CHEMISTRY OF $\beta$-ARYL GLUTACONIC ACIDS.

Part II. Condensations with Phenolic Ethers.

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Introduction.

In Part I of this series, the $\beta$-(2-methoxy-naphthyl)-glutaconic acid was found to be the first case of a glutaconic acid of the $\beta$-aryl type to be separated in geometrically isomeric forms, and later on it was found possible to transform all the naphthol substituted glutaconic acids into their geometrical isomerides. In a search for more glutaconic acids belonging to the $\beta$-aryl type exhibiting geometrical isomerism, the author happened to condense $p$-cresol-ethylether with acetone-dicarboxylic acid. This condensation, however, gave only one form of a $\beta$-(2-ethoxy-5-methyl-phenyl)-glutaconic acid (I), besides two other new acids melting at 205°C and 232°C. These acids were found to belong to an entirely new type of compounds which could be derived from glutaconic acids, and form the subject of the present investigation.

The equivalents and empirical formulæ of these acids were of a grade differing from the glutaconic acid by about one molecule of $p$-cresol-ethylether, and this combined with their monobasic character, suggested their probable formation by interaction of the cresolether with one of the carboxylic groups of the glutaconic acid during the reaction. However, when it was attempted to condense the glutaconic acid (I) with $p$-cresol-ethylether in the presence of concentrated sulphuric acid as in the original reaction, no reaction was observed to proceed in the expected manner. Similar condensation products of phthalic and succinic acids with aromatic hydrocarbons or phenolic ethers have been obtained in the past from their anhydrides, by the application of Friedel and Crafts' reaction. This reaction

3 Pechmann, Ber., 1889, 13, 1612; Burker, A.ch. (5) 26, 435, 499; Nourrison, Ber., 19, 2013; Ullmann and Schmidt, Ber., 52, 2098; Bentley, Gardener and Weizmann, J.C.S., 1907, 1626.
was found unworkable in the present case, in that, the glutaconic anhydride, being an unsaturated compound, was itself attacked by aluminium chloride. Moreover, zinc chloride or phosphorus pentoxide could not be used here as condensing agents, for they transformed the glutaconic acid into its anhydride, which prevented further reaction. The desired condensation, however, was found to get effected, in the presence of 80% sulphuric acid, appreciable quantities of the acids m.p. 205°C. and 232°C. being formed.

The monocarboxylic acid m.p. 205°C., however, did not absorb any bromine from bromine water, did not decolourise alkaline potassium permanganate solution and gave no semicarbazone, thus indicating an absence of any double bond or a ketonic group in itself. This went against the above supposition about its formation. When treated with 80% sulphuric acid this monocarboxylic acid gave the known 6-methyl-coumarin-4-acetic acid, while the action of concentrated sulphuric acid produced together with this coumarin acid, a neutral compound m.p. 184°C. with an empirical formula showing a loss of one molecule of ethyl alcohol during its formation. This neutral compound, on boiling with caustic alkalies, went slowly in solution, and on subsequent acidification produced an acid, which decomposed at 110°C. and gave back the neutral compound. This new acid was also extremely unstable giving back the original neutral compound even on simple crystallisation; this suggested an existence of a lactone ring similar to that in the coumarins, in the latter. Hydrolysis and subsequent ethylation of the neutral compound to prevent this lactone-ring closure, yielded, instead of the original monocarboxylic acid m.p. 205°C., a new dicarboxylic acid m.p. 219°C. with an empirical formula showing an excess of one molecule of ethyl alcohol over the monocarboxylic acid. This indicated the presence of a lactone ring also in the monocarboxylic acid m.p. 205°C. which was proved by its transformation into the dicarboxylic acid m.p. 219°C. by hydrolysis and ethylation. On the other hand, the dicarboxylic acid m.p. 219°C. was also found to give, by the action of sulphuric acid, a mixture of the monocarboxylic acid m.p. 205°C., the neutral compound m.p. 184°C. and the 6-methyl-coumarin-4-acetic acid (VI).

It was therefore concluded that the dicarboxylic acid m.p. 219°C. was the primary product of the reaction formed evidently by the addition of one molecule of \( p \)-cresol-ethylether to the \( \beta \)-(2-ethoxy-5-methyl-phenyl)-glutaconic acid (I); the monocarboxylic acid m.p. 205°C. (II) and the neutral compound m.p. 184°C. (V) being its mono and dilactones. Such direct additions of aromatic hydrocarbons or phenolic ethers to a double bond,

