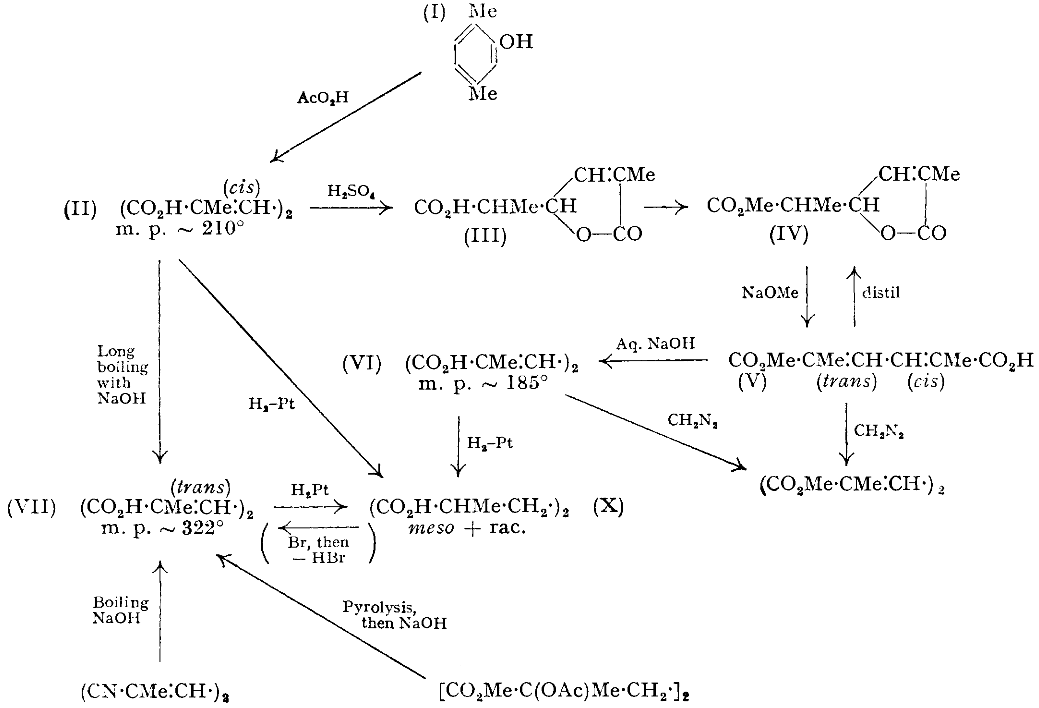
* Part III, *J.*, 1951, 3398.

provided αα′-dimethyl-*cis-trans*-muconic acid (VI) with m. p. 182—185°. This acid and the half-ester (V) both yielded the same dimethyl ester, m. p. 26—27°, showing that no change of geometrical configuration had occurred during the hydrolysis stage (V) ⟶ (VI). When distilled under reduced pressure, the half-ester (V) readily relactonised to (IV).

The trans-trans-*Acid.*—Inversion of αα′-dimethyl-*cis-cis*-muconic acid (II) by the prolonged action of boiling sodium hydroxide solution yielded a mixture from which the *trans-trans*-acid (VII), m. p. 320—322°, was separated : its dimethyl ester had m. p. 99—100°. A more satisfactory route to the *trans-trans*-acid (VII) was the vapour-phase pyrolysis at 650° of methyl αα′-diacetoxy-αα′dimethyladipate (VIII), followed by alkaline hydrolysis of the neutral fraction. The diacetoxy-ester (VIII) was prepared from acetonylacetone biscyanohydrin (XIV) as outlined later. Dehydration of this biscyanohydrin afforded in poor yield the diene-dinitrile (IX), alkali hydrolysis of which also provided αα′-dimethyl-*trans-trans*-muconic acid (VII). Less satisfactory was the dehydrobromination with potassium hydroxide of αα′-dibromo-αα′-dimethyladipic ester obtained from mixed *meso*- and racemic αα′-dimethyladipic acids (X) : a high-melting product was given which from its properties was essentially αα′-dimethyl-*trans-trans*-muconic acid, but repeated crystallisation failed to raise the melting point above 306—308°.



