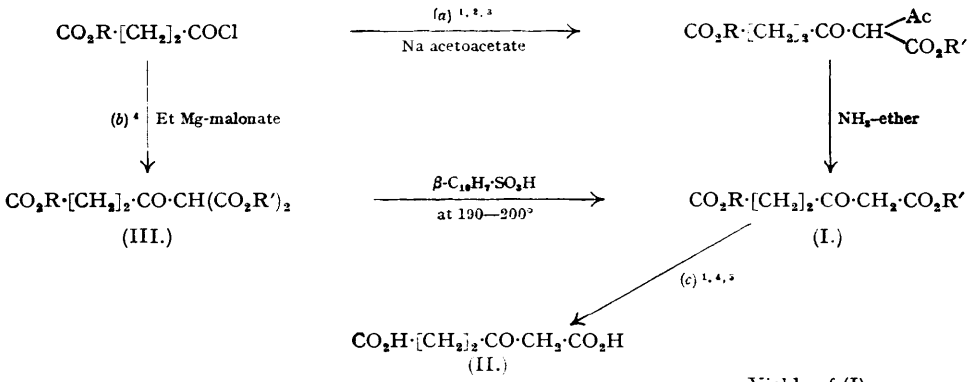
460. *Unsaturated Lactones and Related Substances. Part III. α-Ketoadipic Acid and γ-Carboxymethylenebutanolide.*

By Ulli Eisner, J. A. Elvidge, and R. P. Linstead.

A two-stage process for the preparation of β-ketoadipic acid (II) in 70—80% overall yield from (readily available) β-carbethoxypropionyl chloride is described. Cyclodehydration of (II) to γ-carboxymethylenebutanolide (V) is best effected with acetyl chloride–hydrogen chloride: under other conditions the corresponding lactonic acid anhydride (IV) is obtained, which with water affords (V) and (II), and with methanol, methyl β-ketoadipate and (V). Hot acetic anhydride reacts with (V) to yield the mixed anhydride with acetic acid (VII). The structure of the lactonic acid (V) is proved by its oxidation to oxalic and succinic acids. The lactone ring of (V) is opened by water, methanol containing hydrogen chloride, aqueous ammonia, and aniline to give respectively β-ketoadipic acid, methyl lævulate, lævulamide, and lævulanilide. The lactonic ester (VI) reacts with aniline to form methyl β-anilidopropionylacetate and with sodium methoxide in methanol to form methyl β-ketoadipate. Hydrogenation of the unsaturated lactonic acid (V) yields only adipic acid, and no saturated lactonic acid.

The dehydration of γ-keto-acids is a standard method of making unsaturated γ-lactones (see, *e.g.*, Kuehl, Linstead, and Orkin, Part I, *J.*, 1950, 2213). We have now examined the possibility of obtaining an unsaturated lactonic acid from a keto-dibasic acid. The product is of interest as having a double bond in an unusual position, exocyclic to the γ-lactone ring; moreover, the presence of a free carboxyl provides a functional group capable of modification and thus increases the possible range of variation in physiological activity.

The acid selected for study was β-ketoadipic acid. Its esters (I) have been prepared from the half-esters, half-chloride of succinic acid by the routes (*a*) and (*b*), and the acid itself (II) by their hydrolysis (*c*) with cold concentrated hydrochloric acid:



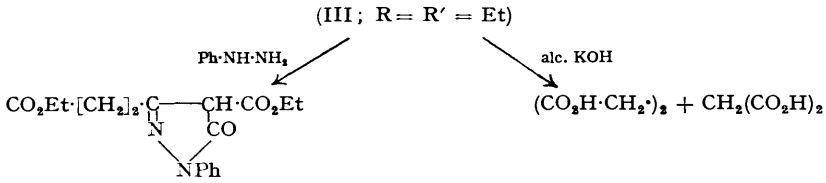
Yields of (I):
unstated (R = R′ = Me)
27% (R = Me, R′ = Et)
11% (R = R′ = Et)
40% ,,

[1] Bardhan, *J.*, 1936, 1848.
[2] Ruggli and Maeder, *Helv. Chim. Acta*, 1942, **25**, 936.
[3] Stevens and Beutel, *J. Amer. Chem. Soc.*, 1943, **65**, 449.
[4] Riegel and Lilienfeld, *ibid.*, 1945, **67**, 1273.
[5] Richter, *Helv. Chim. Acta*, 1949, **32**, 2318.