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4 Dey, J.C.S., 1915, 1636.
are known to happen in the case of styro", 5 and cinnamic acid. 6 Thus here the dicarboxylic acid m.p. 219° C. can be represented by either of the structures (III) and (IV), according to which carbon atom along the double bond, the nucleus of the phenolic ether is attached. The symmetrical structure (III) designating the dicarboxylic acid as \( \beta \beta'-(22'-\text{diethoxy-55'}-\text{dimethyl-diphenyl}) \)-glutaric acid, is the more probable one, because an acid of the structure (IV) would give in addition to the 6-methyl-coumarin-4-acetic acid (VI), an acid of the formulae (VII) by the action of sulphuric acid; no such acid was detected. These reactions and all the products could be represented as:

\[ 
\text{monocarboxylic acid m.p. 232°C.} 
\]

\[ 
\text{\begin{align*}
\text{H}_2\text{C} & \quad \text{CH}_3 \\
\text{C}_6\text{H}_5 & \\
\text{\text{-etylether}} & \end{align*}} 
\]

\[ 
\text{\begin{align*}
\text{H}_2\text{C} & \quad \text{CH}_3 \\
\text{CH}_3 & \\
\text{OC}_2\text{H}_5 & \end{align*}} 
\]

\[ 
\beta\text{-Substituted glutaric esters are known to condense with oxalic ester, but the reaction is more difficult when there are two methyl groups in the \( \beta \)-position. 7 The esters of the present glutaric acid could not be made to condense with oxalic ester. This may be due to the fact that there are two much heavier phenolic ether groups in the \( \beta \)-position, which cause a kind of steric hindrance as in the case of \( \beta \beta \)-dimethyl-glutaric esters.}

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5 König, Ber., 23, 3145; Krämer and Spilker, Ber., 23, 3169, 3269.
6 Libermann and Hartmann, Ber., 24, 2582; 25, 957.
7 Dieckemann, Ber., 1930, 32; Komppa, Annalen, 368, 126.
In the other monocarboxylic acid m.p. 232° C., the absorption of bromine from bromine water, the instantaneous decolourisation of alkaline potassium permanganate solution, and the easy formation of semicarbazone indicated the existence of unsaturation and a ketone group. This showed that it had been formed by the elimination of a molecule of water between one of the carboxylic groups of the glutaronic acid (I) and the nuclear hydrogen atom of \( p \)-cresol-ethylether. A similar monocarboxylic acid melting at 252° C. had been obtained previously by the condensation of \( p \)-cresol-methylether with acetone-dicarboxylic acid. It has now been found possible to synthesise this also by the condensation of \( p \)-cresol-methylether with \( \beta \)-(2-methoxy-5-methyl-phenyl)-glutaronic acid (VIII) in the presence of 80% sulphurous acid. It was observed that no glutaric acid like (III) was formed in either of these condensations; the compound could however be synthesised from the dilactone (V) by hydrolysis and methylation. This monocarboxylic acid m.p. 252° C. could be designated by either the structure (IX) or (X), depending upon which of the carboxylic groups of the glutaronic acid had taken part in the reaction.

By the action of 80% sulphurous acid, the monocarboxylic acid m.p. 252° C. produced an indone-acetic acid m.p. 218° C. by the loss of one molecule of \( p \)-cresol-methylether, which was identical with the one described by Gogte and Limaye; but the action of concentrated sulphuric acid yielded, in addition to the indone-acetic acid, a neutral compound m.p. 214° C. by a loss of water caused by the internal condensation of the carboxylic group with the ring. If the structure (IX) be assumed for the monocarboxylic acid, the indone-acetic acid will have the formula (XI) and the neutral compound (XIII). Then the decarboxylation product (XII) of the indone-acetic acid will not contain a reactive-\( \text{CH}_2\)-CO-group in the ring, but such a group will be present in the neutral compound. If, on the other hand, the structure (X) represents the monocarboxylic acid, the situation will be exactly reversed and thus a decision between these two alternative formulæ (IX) and (X) can easily be made by examining whether the decarboxylation product of the indone-acetic acid or the neutral compound m.p. 214° C. contains a reactive methylene group by condensing with aromatic aldehydes.

It was observed that the neutral compound m.p. 214° C. (XIII) easily condensed with benzaldehyde whereas the decarboxylation product (XII) remained inert, thus supporting the formula (IX) for the monocarboxylic acid m.p. 252° C. This structure is further supported by the observation that

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the esters of the monocarboxylic acid also contained no reactive-CH$_2$-CO-group condensing with benzaldehyde, as would be the case if formula (X) were correct. In the formula (IX), the carboxylic group of the glutaconic acid is represented as attached at the ortho-position to the methoxy group of the $\beta$-cresol-methylether, as this is the only reactive position in the nucleus. The monocarboxylic acid m.p. 252° C. can therefore be designated as 2-2'-dimethoxy-5-5'-dimethyl-chalkone-$\alpha$-acetic acid, and the indone-acetic acid as 7-methoxy-4-methyl-3-keto-indene-acetic acid. The fact that in the formation of these acids, the carboxylic group of the glutaconic acid (VIII) situated at the end of a conjugated system of double bonds, has taken part in the reactions, is in harmony with its increased reactivity. These reactions and the above-mentioned products are represented as:

\[
\begin{align*}
\text{OCH}_3 & \quad \text{CH=COOH} \\
\text{CH}_3 & \quad \text{COOH} \\
\end{align*}
\]