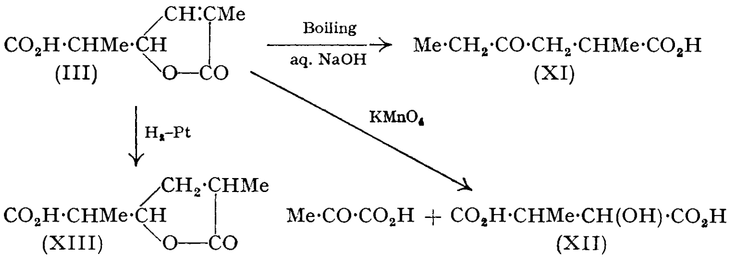
Configurations.—The configurations of the three acids (II), (VI), and (VII) followed unambiguously from the methods of preparation. The high-melting, sparingly soluble isomer (VII), obtained by elimination processes from disubstituted αα′-dimethyladipic acids, was expected to have an all-*trans*-configuration. This isomer could not be lactonised. The acid (II) obtained by fission of aromatic material was most likely the *cis-cis*-isomer. It lactonised readily to (III). Moreover, it could be isomerised to the high-melting acid (VII) directly and to a third isomer (VI) *via* its lactone (III). Being derived *via* the elimination reaction (IV) ⟶ (V), this third isomeric αα′-dimethylmuconic acid (VI) was expected to have the *cis-trans*-configuration. That the configuration was *cis* about the double bond αβ to the unesterified carboxyl in its half ester (V) was shown by the ready re-lactonisation to (IV).

The αγ-diene structures of the αα′-dimethylmuconic acids were confirmed by their behaviour on reduction, and by light-absorption measurements. On catalytic hydrogenation, each of the three acids (II), (VI), and (VII) took up 2 mols. of hydrogen and afforded a mixture of *meso-* and racemic αα′-dimethyladipic acids (X) from which the *meso*-acid was separated in a pure state and compared with authentic material. The ultra-violet light absorption properties of the αα′-dimethylmuconic acids and their methyl esters are recorded in the Table. The shift of the main absorption band to 2800 Å, from 2580 Å in the parent muconic acids (*J.*, 1950, 2235), can be ascribed to hyperconjugation involving the two α-methyl groups. The positions of the main absorption maxima are practically the same for each of the isomeric αα′-dimethylmuconic acids and their esters, whilst there is a small increment in the intensity of absorption for each *cis* ⟶ *trans* inversion. These characteristics, which may be correlated with extended *s-trans*-configurations for all of the geometrical isomers, resemble those of the muconic and β-methylmuconic acids (*J.*, 1950, 2235; 1951, 3386).

Intermediates.—The product, m. p. 127°, of the sulphuric isomerisation of αα′-dimethyl-*cis-cis*-muconic acid was assigned the Δ^α^-butenolide structure (III) on the following evidence (cf. Elvidge, Linstead, Orkin, Sims, Baer, and Pattison, *J.*, 1950, 2228). The neutralisation and saponification equivalents indicated that the compound was a monobasic lactonic acid. The presence of the 5-membered unsaturated lactone ring was shown by the hydrolysis with boiling alkali to αδ-dimethylævulic acid (XI), isolated as the known semicarbazone. The Δ^{α}-position of the double bond followed from the oxidation with permanganate to pyruvic acid and β-methylmalic acid (XII), which were respectively isolated as the 2 : 4-dinitrophenylhydrazone and bisphenylhydrazide. Confirmation of the Δ^{α}-structure (III) was provided by the light absorption (end absorption only), by esterification with methanolic hydrogen chloride, which proceeded without ring-fission, to give (IV), and by hydrogenation to the saturated lactonic acid (XIII). As expected on the basis of one-sided addition of hydrogen, this reduction product (XIII) seemed to be a single racemate.