The decarbethoxylation stage of method (*b*) gave very variable results in our hands and the overall yield of ethyl β-ketoadipate (I; R = R′ = Et) was seldom more than 16%. We therefore examined Lukeš, Kastner, Gut, and Herben's synthesis (*Coll. Czech. Chem. Comm.*, 1947, **12**, 647). These authors found that ethanolysis of the readily available benzoyl derivative of furfuraldehyde cyanohydrin gave 45% of a product which contained ethyl β-ketoadipate, although this could not readily be isolated in a state of purity. We have confirmed this result and the method offers no advantage.

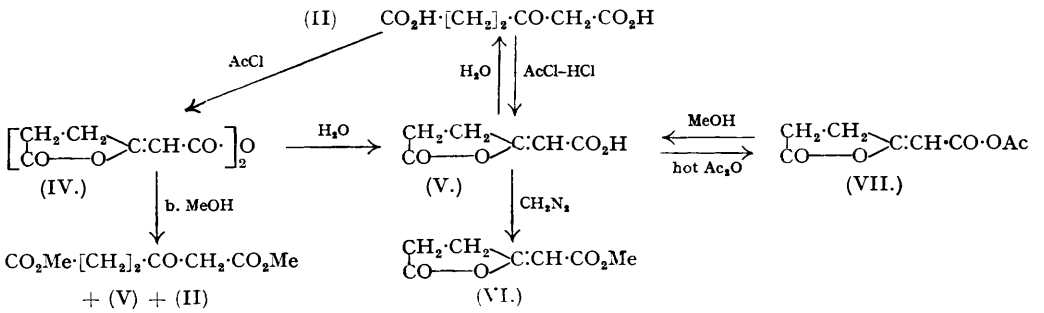
We next attempted to modify Riegel and Lilienfeld's synthesis (*b*) by isolating the intermediate triester (III) and hydrolysing this directly to β-ketoadipic acid. This route proved highly satisfactory. From the reaction of β-carbethoxypropionyl chloride with ethyl magnesiomalonate, ethyl β-keto-α-carbethoxyadipate (III; R = R′ = Et) was easily separated by vacuum distillation, in yields of 70—80%. The triester was characterised by formation of

the phenylpyrazolone, and the structure was proved by hydrolysis with cold alcoholic potassium hydroxide to malonic and succinic acids, which were isolated quantitatively :



Treatment of the triester (III; R = R′ = Et) with cold concentrated hydrochloric acid, followed by evaporation of the solution to dryness at 30—35° under reduced pressure, readily afforded β-ketoadipic acid (II) in quantitative yield. Previous workers, when effecting the similar stage (*c*) (above), have isolated the β-ketoadipic acid by evaporation of the hydrolysate over potassium hydroxide in a vacuum desiccator at room temperature, a process which even on the quite small scale is unduly lengthy.