(VIII) \hspace{1cm} \hspace{1cm} \hspace{1cm}

\[
\begin{align*}
\text{OCH}_3 & \quad \text{C=CH-COOH} \\
\text{CH}_3 & \quad \text{COOH} \\
\end{align*}
\]

(IX) \hspace{1cm} \hspace{1cm} \hspace{1cm}

\[
\begin{align*}
\text{OCH}_3 & \quad \text{C=CH-COOH} \\
\text{CH}_3 & \quad \text{COOH} \\
\end{align*}
\]

(X)

The corresponding monocarboxylic acid m.p. 232° C. obtained in the condensation of $\beta$-cresol-ethylether, gave by the action of sulphuric acid, an indone-acetic acid m.p. 216° C. and a neutral compound m.p. 165° C. This indone-acetic acid could not however be obtained from the $\beta$-(2-ethoxy-5-methyl-phenyl)-glutaconic acid (I) by the action of sulphuric acid, the 6-methyl-coumarin-4-acetic acid being the sole product in this case.

**Conclusion.**

Pechmann's condensation consists primarily in the elimination of a molecule of water between the enolic hydroxylic group of the $\beta$-ketonic ester and the nuclear hydrogen atom of the phenol, whereas in the Simonis' reaction, it is the carboxylic group of the $\beta$-ketonic ester that eliminates water with the latter. In the present condensations of $\beta$-cresol-methyl and ethyl-ethers with acetone-dicarboxylic acid, both these reactions apparently happen simultaneously to produce the chalkone-acetic acids, and thus they
can be looked upon as a combination of Pechmann's and Simonis' reactions. Similarly the glutaric acid condensation can be called a combination of Pechmann's and Krämer's reaction.

The $\beta$-(2-methoxy-5-methyl-phenyl)-glutaconic acid (VIII) by the action of sulphuric acid, produces the indone-acetic acid (XI) as well as the 6-methyl-coumarin-4-acetic acid (VI), whereas the $\beta$-(2-ethoxy-5-methyl-phenyl)-glutaconic acid (I) gives only the latter coumarin acid, no trace of any indone-acid being obtained. The chalkone-acetic acids m.p. 252°C and 232°C. (IX) on the other hand, give only the indone-acids (XI) under these circumstances, and not even a trace of the coumarin acid. It thus appears that in the $\beta$-(2-ethoxy-5-methyl-phenyl)-glutaconic acid (I) and in both the chalkone-acetic acids, there is a restricted rotation round the bond joining the $\beta$-carbon atom of the glutaconic acid to the phenolic ether (shown in thick line). Consequently the $\beta$-(2-ethoxy-5-methyl-phenyl)-glutaconic acid can be represented only by the formula (XIV) and the chalkone-acetic acid by (XVI). Thus it must be presumed that in the condensation of this glutaconic acid with $p$-cresol-ethylether, the formation of the chalkone-acetic acid has been preceded by the change of the glutaconic acid from the structure (XIV) to (XV) which alone is capable of producing the indone-acid.

\[ \text{HOOC-CH}_2\text{CH}_2\text{COOH} \quad \text{HOOC-CH}_2\text{CH}={}\text{COOH} \quad \text{HOOC-CH}_2\text{CH}={}\text{CO} \quad \text{C}_1 \]

\[ \text{CH}_2\text{COOH} \quad \text{CH}={}\text{COOH} \quad \text{CH}={}\text{CO} \quad \text{RO} \]

\[ \text{RO} \quad \text{RO} \quad \text{RO} \]

\[ \text{(XIV)} \quad \text{(XV)} \quad \text{(XVI)} \]

This great difference in the resulting condensation products, caused by the mere replacement of the methoxy group in the $p$-cresol-methyl-ether by ethoxy group, is striking.

**Experimental.**

Condensation of $p$-cresol-ethylether with acetone-dicarboxylic acid.—Citric acid (200 g.) was finely powdered and covered with concentrated sulphuric acid (240 c.c.). The mixture was shaken well and fuming sulphuric acid (20 per cent. SO$_3$; 80 c.c.) was gradually added. Immediately a vigorous reaction commenced with frothing and evolution of carbon monoxide, which was completed by heating on a water-bath at 60°C. with shaking at intervals, till a clear orange solution was obtained. It was cooled in a freezing mixture to a temperature of about 2–3°C. and $p$-cresol-ethylether (65 c.c.) was gradually added with shaking. After keeping at this temperature
for 3½ hours, the reaction mixture was poured on 1000 g. of cracked ice, when the sticky mass thus separated turned into a brittle cake on keeping overnight. This was filtered, dissolved in dilute sodium carbonate solution, this solution washed with ether to remove any unchanged p-cresol-ethyl-ether and other neutral impurities and acidified. The semisolid mixture of acids thus obtained became granular on rubbing and keeping overnight with water. Yield 47 g.