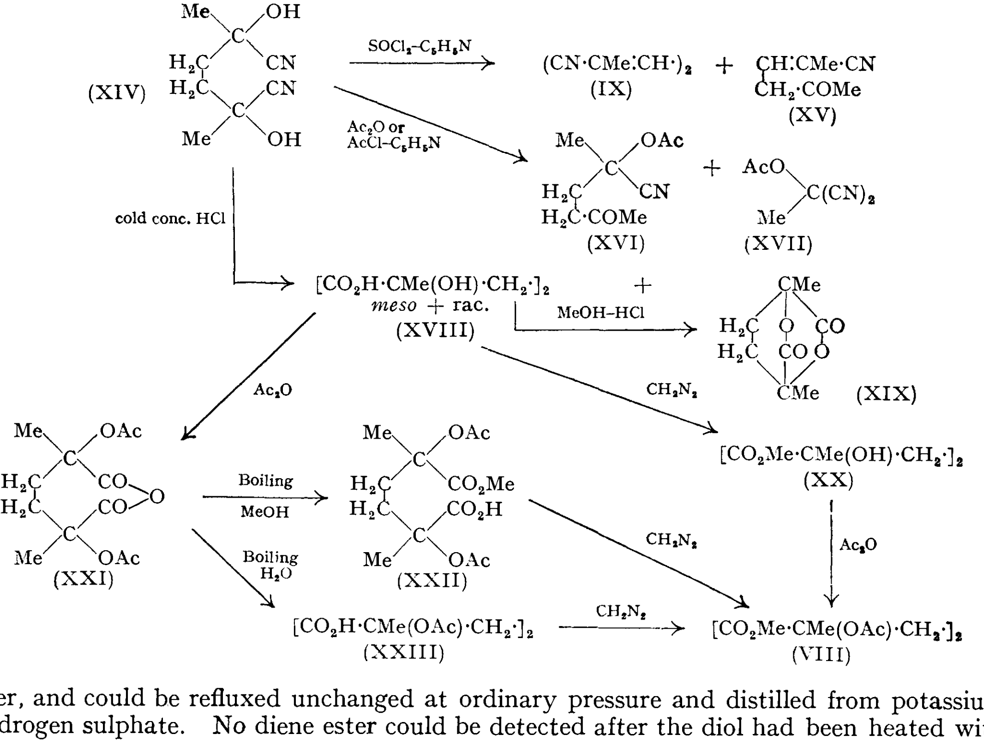
Compound		$\lambda_{max.}$, Å	ε	Solvent
$CO_2H{\cdot}CMe{:}CH{\cdot}CH{:}CMe{\cdot}CO_2H$	*cis-cis*	2700 2810	20 400 20 400	H_2O
	cis-trans	2690 2800	24 000 25 500	EtOH
	trans-trans	2820	31 450	MeOH
$CO_2Me{\cdot}CMe{:}CH{\cdot}CH{:}CMe{\cdot}CO_2Me$	*cis-cis*	2800	24 750	MeOH
	cis-trans	2800	31 600	MeOH
	trans-trans	2820	33 300	MeOH
CN·CMe:CH·CH:CMe·CN		2680 2760 *	27 700 26 400	MeOH
		2250	7 100	EtOH

* Inflection.



Acetonylacetone biscyanohydrin (XIV), utilised for the preparation of (IX) and (VIII), was prepared by the action of liquid hydrogen cyanide on acetonylacetone, and was not stable enough to be purified by distillation or recrystallisation. The dehydration of the biscyanohydrin to the αα′-dimethylmucononitrile (IX) was effected with thionyl chloride in dioxan–pyridine. The reaction proceeded in very low yield, much resin was formed, and the dinitrile (IX) was accompanied by a ketonic product. The analysis of the derived 2 : 4-dinitrophenylsemicarbazone indicated that the ketone was C_7H_9ON; and therefore the structure (XV) seems most likely. Treatment of acetonylacetone biscyanohydrin (XIV) with acetic anhydride alone, or with acetyl chloride in pyridine, gave the related acetoxy-ketone (XVI), isolated as the 2 : 4-dinitrophenylhydrazone, together with α-acetoxy-α-methylmalononitrile (XVII), m. p. 67—68°. The last is known to arise from the action of hydrogen cyanide on acetic anhydride (Nef, *Annalen*, 1895, **287**, 265). It is apparent from these results that acetonylacetone biscyanohydrin very readily dismutates with loss of hydrogen cyanide and that the monocyanohydrin thus produced is sufficiently stable to undergo dehydration [to (XV)] and acetylation [to (XVI)].

Hydrolysis of the biscyanohydrin (XIV) with cold concentrated hydrochloric acid proceeded normally to give in moderate yield a mixture of *meso*- and racemic αα′-dihydroxy-αα′-dimethyladipic acids (XVIII) (not separated), together with some of the dilactone (XIX) (Zelinsky and Isajew, *Ber.*, 1896, **29**, 819; Fittig, *Annalen*, 1907, **353**, 1). Attempted esterification of the acids (XVIII) with methanolic hydrogen chloride afforded only the dilactone (XIX), whilst reaction with diazomethane was unsatisfactory in that the acid was sparingly soluble and the necessarily prolonged treatment led to a product difficult to purify. Nevertheless, sufficient methyl αα′-dihydroxy-αα′-dimethyladipate (XX) was obtained for dehydration experiments. The dihydroxy-ester was extremely stable, however, and could be refluxed unchanged at ordinary pressure and distilled from potassium hydrogen sulphate. No diene ester could be detected after the diol had been heated with phosphoric oxide or with boric acid. Attention was therefore turned to the diacetoxy-derivative (VIII), for which a route alternative to the direct acetylation of the dihydroxy-ester (XX) was desirable.