Lactonisation of β-Ketoadipic Acid.—First attempts to lactonise β-ketoadipic acid by heating it with acetyl chloride afforded mainly a neutral product, $C_{12}H_{10}O_7$, m. p. 164°, which gave no coloration with ferric chloride, unlike β-ketoadipic acid or its esters which give, respectively, a purple and a deep red. It appeared to be the anhydride (IV) of the required lactonic acid. In agreement with this formulation, the substance was found to react with water at room temperature, yielding the desired lactonic acid, $C_6H_6O_4$. This also failed to give an immediate coloration with ferric chloride, but after being warmed with water the solution gave a reddish colour with that reagent. This corresponds to the hydrolysis of the lactonic acid to β-ketoadipic acid, a reaction which was subsequently demonstrated by the isolation of the latter as the sole product. Treatment of the lactonic acid with ethereal diazomethane afforded the crystalline methyl ester (VI). Suitably prolonged treatment of the anhydride (IV) with water gave a mixture of lactonic acid (V) and β-ketoadipic acid, whilst from the reaction of the anhydride with boiling methanol, the lactonic acid (V) and methyl β-ketoadipate were isolated, together with some β-ketoadipic acid. The methyl ester (VI) of the lactonic acid was not obtained. The results suggested that the lactonic ester (VI) reacts more readily with methanol than the acid (V). In an attempt to convert the lactonic acid (V) into the anhydride (IV) by warming with acetic anhydride, a high yield of the mixed anhydride (VII) was obtained. With methanol, (VII) afforded the lactonic acid (V) quantitatively : the other product of reaction was presumbly methyl acetate.

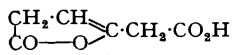


When β-ketoadipic acid was heated with redistilled acetyl chloride or treated for longer periods with acetic anhydride at room temperature, 70% yields of a crude solid were obtained. By fractional crystallisation, the lactonic acid (V) was isolated in about 10% yield : the remainder of the material consisted of a mixture of the anhydride (IV) with a small amount of another neutral substance of m. p. 189°, which was sparingly soluble in the common solvents. From its analysis and ultra-violet light absorption spectrum this substance appeared to be isomeric with the anhydride, but it was recovered unchanged after treatment with cold water. Lack of material precluded its further investigation.

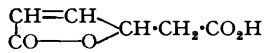
Treatment of β-ketoadipic acid with acetic acid which had been saturated with dry hydrogen chloride proved abortive, since the starting material was recovered. Treatment at room temperature with acetyl chloride containing hydrogen chloride, however, afforded the lactonic

acid as main product. By this method the pure lactonic acid (V) could readily and consistently be obtained from β-ketoadipic acid in 40—50% yield.

The structure of the lactonic acid was determined by oxidation with potassium permanganate. Succinic acid and oxalic acid were isolated in high yield, proving that the formulation as γ-carboxymethylenebutanolide (V) was correct. The isomeric lactonic acids (VIII) and (IX) would not give succinic acid under the conditions employed.



(VIII.)



(IX.)

During the course of this work a communication by Richter appeared (*Helv. Chim. Acta*, 1949, **32**, 2318) which described the preparation of the lactonic acid methyl and ethyl esters from the corresponding half esters of β-ketoadipic acid (I; R = H) by cyclisation under comparatively vigorous conditions. Richter's description of the lactonic methyl ester indicated that it was identical with our product (VI), and consequently his oxidation results, *e.g.*, formation of oxalic acid, and of succinic acid and its anhydride on ozonolysis, also serve to support the exocyclic double-bond structure (V) for the lactonic acid. Very recently, Richter (*ibid.*, 1950, **33**, 20) has claimed the preparation of the lactonic acid (V) in 2·5% yield by treating methyl ethyl β-ketoadipate (I; R = Me, R′ = Et) with concentrated sulphuric acid. We think it highly probable, however, from his description of the product, its melting point, and failure to react with diazomethane or immediately with aqueous sodium carbonate, that it is not the lactonic acid (in spite of the analysis quoted) but is identical with the anhydride (IV) described above.