β-(2-ethoxy-5-methyl-phenyl)-glutaronic acid.—The above mixture of acids was treated with 4 litres of boiling water and filtered, when the filtrates on cooling deposited crystals of the glutaronic acid. It was recrystallised from water as colourless short rods m.p. 153°C. (decomp.). On treating with concentrated sulphuric acid at 60°C., or 80% sulphuric acid overnight, it gave only the 6-methyl-coumarin-4-acetic acid m.p. 180°C. (decomp.) (Found: Eq=132; C=63.44%; H=6.6%; C₄H₆O₅ requires Eq=132; C=63.6%; H=6.6%).

The hydroxy-anhydride crystallised in colourless needles from benzene, m.p. 112°C. It titrates as a monobasic acid and gives phenolic colouration with ferric chloride in cold alcoholic solution (Found: Eq=243; C=68.15%; H=5.6%; C₁₄H₁₄O₄ requires Eq=246; C=68.29%; H=5.69%).

The semianilide, prepared from the hydroxy anhydride and aniline in benzene solution, crystallised from 60% aqueous methyl alcohol in hexagonal plates m.p. 136°C. It decomposed after 150°C. temperature to give the anil described below (Found: C=70.5%; H=6.1%; C₂₀H₂₉O₄N requires C=70.8%; H=6.16%).

The hydroxy-anil crystallised from 80% alcohol in yellowish silky needles m.p. 163°C. (Found: C=74.5%; H=5.80%; C₂₀H₂₉O₄N requires C=74.76%; H=5.80%).

The monolactone of ββ’-(22’-diethoxy-55’-dimethyl-diphenyl)-glutaric acid.—The water insoluble residue in the above (about 15 g.), on crystallisation from alcohol, melted between 190–200°C. This was esterified by alcohol and sulphuric acid and the resulting mixed esters were, by fractional crystallisation from 80% methyl alcohol, separated into two fractions, the more insoluble one melting at 124°C., and the other at 110–115°C. Hydrolysis of the former gave the monolactonic acid which crystallised from alcohol in stout colourless needles, m.p. 205°C. yield 8 g. The acid titrated as monobasic acid and gave an insoluble barium salt in the cold. The acid was soluble in alcohol, acetic acid, acetone, and insoluble in water, benzene, petrol or chloroform (Found: Eq=356; C=71.00%; H=6.12%; C₂₁H₂₉O₅ requires Eq=354; C=71.2%; H=6.2%).
The ethyl-ester crystallised from methyl alcohol in colourless hexagonal rods m.p. 124° C. (Found: C=72·1%; H=6·72%; \text{C}_2\text{H}_2\text{O}_5 \text{requires} \ C=72·25\%; \text{H}=6·8\%).

The 22'-diethoxy-55'-dimethyl-chalkone-\alpha-acetic acid.—The more soluble fraction of the mixed ethyl esters melting between 110–115° C., was hydrolysed by alcoholic potash, and the resulting mixture of acids melting between 195–215° C., was dissolved in hot 15% sodium hydroxide solution. On cooling the solution gradually, colourless shining leaflets of a sodium salt separated, which were collected at the pump under strong suction, washed with small amounts of 10% sodium carbonate solution, and acidified in cold by hydrochloric acid. The acid coming out as a fine precipitate was filtered and crystallised from a large amount of alcohol in colourless rectangular plates m.p. 232° C. yield 2 g. The acid is soluble in acetone, sparingly so in alcohol and acetic acid, and insoluble in other organic solvents. It gave an insoluble barium salt in the cold. Its solution in alkali instantaneously decolourised potassium permanganate solution. Its esters did not condense with aromatic aldehydes (Found: C=72·00%; H=6·7%; \text{Ba=14·70%; C}_2\text{H}_2\text{O}_5 \text{requires} \ C=72·25\%; \text{H}=6·8\%; (\text{C}_2\text{H}_2\text{O}_5)\text{Ba requires} \ \text{Ba}=15·25\%).

The ethyl-ester prepared by alcohol and sulphuric acid, crystallised from 80% methyl alcohol in colourless parallelogramic plates, m.p. 133° C. (Found: C=72·9%; H=7·24%; \text{C}_2\text{H}_2\text{O}_5 \text{requires} \ C=73·2\%; \text{H}=7·32\%).