The mixed αα′-dihydroxy-αα′-dimethyladipic acids (XVIII) were heated with acetic anhydride, and the product subjected to short-path vacuum-distillation. The diacetoxy-anhydride (XXI) was thus obtained in good yield. It reacted only slowly with boiling methanol to give the half methyl ester (XXII), however, and a better route to the diacetoxy-diester (VIII) than (XXI) $\xrightarrow{\text{MeOH}}$ (XXII) $\xrightarrow{CH_2N_2}$ (VIII) was the hydrolysis of the anhydride (XXI) with boiling water to the αα'-diacetoxy-acid (XXIII) followed by esterification with diazomethane. Vapour-phase pyrolysis of the diacetoxy-diester (VIII) thus prepared, followed by hydrolysis of the pyrolysate, then yielded αα'-dimethyl-*trans-trans*-muconic acid, as already mentioned. The mode of formation and stability of the anhydride (XXI) are in agreement with the findings of Adams and Anderson (*J. Amer. Chem. Soc.*, 1951, **73**, 136) who studied the action of acetic anhydride on some ααα'α'-tetramethyl-substituted dibasic acids.

EXPERIMENTAL

*αα'-Dimethyl-*cis-cis*-muconic Acid.*—A solution of *p*-xylenol (90 g.) in 12·7% peracetic acid (1·1 l.) was kept at 0° for several hours, then at room temperature for 7 days. The precipitated *αα'-dimethyl-*cis-cis*-muconic acid* (14 g.) was washed with acetic acid and recrystallised from ethanol; it then had m. p. 208—210° (prismatic needles) (Found: C, 56·7; H, 6·2%; equiv., 85·3. $C_8H_{10}O_4$ requires C, 56·5; H, 5·9%; equiv., 85·1). Similar oxidation of 10 g. of *p*-xylenol afforded only 0·7 g. of diene acid, and from the filtrate, by evaporation under reduced pressure, yellow *p*-xylo-2 : 5-quinone (5 g.) was isolated, m. p. 120—121° (lit., m. p. 125°) (Found: C, 70·7; H, 5·59. Calc. for $C_8H_8O_2$: C, 70·6; H, 5·9%).

*Methyl αα'-dimethyl-*cis-cis*-muconate*, prepared from the foregoing acid by shaking it with ethereal diazomethane, crystallised from aqueous ethanol as laths, m. p. 69—70° (Found: C, 60·3; H, 7·1. $C_{10}H_{14}O_4$ requires C, 60·6; H, 7·1%).

γ-(1-Carboxyethyl)-α-methyl-Δ$^{\alpha}$-butenolide (*2 : 4-Lactone of 4-Hydroxyhex-2-ene-2 : 5-dicarboxylic Acid*) (III).—(a) *Preparation.* Dimethyl-*cis-cis*-muconic acid (3 g.) was shaken with cold 80% sulphuric acid (30 c.c.), and after 24 hours the solution was poured on ice, and the bulk of the acid neutralised with ammonia. The solution (acid to Congo-red) was extracted with ether overnight, the extract evaporated, and the residue (2·9 g.) crystallised from ether by cooling to −40°. The *lactonic acid* (III) (2 g.) formed long needles, m. p. 126—127°, from water (Found: C, 56·5; H, 6·0%; equiv., 169; hydrolysis equiv., 77·5. $C_8H_{10}O_4$ requires C, 56·5; H, 5·9%; equivs., 170·2, 85·1).

(b) *Action of alkali.* The lactonic acid (III) (0·5 g.) was heated under reflux with aqueous sodium hydroxide (25 c.c.; 10%) for 30 minutes. The solution was cooled, acidified (to Congo-red), treated with semicarbazide hydrochloride (0·8 g.) and saturated aqueous sodium acetate (5 c.c.), and kept overnight. The precipitated semicarbazone of αδ-dimethyl-lævulic acid (0·15 g.) was recrystallised from methanol and had m. p. 157° (lit., m. p. 153°) (Found: N, 21·3. Calc. for $C_8H_{15}O_3N_3$: N, 20·9%).

(c) *Oxidation.* To an ice-cooled, stirred solution of the lactonic acid (III) (1 g.) in water (100 c.c.), potassium permanganate (1·24 g.) in water (200 c.c.) was slowly added. The filtrate from the manganese dioxide was acidified with sulphuric acid and extracted with ether overnight. Evaporation of the extract left an oil, a portion of which with Brady's reagent afforded the 2 : 4-dinitrophenylhydrazone of pyruvic acid (recrystallised from methanol), m. p. and mixed m. p. 213—214°. The remainder of the oil was kept at 80°/15 mm. to remove pyruvic acid, and the residue was then treated with ethereal diazomethane. The solution was evaporated under reduced pressure and the residue heated with an excess of phenylhydrazine under reflux for 3 hours. The excess of the reagent was removed at 120°/15 mm. and the residue triturated with ether to give a white solid, which had m. p. 231—232° (from a bath at 220°) alone and when mixed with β-methylmalic bisphenylhydrazide, and which gave a purple colour when treated in concentrated sulphuric acid solution with ferric chloride (Wislicenus, *Ber.*, 1892, **25**, 196). Authentic β-methylmalic bisphenylhydrazide was prepared similarly from phenylhydrazine and ethyl β-methylmalate. The latter ester (17 g.), b. p. 97°/1 mm., n_D^{26} 1·4321, was obtained by hydrogenation (in ethanol over Adams's catalyst) of 20 g. of ethyl α-oxalopropionate, b. p. 83°/1·5 mm., n_D^{25} 1·4280, prepared from ethyl oxalate and ethyl propionate (*Org. Synth.*, Coll. Vol. II, p. 272).