The lactonic acid (V) has a γδ-double bond exocyclic to a γ-lactone ring. In most of its reactions, it resembles a βγ- rather than an αβ-unsaturated γ-lactone. For instance, when it was refluxed with dry methanol containing a trace of hydrogen chloride, methyl lævulate was formed, being isolated in 43% yield as its 2 : 4-dinitrophenylhydrazone. With boiling absolute methanol alone, (V) underwent no change during 2·5 hours, while even after being refluxed with methanol containing 0·5% of water, it was recovered very largely unchanged. The slow ring-opening with cold water to β-ketoadipic acid has already been mentioned. After treatment of (V) with concentrated aqueous ammonia, followed by vacuum evaporation at room temperature, a white deliquescent solid was obtained. With water, or on being warmed with organic solvents, this material evolved carbon dioxide and afforded a neutral product identified as lævulamide : with acid 2 : 4-dinitrophenylhydrazine solution it gave the dinitrophenylhydrazone of lævulic acid. On keeping the lactonic acid (V) with aniline in a solvent lævulanilide was formed, and the lactonic ester (VI) under these conditions gave methyl β-anilidopropionylacetate (compare βγ-angelicalactone, Part I, *loc. cit.*). With sodium methoxide in absolute methanol the lactonic ester (VI) afforded methyl β-ketoadipate which was isolated and identified by conversion into the semicarbazone and known phenylpyrazolone. The lactonic acid (V) failed to react with *p*-nitrotoluene-ω-thiol. The ready loss of carbon dioxide which occurred in the ring-opening reactions of the lactonic acid (V) is noteworthy.

Hydrogenation of the ester (VI) in the presence of platinum resulted in an uptake of 2 mols. of hydrogen, and an oil was obtained which on warming with aqueous hydrochloric acid afforded adipic acid. Complete hydrogenation of the lactonic acid (V) under similar conditions gave adipic acid direct. 50% Hydrogenation of (V) gave a mixture of adipic acid and unchanged lactone (V). The behaviour on reduction of the unsaturated system present in (V) and (VI) resembled many of the results of Jacobs and Scott (*J. Biol. Chem.*, 1930, **87**, 601; 1931, **93**, 139), who found that αβ-unsaturated lactones gave normal dihydro-products but that many βγ-unsaturated γ-lactones were fully hydrogenated to deoxy-acids. However, β-substitution was a factor which reduced the capacity of Δ^{β}-lactones for this abnormal reaction. Our new lactonic acid (V) has the double bond next to the point of lactonisation and resembles Jacobs and Scott's simple βγ-unsaturated γ-lactones in its complete conversion into deoxy-acid.

Experimental.

Ethyl β-Keto-α-carbethoxyadipate.—According to the directions of Riegel and Lilienfeld (*loc. cit.*), β-carbethoxypropionyl chloride (60 g., b. p. 98°/15 mm.), prepared in 91% yield from succinic anhydride (40 g.; recrystallised from acetic anhydride), was added in ether (50 c.c.) to an ethereal solution (200 c.c.) of ethyl magnesiomalonate [from ethyl malonate (50·5 g.) and magnesium turnings (7·9 g.)], and the mixture refluxed and stirred for 4 hours. The mixture was cooled, and with continued stirring a cold solution of sulphuric acid (9·5 c.c.) in water (190 c.c.) was slowly added. The ethereal layer was separated, and the aqueous layer extracted once with ether. The combined ethereal solution was washed with a little water, dried (Na_2SO_4), and distilled, finally under reduced pressure. After a small

forerun, *ethyl β-keto-α-carbethoxyadipate* (76·5 g.; 73% calculated on β-carbethoxypropionyl chloride) was collected as a colourless oil, b. p. 144°/0·2 mm., n_D^{20} 1·4506 (Found : C, 54·5; H, 7·0. $C_{13}H_{20}O_7$ requires C, 54·2; H, 7·0%). The ester gives a red coloration with aqueous ethanolic ferric chloride.

The ester (1 g.) in methanol was allowed to react overnight with phenylhydrazine (0·5 c.c.) in 50% acetic acid (5 c.c.), and the solution poured on ice. *Ethyl 5-keto-4-carbethoxy-1-phenylpyrazoline-3-β-propionate* separated from aqueous methanol as cream-coloured needles, m. p. 61—62° (Found : N, 8·5. $C_{17}H_{20}O_5N_2$ requires N, 8·4%).