Semicarbazone was prepared by refluxing the acid with semicarbazide hydrochloride and sodium acetate in alcoholic solution for 3 hours. On cooling, the semicarbazone separated and when recrystallised from alcohol melted at 264° C. (decomp.) (Found: C=65·3%; H=6·4%; \text{C}_2\text{H}_2\text{O}_5\text{N}_3 \text{requires} \ C=66·6\%; \text{H}=6·6\%).

Semicarbazone of the ethyl ester was obtained by refluxing the reactants in alcoholic solution for 7 hours. It crystallised from alcohol in needles m.p. 171° C. (decomp.) (Found: C=66·6%; H=6·85%; \text{C}_2\text{H}_2\text{O}_5\text{N}_3 \text{requires} \ C=66·8\%; \text{H}=7·06\%).

Condensation of \beta-(2-ethoxy-5-methyl-phenyl)-glutaconic acid with \text{p-cresol-ethylether}.—The recrystallised glutaconic acid (10 g.) was finely powdered and dissolved in previously ice-cooled 80% dilute sulphuric acid—1 vol. water: 4 vol. sulphuric acid—(50 c.c.). The \text{p-cresol-ethylether} (20 c.c.) was then added gradually with shaking at intervals. On continuing the shaking until the two layers disappeared—about 2 hours—the clear orange solution was allowed to stand at the room temperature for 20 hours. This reaction mixture was then poured on 200 g. of crushed ice, when a sticky
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mass separated which became granular on keeping overnight. It was filtered, taken up in dilute sodium carbonate, the solution filtered, washed with ether to remove the excess of p-cresol-ethylether, and acidified by hydrochloric acid. The mixed acids were filtered and treated with 400 c.c. of boiling 10% aqueous acetic acid, then with 100 c.c. of boiling water, filtered, and dried. Yield of mixed acids 3.5 g. This was esterified by alcohol and sulphuric acid, and separated into the monolactonic acid m.p. 205° C. yield 2 g., and the chalkone-acetic acid m.p. 232° C. yield 1 g.; exactly as above. The acetic acid filtrate on cooling gave the 6-methyl-coumarin-4-acetic acid.

Action of 80% sulphuric acid on 22'-diethoxy-55'-dimethyl-diphenyl-chalkone-acetic acid: Formation of 7-ethoxy-4-methyl-3-keto-indone-acetic acid.—The chalkone-acetic acid (2.5 g.) was finely powdered and dissolved in 80% sulphuric acid by rubbing and warming a little. The red fluorescent solution on keeping over-night at the room temperature was poured in water, the precipitate taken up in dilute sodium carbonate, filtered and acidified. The acid was crystallised from alcohol in short yellow needles m.p. 216° C. (decomp.); yield 1 g. The acid is sparingly soluble in alcohol and acetic acid and insoluble in water, benzene, petrol or chloroform. It titrates as a monobasic acid and gives intensely coloured solutions with caustic alkalies. This indone acid could not be obtained from the β-(2-ethoxy-5-methyl-phenyl)-glutaconic acid (Found: C=68.21%; H=5.65%; C_{14}H_{14}O_{4} requires C=68.3%; H=5.7%).

The ethyl-ester prepared from the acid by alcohol and sulphuric acid crystallised from 80% alcohol as yellow flat needles m.p. 169° C. (Found: C=69.8%; H=6.45%; C_{15}H_{18}O_{4} requires C=70.0%; H=6.37%).

The semicarbazone was obtained by refluxing the reactants in alcoholic solution for 2 hours. Light needles m.p. 247° C. (decomp.) (Found: C=59.23%; H=5.47%; C_{16}H_{17}O_{4}N_{3} requires C=59.4%; H=5.6%).

The semicarbazone of the ethyl ester crystallised from alcohol in yellow needles m.p. 208° C. (decomp.) (Found: C=61.51%; H=6.25%; C_{17}H_{21}O_{4}N_{3} requires C=61.63%; H=6.34%).

The neutral compound from the above chalkone-acetic acid.—This was obtained by treating the chalkone-acetic acid m.p. 232° (2 g.) with concentrated sulphuric acid (10 c.c.) at a temperature of 60° C. for 1 hour. The precipitate obtained on pouring the resulting fluorescent solution in water gradually became granular on keeping for few hours. It was filtered, treated with dilute sodium carbonate solution, and the insoluble portion was crystallised from methyl alcohol in rectangular plates m.p. 165° C. yield 1.5 g.
(Found: C=75.5%; H=6.46%; C₂₉H₄₄O₄ requires C=75.8%; H=6.5%).