(d) *Hydrogenation.* Absorption by the lactonic acid (III) (0·5 g.) in methanol (20 c.c.) over Adams's catalyst (100 mg.) was complete in 30 minutes (uptake: 2·4 atoms of H). Filtration and evaporation afforded *γ-(1-carboxyethyl)-α-methylbutanolide* (2 : 4-*lactone* of 4-hydroxyhexane-2 : 5-dicarboxylic acid) (XIII), which formed small prisms, m. p. 105—106°, from ether–light petroleum (b. p. 40—60°) (Found: C, 56·15; H, 7·25%; equiv., 179; hydrolysis equiv., 86·5. $C_8H_{12}O_4$ requires C, 55·8; H, 7·0%; equivs., 172·2, 86·1).

(e) *Esterification.* The unsaturated lactonic acid (III) (1·4 g.) was heated with methanol containing 0·3% of hydrogen chloride for 1 hour under reflux, and by distillation, finally at 150—160° (bath-temp.)/20 mm., γ-(1-*carbomethoxyethyl*)-α-*methyl*-Δ^{α}-*butenolide* (2 : 4-*lactone* of 5-carbomethoxy-4-hydroxyhex-2-ene-2-carboxylic acid) (IV) was obtained: it had n_D^{20} 1·4670, solidified at −40°, and had m. p. *ca.* −20° (Found: C, 58·9; H, 6·8. $C_9H_{12}O_4$ requires C, 58·7; H, 6·5%).

Methyl Hydrogen αα'-*Dimethyl*-trans-cis-*muconate.*—(a) *Preparation.* To the preceding lactonic ester (IV) (1·3 g.) in methanol (15 c.c.), methanolic sodium methoxide (2·88 c.c.; 2·54N) was added, and after 15 minutes the solution was evaporated under reduced pressure. Water (10 c.c.) was added and the solution at once acidified with hydrochloric acid, whereupon *methyl hydrogen* αα'-*dimethyl*-trans-cis-*muconate* (0·76 g.) separated: it crystallised from benzene with m. p. 114—115° (Found: C, 58·8; H, 6·7%; equiv., 182; hydrolysis equiv., 90. $C_9H_{12}O_4$ requires C, 58·7; H, 6·5%; equivs., 184·2, 92·1).

(b) *Lactonisation.* When the half ester (0·63 g.) was heated at 160°/18 mm., a liquid distillate (0·57 g.) was collected, which on cooling deposited a few crystals of unchanged starting material, m. p. and mixed m. p. 111—113°. The oil was taken up in ether, the solution washed with aqueous sodium hydrogen carbonate and water, dried (Na_2SO_4), and evaporated, and the residue distilled to yield the Δ^{α}-butenolide (IV) (0·14 g.), n_D^{20} 1·4680.

αα'-*Dimethyl*-cis-trans-*muconic Acid.*—The lactonic ester (IV) (1·3 g.) was treated with methanolic sodium methoxide as described above, the solution evaporated under reduced pressure, and the crude diene half ester warmed with aqueous sodium hydroxide (10 c.c.; N) on the steam-bath for 1 hour. Acidification of the cooled solution afforded αα'-*dimethyl*-cis-trans-*muconic acid* (0·95 g., 86%), m. p. 175—177°, which after repeated crystallisation from water and from ethanol had m. p. 182—185° (prismatic needles) (Found: C, 56·5; H, 5·9%; equiv., 88. $C_8H_{10}O_4$ requires C, 56·5; H, 5·9%; equiv., 85·1).

Methyl αα'-*Dimethyl*-cis-trans-*muconate*, b. p. *ca.* 140°/25 mm., m. p. 26—27°, was obtained by shaking the preceding acid with ethereal diazomethane (Found: C, 60·6; H, 7·3. $C_{10}H_{14}O_4$ requires C, 60·6; H, 7·1%). Treatment of methyl hydrogen αα'-dimethyl-*trans*-*cis*-muconate with ethereal diazomethane, and evaporation of the solution, afforded an identical solid ester.