Alkaline Hydrolysis of Ethyl β-Keto-α-carbethoxyadipate.—The ester (3 g.) was treated overnight with a solution of potassium hydroxide (3 g.) in methanol (10 c.c.), and the solution then acidified with aqueous hydrochloric acid and evaporated to dryness under reduced pressure. Extraction of the residue with acetone afforded a mixture of acids which was treated with ether (45 c.c.). The residue (0·89 g.) had m. p. 184° undepressed by succinic acid, whilst evaporation of the ether gave malonic acid (1·12 g.), m. p. 105—115°, which on recrystallisation had m. p. 136—137° alone and in admixture with an authentic specimen.

β-Ketoadipic Acid.—Ethyl β-keto-α-carbethoxyadipate (76·5 g.) was kept at room temperature with concentrated hydrochloric acid (200 c.c.) for 36 hours. Carbon dioxide was evolved. Distillation of the solution to dryness at 30—35° under reduced pressure afforded a white solid which was freed from some occluded hydrochloric acid by keeping it overnight in a vacuum desiccator containing potassium hydroxide : the β-ketoadipic acid (42 g., yield quantitative) had m. p. 115° (decomp.) and needed no further purification.

Lactonisation Experiments.—(*a*) *The anhydride* (IV). β-Ketoadipic acid (0·8 g.) and acetyl chloride (5 c.c.) were heated under reflux until evolution of hydrogen chloride ceased. On removal of the excess reagent under reduced pressure and addition of dry ether, the residue solidified and had m. p. 150—155°. From ethyl acetate the *anhydride* of γ-carboxymethylenebutanolide (γ-carboxymethylenebutyrolactone) crystallised as prisms, m. p. 164° (Found : C, 54·15; H, 3·75. $C_{12}H_{10}O_7$ requires C, 54·1; H, 3·8%). Light absorption in dry dioxan : maximum at 2470 A., $\varepsilon = 50{,}540$.

(*b*) β-Ketoadipic acid (3 g.) and freshly distilled acetyl chloride (25 c.c.) were heated under reflux for 2 hours. The solution was filtered from a trace of insoluble matter and concentrated under reduced pressure. Trituration of the oily residue with ether gave a white solid which was insoluble in aqueous sodium hydrogen carbonate and which gave no coloration with ferric chloride. From ethyl acetate the isomeric *anhydride* (?) crystallised as beautiful needles, m. p. 189° (Found : C, 54·4, 54·1; H, 3·9, 3·9. $C_{12}H_{10}O_7$ requires C, 54·1; H, 3·8%). Light absorption in dioxan : maximum at 2470 A., $\varepsilon = 51{,}870$. The compound was recovered unchanged (m. p. and mixed m. p. 185—189°) after treatment with water for 16 hours, and appeared not to react with boiling methanol (see below).

(*c*) β-Ketoadipic acid (10·9 g.) was kept with acetic anhydride (35 c.c.) for 3 days at room temperature. The solution was distilled under reduced pressure (bath temp. $\not>50°$), and the residue treated with ether. On crystallisation from ethyl acetate some of the above isomeric compound was isolated, together with crude anhydride (IV) (2·8 g.), m. p. 145—147°.

(*d*) Hydrogen chloride was passed for 15 minutes into a suspension of β-ketoadipic acid (2 g.) in acetic acid (20 c.c.). After 3 days the solution was filtered and evaporated under reduced pressure. The solid residue (1·3 g.) was identified as β-ketoadipic acid by m. p. and the purple coloration afforded with aqueous ferric chloride.

(*e*) *γ-Carboxymethylenebutanolide* (*γ-carboxymethylenebutyrolactone*) (V). β-Ketoadipic acid (10·3 g.) was added to acetyl chloride (80 c.c.) (unredistilled and containing hydrogen chloride) at room temperature. After 24 hours the excess of reagent was distilled under reduced pressure, and the residue (9 g.) crystallised from ethyl acetate–light petroleum (b. p. 60—80°). Colourless needles (4·4 g.; 48%), m. p. 176—179° (decomp.), were obtained which dissolved with effervescence in aqueous sodium hydrogen carbonate and gave no coloration with aqueous ethanolic ferric chloride. Recrystallisation from ethyl acetate, or chloroform, gave silky needles of pure *γ-carboxymethylenebutanolide* with m. p. 184° (decomp.) (Found : C, 51·0, 50·7; H, 4·3, 4·4. $C_6H_6O_4$ requires C, 50·7; H, 4·25%). Light absorption in dioxan : maximum at 2260 A., $\varepsilon = 19{,}310$.