The *semicarbazone* was obtained by refluxing the neutral compound in alcoholic solution with the reagents for 3 hours, and crystallised from alcohol in parallelogramic plates m.p. 245° C. (decomp.) (Found: C=63·2%; H=6·3%; monosemicarbazone C₂₉H₄₇O₄N₃ requires C=68·4%; H=6·4%; disemicarbazone C₃₂H₃₀O₄N₅ requires C=62·76%; H=6·28%).

*Action of sulphuric acid on the monolactonic acid m.p. 205° C.:* Formation of the dilactone of ββ′-(22'-diethoxy-55'-dimethyl-diphenyl)-glutaric acid.—The recrystallised monolactonic acid (5 g.) was dissolved in concentrated sulphuric acid (20 c.c.) and the solution heated at a temperature of 60° C. for one hour. On pouring in 100 c.c. of ice water and keeping overnight, the crystalline precipitate which separated was filtered and treated with boiling dilute sodium carbonate. The sodium carbonate filtrates on acidification gave the 6-methyl-coumarin-1-acetic acid (yield 1 g.) m.p. 180° C. (decomp.). The neutral dilactone insoluble in sodium carbonate was washed with water and crystallised from 100 c.c. methyl alcohol in colourless pyramids m.p. 184° C. (yield 3 g.) (Found: C=73·90%; H=5·14%; C₁₅H₁₄O₄ requires C=74·00%; H=5·2%). Action of 80% sulphuric acid on the monolactonic acid overnight produced only the 6-methyl-coumarin-4-acetic acid, and no neutral dilactone. The dilactone slowly went in solution in boiling caustic alkalies, which on acidification carefully after cooling in ice gave an acid, which decomposed at 110° C. and produced the original dilactone. This acid gave intense phenolic colouration with ferric chloride in cold alcoholic solution which disappeared on warming. All the attempts to purify this acid were rendered futile, each time the dilactone being the resulting product.

*Hydrolysis and ethylation of the dilactone m.p. 184° C.:* Formation of ββ′-(22'-diethoxy-55'-dimethyl-diphenyl)-glutaric acid.—The neutral dilactone (1·5 g.) was finely powdered and refluxed with (30 c.c.) of 25% sodium hydroxide solution, when it gradually dissolved. The pale yellow solution was filtered and heated on a small flame just to boiling, while freshly distilled diethyl-sulphate (6 c.c.) was gradually run in during about 20 minutes; shaking the reaction mixture at frequent intervals. The resulting liquid was refluxed for 15 minutes, when the diethyl ester of the glutaric acid separated as a yellow oil, which solidified to a colourless crystalline mass on cooling to the room temperature. It was filtered, dried in a vacuum over calcium chloride, and crystallised from methyl alcohol, obtaining thus (1·2 g.) of colourless parallelogramic plates m.p. 82° C. Hydrolysis of the diethyl ester with alcoholic potash furnished the glutaric acid which crystallised from alcohol in colourless parallelogramic plates, m.p. 219° C.
Some more of the glutaric acid was obtained by cooling the above alkali filtrates in ice, when its sodium salt separated as colourless silky needles. These were filtered, treated with boiling dilute hydrochloric acid for a while, again filtered, washed with water, and taken up in dilute sodium carbonate solution. Any undissolved neutral product was filtered out and the solution acidified, thus giving (0.5 g.) more of the glutaric acid. The glutaric acid is soluble in acetone and acetic acid, sparingly so in alcohol or ethyl acetate and insoluble in water, petrol, or benzene. It gave an insoluble barium salt in cold (Found: C=68.92%; H=6.96%; Eq=201; C\textsubscript{23}H\textsubscript{28}O\textsubscript{6} requires C=69.00%; H=7.00%; Eq=200. Found: Ba=25.2%; C\textsubscript{23}H\textsubscript{28}O\textsubscript{6}Ba requires Ba=25.6%).

The glutaric acid, by warming with concentrated sulphuric acid, gave a mixture mainly of the dilactone m.p. 184°C. and 6-methyl-coumarin-4-acetic acid, with a small amount of the monolactonic acid m.p. 205°C. Similarly the monolactonic acid (2 g.) by hydrolysis and ethylation with 25% sodium hydroxide (25 c.c.) and diethyl sulphate (5 c.c.) gave the glutaric acid m.p. 219°C. (decomp.).

The diethyl ester could also be prepared from the glutaric acid by alcohol and sulphuric acid (Found: C=70.8%; H=7.8%; C\textsubscript{27}H\textsubscript{36}O\textsubscript{6} requires C=71.00%; H=7.90%).

The dimethyl ester crystallised from methyl alcohol in colourless flat needles, m.p. 105°C. (Found: C=69.90%; H=7.4%; C\textsubscript{25}H\textsubscript{32}O\textsubscript{6} requires C=70.10%; H=7.47%).