Acetonylacetone Biscyanohydrin.—(a) *Preparation.* Acetonylacetone (25 g.), containing a few drops of concentrated potassium hydroxide solution, was stirred at 0° for 24 hours with liquid hydrogen cyanide (50 c.c.). Removal of the excess of the latter by passage of nitrogen for 3 hours afforded the biscyanohydrin as a labile solid.

(b) *Dehydration with thionyl chloride.* The biscyanohydrin was dissolved in dry dioxan, pyridine (200 c.c.) was added, and then with ice-cooling and stirring thionyl chloride (60 c.c.) was run in during 4 hours. After a further 4 hours, the cooling-bath was removed, and 24 hours later the mixture was poured into water. On shaking of the mixture with ether, some dark solid separated. The mixture was filtered through kieselguhr and the filtrate extracted with ether. The ethereal layer was separated, washed with dilute sulphuric acid and water, dried (Na_2SO_4), and evaporated. Distillation of the residue at 60—120°/0·5 mm. afforded a mixture of a liquid with some solid (0·8 g.), m. p. 134—138° raised to 141—145° by crystallisation from ethanol. A portion of the solid (100 mg.) in benzene was chromatographed on alumina (10 g.). From the first fractions, αα'-*dimethylmucononitrile* (IX) was isolated as prisms, m. p. 146—147° (Found: C, 72·7; H, 6·5; N, 20·9. $C_8H_8N_2$ requires C, 72·7; H, 6·1; N, 21·2%). Repeated fractionation of the liquid distillate gave an oil, b. p. 50—56°/0·5 mm., n_D^{21} 1·4578—1·4582, $E_{1\,\text{cm.}}^{1\%}$ 100 at 2300 Å., which afforded a 2 : 4-*dinitrophenylsemicarbazone*, m. p. 212—214°, from ethyl acetate (Found: N, 24·5. $C_{14}H_{14}O_5N_6$ requires N, 24·3%).

(c) *Action of acetic anhydride.* The biscyanohydrin from 25 g. of acetonylacetone was heated under reflux with an excess of acetic anhydride for 2 hours, the solution was poured into water, and the mixture warmed to decompose unchanged anhydride. The cooled solution was extracted with ether, and the extract was washed with aqueous sodium carbonate and water, dried (Na_2SO_4), and evaporated. Distillation of the residue at 28 mm. gave two main fractions, b. p. 90—110° and 110—140°. The first fraction solidified, was crystallised from dilute ethanol, and identified as α-acetoxy-α-methylmalononitrile (XVII), m. p. 67—68° (Found: C, 52·0; H, 4·6; N, 19·8. Calc. for $C_6H_6O_2N_2$: C, 52·1; H, 4·4; N, 20·3%). Nef (*loc. cit.*) recorded m. p. 70°. The second fraction had b. p. 167—168°/20 mm. on refractionation, and gave a 2 : 4-*dinitrophenylhydrazone* which crystallised from methanol with m. p. 145·5—146·5° (Found: N, 19·2; 19·5. $C_{15}H_{17}O_6N_5$ requires N, 19·3%).

(d) *Hydrolysis to* (XVIII). The biscyanohydrin from 25 g. of acetonylacetone was stirred with ice-cold concentrated hydrochloric acid (70 c.c.) for 24 hours. The mixture was then heated on the steam-bath for 2 hours, cooled in ice, and filtered. From water (charcoal), the mixture of *meso-* and racemic αα'-dihydroxy-αα'-dimethyladipic acids (XVIII) separated with m. p. 203—205° (decomp.) (Found : C, 46·4; H, 6·7. Calc. for $C_8H_{14}O_6$: C, 46·6; H, 6·8%). The mother-liquors from the crude acid were evaporated to dryness and the residue extracted with ethanol. Evaporation of the ethanol and crystallisation of the solid from water afforded small prisms of the dilactone (XIX), m. p. 95—96° (Found : C, 56·7; H, 6·1. Calc. for $C_8H_{10}O_4$: C, 56·5; H, 5·9%). Fittig (*loc. cit.*) gives the same m. p. The dilactone (XIX), m. p. 91—92° and mixed m. p. 93—94°, was also obtained when the dihydroxy-dimethyladipic acid (XVIII) was heated under reflux with 5% methanolic hydrogen chloride for 2 hours. After treatment of the dilactone with aqueous sodium hydroxide, or with methanolic sodium methoxide, only αα'-dihydroxy-αα'-dimethyladipic acid was isolated, m. p. and mixed m. p. 203—204° (decomp.).