A second preparation from β-ketoadipic acid (15 g.) and acetyl chloride (150 c.c.) gave a crude solid (8·25 g.) which on crystallisation from ethyl acetate–light petroleum (b. p. 60—80°) afforded needles, m. p. 176—177° (decomp.), of the lactonic acid (V) (6 g.) in 45% yield. Such material was sufficiently pure for further use.

γ-Carbomethoxymethylenebutanolide (VI).—Treatment of the lactonic acid (V) with ethereal diazomethane and evaporation of the solution under reduced pressure yielded a neutral solid. γ-Carbomethoxymethylenebutanolide formed laths, m. p. 110°, from ether–light petroleum (b. p. 40—60°) (Found : C, 53·9, 54·2; H, 4·7, 5·3. Calc. for $C_7H_8O_4$: C, 53·9; H, 5·1%). Richter (*Helv. Chim. Acta*, 1949, **32**, 2318) records m. p. 108°.

Oxidation of γ-Carboxymethylenebutanolide.—Potassium permanganate (0·90 g.; 3 atoms of O) in water (35 c.c.) was added during 1·5 hours to a stirred solution of the lactonic acid (0·40 g.) in 2·5% aqueous sodium hydrogen carbonate (30 c.c.) kept at 0° to −2°. Water (30 c.c.) was added, the mixture was warmed to coagulate manganese dioxide and filtered, and the residue extracted with warm 1% aqueous sodium hydrogen carbonate (20 c.c.). The combined filtrate was acidified with dilute hydrochloric acid, the reaction adjusted to pH 4 with ammonia, and concentrated calcium chloride solution (5 c.c.) added. The white precipitate of calcium oxalate was collected, washed with water, and dried to constant weight; yield, 0·279 g. (77%). Treatment with 2N-sulphuric acid (15 c.c.) and extraction with ether (7 times) afforded oxalic acid (0·159 g.), m. p. and mixed m. p. 100° with resolidification and m. p. 185—188° (decomp.). The filtrate from the calcium oxalate was extracted continuously with ether for

20 hours. Evaporation of the ether gave a completely crystalline residue (0·229 g.; 69%), which was soluble with effervescence in aqueous sodium hydrogen carbonate, and had m. p. 184—185° alone or in admixture with succinic acid.

Reactions of the Anhydride (IV).—(a) *With water.* The anhydride (185 mg.) was treated with a little water which was then removed *in vacuo* over sulphuric acid. Repetition of the treatment afforded a residue, m. p. 173—176° (decomp.), which on recrystallisation from ethyl acetate–light petroleum (b. p. 60—80°) had m. p. 185° (decomp.) undepressed in admixture with γ-carboxymethylenebutanolide. Further treatment of the residue with aqueous acetone, followed by evaporation, gave β-ketoadipic acid, m. p. 115—120° (decomp.) (purple ferric chloride colour).

(b) *With methanol.* The anhydride (2·8 g.; crude) and excess of methanol were heated under reflux for 4 hours. When the solution was cooled, the neutral isomeric compound (0·44 g.), m. p. 172—174°, separated. The filtrate was evaporated under reduced pressure, the residue dissolved in ethyl acetate, and the solution extracted with saturated aqueous sodium hydrogen carbonate (12 c.c.). Evaporation of the ethyl acetate left a neutral oil which failed to crystallise, gave a strong red coloration with aqueous ethanolic ferric chloride, and was evidently methyl β-ketoadipate. On cautious acidification of the aqueous extract, γ-carboxymethylenebutanolide (0·29 g.) separated, m. p. 180° (decomp.). Concentration of the mother-liquors in a vacuum desiccator yielded β-ketoadipic acid (0·7 g.), m. p. 117° (decomp.) (purple ferric chloride colour).