Unlike the glutaric acids, these glutaric esters do not condense with aromatic aldehydes. On condensing the dimethyl ester (1 mol.) with dimethyl oxalate (3 mols.) in the presence of sodium methoxide, according to Dieckemann's method, most of it was recovered unchanged. Very small amount of a substance melting above 160°C. was however obtained as a more soluble fraction, which on further examination appeared to be a complex mixture.

The anhydride was prepared from the glutaric acid by the action of acetic anhydride or by thermal decomposition at 220°C. temperature. It crystallised from benzene in colourless flat rods, m.p. 189°C. It is insoluble even in caustic alkalies, and does not give any colouration with ferric chloride in cold alcoholic solution: (Found: C=72.08%; H=6.73%; C\textsubscript{29}H\textsubscript{26}O\textsubscript{5} requires C=72.25%; H=6.8%).

The acid-anilide of the glutaric acid was prepared from the above anhydride and aniline in benzene solution, and crystallised from 80% alcohol in colourless silky needles m.p. 198°C. (decomp.) (Found: C=73.00%; H=6.7%; C\textsubscript{27}H\textsubscript{32}O\textsubscript{6}N requires C=73.24%; H=6.9%).
The anil is formed by the action of aniline on the glutaric acid at a temperature of 220°C or by the decomposition of the above acid anilide at its melting point. It was crystallised from alcohol in colourless rectangular prisms m.p. 216°C. It is insoluble in even boiling caustic alkalies and does not give any colouration with ferric chloride (Found: C=75.9%; H=6.62%; C₂₅H₃₁O₄N requires C=76.15%; H=6.78%).

ββ'-(22'-dimethoxy-55'-dimethyl-diphenyl)-glutaric acid.—This dimethoxy acid corresponding to the diethoxy, could not be had either in the condensation of p-cresol-methylether with acetone-dicarboxylic acid, or by condensing the β-(2-methoxy-5-methyl-phenyl)-glutaconic acid with p-cresol-methyl ether (see below). This glutaric acid was however prepared from the above dilactone m.p. 184°C by hydrolysis and methylation. The compound crystallised from alcohol in colourless rectangular prisms, m.p. 192°C (decomp.). It gave an insoluble barium salt in cold (Found: C=67.62%; H=6.38%; Eq.=188; C₂₅H₂₅O₄ requires C=67.74%; H=6.45%; Eq.=186).

Condensation of p-cresol-methylether with acetone-dicarboxylic acid (improved method).—Finely powdered citric acid (200 g.) was mixed with concentrated sulphuric acid (200 c.c.) and fuming sulphuric acid (20% SO₃, 120 c.c.) was later added. The mixture was shaken well and heated on a water bath at 60°C. temperature till the evolution of carbon monoxide stopped and a clear orange solution was obtained. This was cooled in a freezing mixture, p-cresol-methylether (80 c.c.) gradually added with shaking and the reaction mixture, on standing for 3 hours, poured over 800 g. of crushed ice. The thus separated sticky solid became crystalline on keeping overnight, was then filtered, and treated with dilute sodium carbonate solution to remove any unchanged p-cresol-methylether, when on acidification 52 g. of mixed acids were obtained. This was treated with boiling 10% acetic acid (1000 c.c.) and filtered, when the filtrate on cooling deposited crystals of the β-(2-methoxy-5-methyl-phenyl)-glutaconic acid. The glutaconic acid crystallised from water in colourless rectangular plates m.p. 167°C (decomp.). Gogte and Limaye give the m.p. 169°C (decomp.).

22'-dimethoxy-55'-dimethyl-chalkone-a-acetic acid.—The portion insoluble in acetic acid in above, was crystallised from alcohol. This was dissolved in least amount of boiling 10% sodium carbonate solution, which on cooling deposited the sodium salt of the chalkone-acetic acid as colourless leaflets. These were collected at the pump under strong suction, acidified with hydrochloric acid, and the chalkone-acetic acid thus obtained was recrystallised from alcohol in colourless parallelogramic plates, m.p. 252°C. yield 12 g. The acid is a remarkably stable compound being unchanged even on fusion.
with solid potash. It is soluble in acetone, sparingly so in acetic acid or alcohol, and insoluble in other organic solvents. It gave an insoluble barium salt in cold. Its ethyl ester did not condense with aromatic aldehydes (Found: C=71.00%; H=6.13%; Eq. =346; C_{22}H_{22}O_{6} requires C=71.2%; H=6.2%; Eq. =354. Found: Ba=15.6%; (C_{22}H_{21}O_{4})_{2}Ba requires Ba=16.25%).

*The ethyl-ester crystallised from 70% methyl alcohol in parallelogramic plates m.p. 122° C. (Found: C=72.1%; H=6.7%; C_{23}H_{26}O_{5} requires C=72.24%; H=6.8%).