Methyl αα'-Dihydroxy-αα'-dimethyladipate.—Treatment of the acid (XVIII) with ethereal diazomethane for 2 hours, filtration, and evaporation gave the *methyl* ester (XX) which formed prisms, m. p. 111—112°, from water (Found : C, 51·6; H, 7·8. $C_{10}H_{18}O_6$ requires C, 51·3; H, 7·7%).

Attempts to Dehydrate the Hydroxy-ester (XX).—(i) Methyl αα'-dihydroxy-αα'-dimethyladipate was unchanged (m. p. and mixed m. p.) after being boiled for 5 minutes and then distilled at ordinary pressure. (ii) An intimate mixture of the hydroxy-ester (0·5 g.) and potassium hydrogen sulphate (0·1 g.) was kept at 120° for 30 minutes and at 160° for a further 30 minutes. A solution of the product in water did not rapidly decolorise dilute aqueous potassium permanganate. (The αα'-dimethylmuconic acids are oxidised at once). Neither was any unsaturated material produced by keeping the hydroxy-ester (1 g.) and potassium hydrogen sulphate (1 g.) at 140—150° for 8 hours. (iii) The hydroxy-ester (0·5 g.) and phosphoric oxide (0·5 g.) were heated together at 140° for 15 minutes. The product was treated with ice-water, and the solid crystallised from aqueous ethanol : it had m. p. 105—106° and did not decolorise aqueous potassium permanganate. (iv) After heating of the hydroxy-ester (0·3 g.) with boric acid (0·3 g.) at 130° for 20 minutes no boron-free product could be isolated.

αα'-Diacetoxy-αα'-dimethyladipic Anhydride.—(a) *Preparation.* A solution of the acid (XVIII) in acetic anhydride was heated under reflux for 30 minutes, then evaporated under reduced pressure, and the residue subjected to short-path distillation at 140°/10^{-4} mm. The distillate solidified on trituration with ether and was crystallised from dioxan–ether, to give the *anhydride* (XXI) as prisms, m. p. 163—164° (Found : C, 53·1; H, 6·0. $C_{12}H_{16}O_7$ requires C, 52·9; H, 5·9%).

(b) *Reaction with methanol.* Heating of the anhydride (338 mg.) with methanol under reflux overnight, and evaporation of the solution, yielded methyl hydrogen αα'-diacetoxy-αα'-dimethyladipate (XXII), which separated from aqueous methanol as hexagonal plates of the *monohydrate* (225 mg.), m. p. 95—97° (Found : C, 48·65; H, 6·9. $C_{13}H_{20}O_8,H_2O$ requires C, 48·45; H, 6·8%). After being kept at 60°/0·1 mm. for several hours, the solid anhydrous *half ester* was obtained (Found : C, 51·5; H, 6·7. $C_{13}H_{20}O_8$ requires C, 51·3; H, 6·6%).

(c) *Reaction with water.* The undistilled anhydride from 12 g. of the acid (XVIII) was heated with water until dissolved. On cooling of the solution, *αα'-diacetoxy-αα'-dimethyladipic acid* (XXIII) separated : from aqueous ethanol it formed prisms (13·3 g.), m.p. 207—208° (Found : C, 49·3; H, 6·4% ; equiv., 146. $C_{12}H_{18}O_8$ requires C, 49·3; H, 6·2% ; equiv., 145·1).

Methyl αα'-Diacetoxy-αα'-dimethyladipate.—(i) Treatment of the preceding acid (XXIII) (13·3 g.) with an excess of ethereal diazomethane and evaporation of the solution yielded the *methyl* ester (VIII) (13·6 g.) which was crystallised from methanol and then benzene, to give square plates, m. p. 163—164° (Found : C, 52·9; H, 7·1% ; hydrolysis equiv., 80·6. $C_{14}H_{22}O_8$ requires C, 52·8; H, 6·9% ; equiv., 79·6). (ii) An identical ester (2·6 g.) (mixed m. p.) was obtained by heating methyl αα'-dihydroxy-αα'-dimethyladipate (XX) (3·1 g.) with an excess of acetic anhydride for 2 hours, evaporating the solution, and crystallising the residue from ethanol. (iii) The dimethyl ester, m. p. 158—160°, was also obtained from methyl hydrogen αα'-diacetoxy-αα'-dimethyladipate (XXII) and ethereal diazomethane.

*αα'-Dimethyl-*trans-trans-*muconic Acid.*—(a) *Inversion of the* cis-cis-*acid.* αα'-Dimethyl-*cis-cis*-muconic acid (0·5 g.) was heated under reflux with 20% aqueous sodium hydroxide for 7 hours. The solution was cooled and acidified with dilute sulphuric acid, and the precipitate crystallised from methanol, to yield small prisms of *αα'-dimethyl-*trans-trans-*muconic acid* (50 mg.), m. p. 320—322° (Found : C, 57·2; H, 6·9. $C_8H_{10}O_4$ requires C, 57·0; H, 7·1%).