Reactions of γ-Carboxymethylenebutanolide and its Methyl Ester.—(a) *With acetic anhydride.* A solution of the lactonic acid (1 g.) in acetic anhydride (15 c.c.) was heated on the steam-bath for 3 hours. Evaporation under reduced pressure gave an oil which on trituration with a small volume of dry ether set solid (1 g.), m. p. 70—80°. From ether–light petroleum (b. p. 60—80°) the *mixed anhydride* (VII) of γ-carboxymethylenebutanolide with acetic acid separated as shiny plates, m. p. 72° (Found: C, 52·2; H, 4·3. $C_8H_8O_5$ requires C, 52·2; H, 4·35%). The compound dissolved gradually in aqueous sodium hydrogen carbonate and gave no coloration with aqueous ethanolic ferric chloride.

A solution of the mixed anhydride (0·5 g.) in methanol (5 c.c.) was kept at room temperature overnight and then evaporated under reduced pressure. The completely crystalline residue gave no coloration with ferric chloride and had m. p. 172—175° (decomp.) undepressed by γ-carboxymethylenebutanolide.

The lactonic acid (0·3 g.) was kept overnight with acetic anhydride (3 c.c.). On removal of the solvent under reduced pressure a solid was obtained (0·3 g.), m. p. 154—158°, which after crystallisation (twice) from ethyl acetate had m. p. 189° alone and in admixture with the "isomeric anhydride" described above.

(b) *With water.* The lactonic acid (0·4 g.), dioxan (3·5 c.c.), and water (2·5 c.c.) were kept at room temperature for 3 days. Undissolved lactonic acid (0·115 g.), m. p. 170—174° (decomp.) (no ferric chloride colour), was collected, and the filtrate evaporated *in vacuo* over calcium chloride to yield readily water-soluble β-ketoadipic acid (0·30 g.), m. p. 109—111° (decomp.) (purple colour with ferric chloride).

(c) *With methanol.* (i) The lactonic acid (0·544 g.) was recovered unchanged (m. p. 182—183°, decomp.) after being refluxed with methanol (20 c.c.; dried over magnesium methoxide) for 2·5 hours. (ii) The recovered lactonic acid was heated under reflux for 2·5 hours with methanol (20 c.c.) containing 0·5% of water. Removal of the solvent under reduced pressure left a crude solid, m. p. 157—160° (decomp.), which gave a faint red coloration with aqueous ethanolic ferric chloride. Recrystallisation from chloroform yielded the lactonic acid, m. p. 185° (decomp.). (iii) A solution of the lactonic acid (0·7 g.) in dry methanol (20 c.c.) containing a trace of dry hydrogen chloride was refluxed for 2·5 hours, and then evaporated under reduced pressure. The residue was a neutral oil (red ferric chloride colour): it reacted with an alcoholic solution of 2 : 4-dinitrophenylhydrazine sulphate to yield the dinitrophenylhydrazone of methyl lævulate (0·67 g.; 43%), m. p. 130—131° raised to 138° on recrystallisation from methanol. A mixture with an authentic specimen had m. p. 138°. (iv) The lactonic acid methyl ester (VI) (1·53 g.) was added to a solution of sodium (0·23 g.; 1 mol.) in dry methanol (50 c.c.), and after 10 minutes the solvent was removed under reduced pressure and the residue treated with dilute hydrochloric acid and ether. The ether was washed with aqueous sodium hydrogen carbonate and evaporated to give an oil (1·18 g.; 64%). This reacted with alcoholic semicarbazide hydrochloride in the presence of aqueous sodium acetate to yield the *semicarbazone* of methyl β-ketoadipate (plates, m. p. 109°, from benzene, identical with a preparation from authentic methyl β-ketoadipate) (Found: N, 17·25. $C_9H_{15}O_5N_3$ requires N, 17·1%) and the known methyl 1-carbamido-5-ketopyrazoline-3-β-propionate which formed prismatic needles, m. p. 171°, from ethanol. Ruggli and Maeder (*Helv. Chim. Acta*, 1942, **25**, 961) gave m. p. 172°.