*The semicarbazone was obtained by refluxing the alcoholic solution of the chalkone-acetic acid with semicarbazide hydrochloride and sodium acetate for 4 hours. When recrystallised from alcohol, it melted at 277° C. (decomp.) (Found: C=64.00%; H=5.92%; C_{22}H_{24}O_{10}N_{3} requires C=64.24%; H=6.08%).

*The semicarbazone of the ethyl-ester crystallised from alcohol in colourless needles m.p. 219° C. (decomp.) (Found: C=65.38%; H=6.44%; C_{24}H_{29}O_{5}N_{3} requires C=65.6%; H=6.6%).

Synthesis of the chalkone-acetic acid m.p. 252° C. from β-(2-methoxy-5-methyl-phenyl)-glutaconic acid and p-cresol-methylether.—The glutaconic acid (5 g.) was finely powdered and dissolved in previously ice-cooled dilute—4 vols. acid: 1 vol. water—sulphuric acid (40 c.c.). p-cresol-methylether (10 c.c.) was then gradually added with shaking and the whole allowed to stand overnight at the room temperature. On pouring the reaction mixture on 100 g. of powdered ice, a partly sticky mass, becoming granular on keeping for few hours, separated. It was filtered, washed, treated with 100 c.c. of boiling 10% aqueous acetic acid, and filtered. The chalkone-acetic acid insoluble in acetic acid, was purified as above. Yield 1.5 g. The acetic acid filtrates on cooling gave the 6-methyl-coumarin-4-acetic acid.

Action of sulphuric acid on the chalkone-acetic acid m.p. 252° C.—On keeping a solution of the chalkone-acetic acid (2 g.) in 80% sulphuric acid (15 c.c.) overnight at room temperature, the indone-acetic acid (1.1 g.) melting at 218° C. (decomp.), was obtained, and was found identical with that described by Gogte and Limaye. Action of concentrated sulphuric acid (10 c.c.) on the glutaconic acid (2 g.) at 60° C. for 1 hour, gave on pouring the reaction mixture in water and filtering, 1.4 g. of a precipitate. It was washed with boiling water, treated with boiling dilute sodium carbonate solution and

* These three compounds had been described in the M.Sc. Thesis of the author, but the melting points of the latter two were given as 272° C., and 212° C., and their method of preparation was also different.
separated into 0.6 g. of the above indole-acetic acid and 0.8 g. of a neutral compound. This was recrystallised from 40 c.c. of alcohol in parallelogramic plates m.p. 214°C. (Found: C=74.87%; H=5.82%; C_{21}H_{20}O_{4} requires C=75.00%; H=5.95%).

The semicarbazone of the neutral melted at 253°C. (decomp.) (Found: C=61.65%; H=5.6%; disemicarbazone, C_{25}H_{22}O_{4}N_{5} requires C=61.30%; H=5.78%; monosemicarbazone C_{25}H_{23}O_{4}N_{5} requires C=67.17%; H=5.85%).

Benzylidene derivative of the neutral.—The neutral compound was dissolved in alcohol and refluxed with benzaldehyde and alcoholic potash for one hour. Alcohol was evaporated, the residue rubbed with water to remove the alkali, and the unreacted benzaldehyde removed with steam. On crystallisation from alcohol the benzylidene compound melted at 174°C. (Found: C=78.7%; H=5.41%; C_{22}H_{24}O_{4} requires C=79.24%; H=5.66%).

The ethyl-ester of the above chalitone-acetic acid m.p. 252°C., when treated with concentrated sulphuric acid at 50–60°C. produced the ethyl ester m.p. 158°C. of the above indole-acetic acid m.p. 218°C., mainly and a small amount of the indole-acetic acid itself, but the above neutral compound m.p. 214°C. could not be detected. Concentrated nitric acid at room temperature transformed the chalitone-acetic acid into the indole-acetic acid, and hence its oxidation with nitric acid yielded the phthalic anhydride m.p. 186°C. identical with that obtained by Limaye and Gogte^9 (Ref. M.Sc. Thesis of the author).

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NOTE:—With regard to Part I of this series (This Journal Vol. I, No. 1, pp. 48–60) the author wishes to state the following:—The words “while working at the Ranade Institute for his M.Sc. Thesis” should be inserted after the sentence “in extending Limaye and Bhave’s method” (p. 48, line 2 from bottom). The new method of synthesis of β-aryl glutaconic acids described therein, was discovered in the case of the glutaconic acids from β- and m-cresol-methylethers, during the last term of the stay of the author at the Ranade Institute, Poona, and the extension of this new method of synthesis to the glutaconic acids of the naphthol series, was carried out at the Indian Institute of Science, Bangalore.