(b) *By pyrolysis of methyl αα'-diacetoxy-αα'-dimethyladipate.* A stream of nitrogen was passed through the acetoxy-ester (VIII) (7·5 g.) heated at 260—280°, and the issuing vapours were led through a glass tube at 650°, packed with broken glass. The pyrolysate (2·8 g.) was taken up in ether, and the solution washed with aqueous sodium hydrogen carbonate and water, dried (Na_2SO_4), and evaporated. The residue was warmed with an excess of 2N-sodium hydroxide for 2 hours and the solution acidified. From methanol, the αα′-dimethyl-*trans-trans*-muconic acid (0·52 g.) crystallised with m. p. and mixed m. p. 320—322°.

(c) *From the dinitrile* (IX). αα′-Dimethylmucononitrile (0·6 g.) was heated under reflux with 10% aqueous sodium hydroxide until evolution of ammonia ceased. The solution was cooled and acidified, and the precipitate crystallised from methanol. The product (230 mg.) had m. p. 316—318° alone, and 319—320° when mixed with αα′-dimethyl-*trans-trans*-muconic acid.

(d) *By dehydrobromination of αα′-dibromo-αα′-dimethyladipic acid.* αα′-Dimethyladipic acid (Lean, *J.*, 1894, **65**, 99; Noyes and Kyriakides, *J. Amer. Chem. Soc.*, 1910, **32**, 1057) (18 g.) and thionyl chloride (30 g.) were heated together at 40° until evolution of gases ceased. Excess of thionyl chloride was distilled off, iodine (0·05 g.) was added, and bromine (36 g.) run in slowly with stirring whilst the mixture was heated on the steam-bath and illuminated by means of a 100-watt lamp. Next day, the reaction mixture was poured cautiously into ethanol at 0°, and the resulting solution into an excess of water. The oily ethyl αα′-dibromo-αα′-dimethyladipate (24 g.), isolated by extraction with chloroform, was added slowly to a boiling solution of potassium hydroxide (40 g.) in methanol (100 c.c.) and, after 30 minutes, the solid was collected, washed with methanol, and well drained. A solution of the solid in water was stirred with charcoal, filtered, and acidified with concentrated hydrochloric acid, whereupon crude αα′-dimethyl-*trans-trans*-muconic acid was precipitated (1 g.), m. p. 295—300° not raised above 305—307° on repeated crystallisation from water (Found : equiv., 85·3. Calc. for $C_8H_{10}O_4$: equiv., 85·1).

Attempted Lactonisation of the trans-trans-*Acid.*—αα′-Dimethyl-*trans-trans*-muconic acid (46 mg.) was kept with concentrated sulphuric acid for 24 hours and the solution then poured on crushed ice. The *trans-trans*-acid was precipitated, m. p. and mixed m. p. 320—322° (yield, quantitative.)

Methyl αα′-Dimethyl-trans-trans-*muconate.*—By shaking of αα′-dimethyl-*trans-trans*-muconic acid (100 mg.) with ethereal diazomethane until dissolved, and evaporation of the solution, *methyl αα′-dimethyl*-trans-trans-*muconate* (105 mg.) was obtained, with m. p. 99—100° after being crystallised from aqueous methanol (Found : C, 60·6; H, 7·1. $C_{10}H_{14}O_4$ requires C, 60·6; H, 7·1%).

Hydrogenation of the Isomeric αα′-Dimethylmuconic Acids.—(i) αα′-Dimethyl-*cis-cis*-muconic acid (500 mg.) in methanol (50 c.c.) was hydrogenated in the presence of Adams's catalyst (*ca.* 0·1 g.) (hydrogen uptake : 2·25 mols.). The catalyst was filtered off and the solution evaporated to dryness to yield a mixture of *meso*- and racemic αα′-dimethyladipic acids, m. p. 90—97° (no reaction with aqueous alkaline permanganate), which was stirred with boiling benzene. The insoluble portion crystallised from water and had m. p. 137—138° alone and when mixed with authentic *meso*-αα′-dimethyladipic acid of m. p. 141—143°. (ii) Similarly, after hydrogenation of αα′-dimethyl-*cis-trans*-muconic acid (265 mg.) in methanol over Adams's catalyst (hydrogen uptake : 1·95 mols.), *meso*-αα′-dimethyladipic acid was isolated, having m. p. and mixed m. p. 135—137°. (iii) Hydrogenation of the *trans-trans*-acid proceeded analogously to yield a mixture from which *mezo*-αα′-dimethyladipic acid was isolated.

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