(d) *With ammonia.* A solution of the lactonic acid (0·6 g.) in concentrated ammonia (10 c.c.; *d* 0·88) was kept for 4 days and then evaporated to dryness over sulphuric acid, whereupon a deliquescent white solid was obtained. This material evolved carbon dioxide on treatment with organic solvents or water. Evaporation of the aqueous solution afforded somewhat impure lævulamide, m. p. 95—96° (decomp.), which with aqueous 2 : 4-dinitrophenylhydrazine hydrochloride gave a mixture of acidic and neutral derivatives. From methanol, the dinitrophenylhydrazone of lævulic acid formed red needles, m. p. 198° (Found: C, 45·1; H, 4·4; N, 19·4. Calc. for $C_{11}H_{12}O_6N_4$: C, 44·6; H, 4·1; N, 18·9%). A mixture with an authentic specimen (m. p. 206°) had m. p. 201°. The neutral derivative (probably of lævulamide), m. p. *ca.* 198°, could not be adequately purified.

(e) *With aniline.* (i) A solution of the lactonic acid (0·71 g.) and aniline (0·9 c.c.; 2 mols.) in dry dioxan was kept at room temperature overnight, then evaporated under reduced pressure. The residual oil slowly solidified: after being washed with ether, the solid (0·75 g.) was crystallised from benzene to give lævulanilide, m. p. 101—102° (Found: N, 7·55. Calc. for $C_{11}H_{13}O_2N$: N, 7·3%). (ii) A solution of the lactonic acid methyl ester (VI) (135 mg.) and aniline (100 mg.) in alcohol (3 c.c.) was kept at room

temperature for 2 days and then evaporated *in vacuo*. Recrystallisation of the solid from benzene–hexane afforded *methyl β-anilidopropionylacetate* (30 mg.), m. p. 86·5—87·5° (Found: C, 62·85; H, 6·1; N, 5·7. $C_{13}H_{15}O_4N$ requires C, 62·65; H, 6·0; N, 5·6%).

Hydrogenation of γ-Carboxymethylenebutanolide and its Methyl Ester.—(*a*) The lactonic ester (0·162 g.) in alcohol was hydrogenated at ordinary temperature and pressure in the presence of Adams's catalyst (uptake of hydrogen: 53·1 c.c. at 25°/767 mm. Calc. for uptake of 2 mols.: 51·2 c.c.). After filtration and evaporation of the alcohol, the oily residue was taken up in 10% hydrochloric acid, and the solution evaporated to dryness on the steam-bath. The crystalline residue (90 mg.) had m. p. 147—150° undepressed by adipic acid.

(*b*) Hydrogenation of the lactonic acid (0·71 g.) in dry dioxan (35 c.c.) at ordinary temperature and pressure in the presence of Adams's catalyst (150 mg.) occurred slowly and was complete in 8 hours. After filtration from catalyst, the solvent was removed under reduced pressure and the solid residue (0·65 g.), crystallised from water, had m. p. 150—151° alone and in admixture with adipic acid.

(*c*) The lactonic acid (0·7 g.) in dry dioxan (50 c.c.) was 50% hydrogenated at ordinary temperature and pressure in the presence of Adams's catalyst (100 mg.). The allowed uptake of hydrogen (120 c.c. at 15°/759 mm.) took 3 hours. The solution was then filtered, evaporated to dryness under reduced pressure, and the residue fractionally crystallised from ethyl acetate by addition of small volumes of light petroleum (b. p. 60—80°) to yield: (i) Prisms (0·29 g.; 81%), m. p. 147—150° undepressed by adipic acid; (ii) a mixture (51 mg.), m. p. 130—155°, and (iii) unchanged lactonic acid (0·33 g.; 94%), m. p. and mixed m. p. 173—178° (decomp.).

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