

CONTRIBUTION TO THE CHEMISTRY  
OF  
PHENYL GLUTARIC ACIDS

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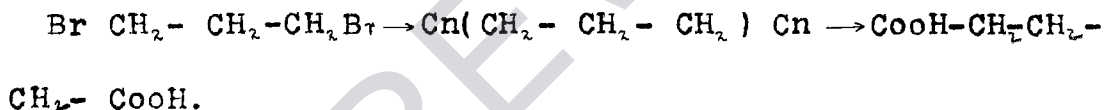
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Aliphatic Glutaric Acids.

Although succinic and glutaric acids have been before the chemical world as a study for some time, presenting an open field of many possibilities, it is only within the last few years that the alkyl derivatives of these acids have become of special interest to investigators. While the knowledge of the aliphatic alkyl succinic and glutaric acids has been materially increased of late by Auwers, Perkin, and others, the corresponding aromatic compounds have been but slightly investigated.

Ordinary glutaric acid was first obtained from amine glutaric acid, which is one of the products formed by the decomposition of albumenoids. Afterwards, glutaric acid was found in wool-sweat and in beet juice. The constitution of glutaric acid and its derivatives is clearly established by the following synthetic reactions:

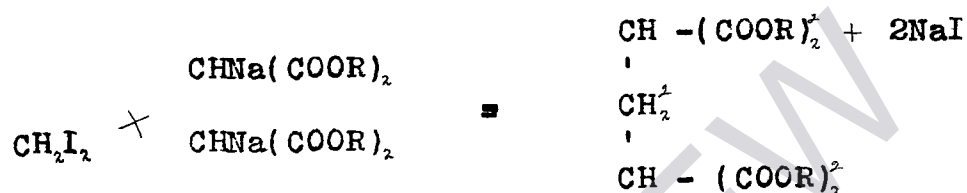
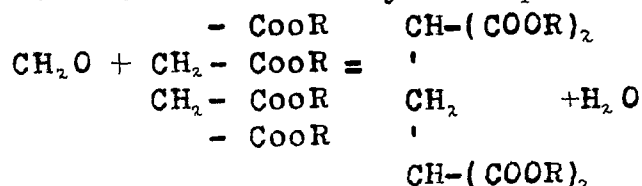
1st.- Trimethylene bromide, treated with potassium cyanide, gives trimethylene cyanide; this on hydralizing yields glutaric acid.



2d. Sodium aceto acetic ester reacts with B Iodopropionic ester forming acetyl glutaric ester, from which glutaric acid is readily obtained.

3d. Form aldehyde condenses with malonic ester forming methylene dimalonic ester. This ester may also be formed by the action of methylene iodide on sodium malonic ester; the latter reaction gives the better yield. The re-

actions involved may be expressed as follows:



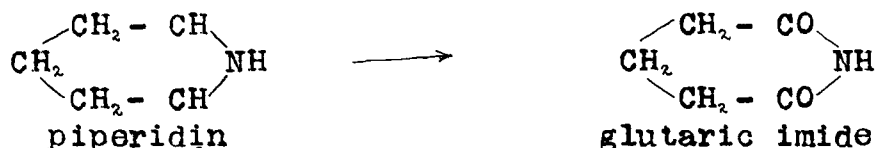
The methylene dimalonic ester on hydralizing in acid solution, loses carbonic anhydride and forms glutaric acid.

Glutaric acid is very soluble in water out of which it crystallizes in glossy prisms, melting at  $97.5^\circ$ . If heated sharply it distills at about  $290^\circ$  unchanged; Upon slow distillation a mixture of the acid and the anhydride is obtained. Of the salts of glutaric acid, the zinc salt is the most characteristic. It is difficultly soluble in cold water (1pt. to 102- at  $18^\circ$ ), less soluble in hot water, a phenomenon quite frequently observed with the salts of the higher dicarboxylic acids; thus when a sat-

urated cold solution is heated, a precipitate of rectangular tablets with reentering angles is formed.

Among the more important general derivatives of glutaric acid may be mentioned the following: dimethyl glutarate- B.P. 236.5° - 237° Sp.gr. at 20° - 1.024; the anhydride M.P. 56° - 57° - B.P., with partial decomposition, 286° - 288°; the nitril (trimethylene cyanide) Sp.gr. at 11° - 0.996 B.P. 142° at pressure of 10 m.m. 276° at normal pressure with decomposition; the imide  $\begin{pmatrix} \text{CH}_2 - \text{CO} \\ \text{CH}_2 - \text{CO} \end{pmatrix} \text{NH}$  bright glistening tablets- M.P. 154.5°.

This imide is of special interest since it may be formed by the oxidation of Piperidin with peroxide of hydrogen. Reaction as hereindicated:



The homologues of glutaric acid are principally obtained by the following reactions: 1st. condensation of aldehydes

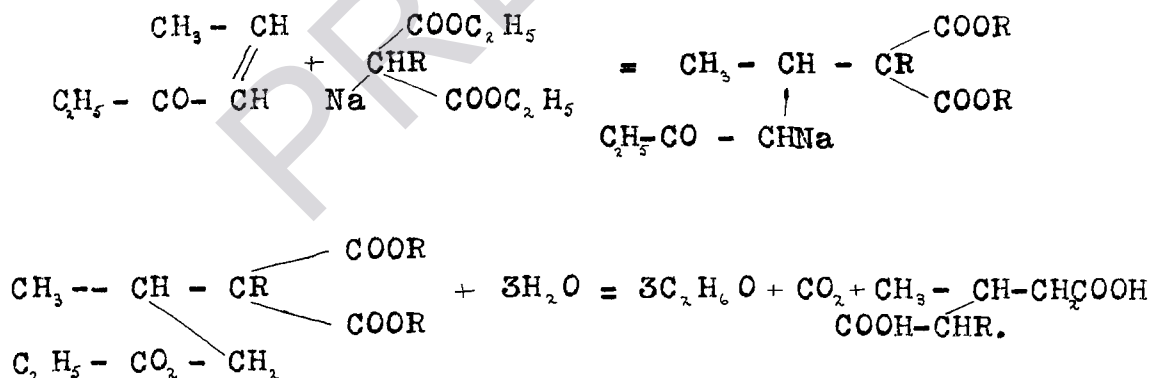
with malonic acid or ester leads to B-monalkyl-glutaric acid.

2d. The action of B-Iodopropionic ester on alkyl acetoacetic ester leads to a mon-alkyl-glutaric acid.

3d. The action of methylene iodide on the sodium compound of  $\alpha$ -cyan fatty acid esters- leads to symmetric - di alkyl- glutaric acids.

4th. The addition of a substituted malonic ester to an unsaturated ester leads to A-B-Alkyl-glutaric acids.-

For example:



Finally the formation of homologues of glutaric acid through reactions which might be expected to lead to the

homologues of succinic acid is interesting.

In the entire group through the variety of structures possible there are many occasions for isomers - especially those corresponding to the symmetrical stereo-isomers of the di-alkyl succinic acids .

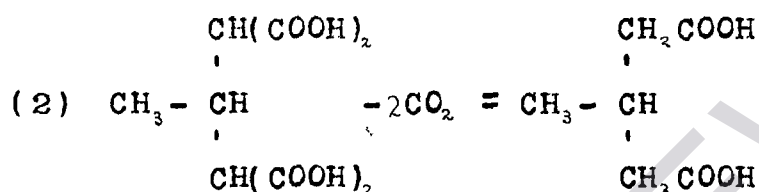
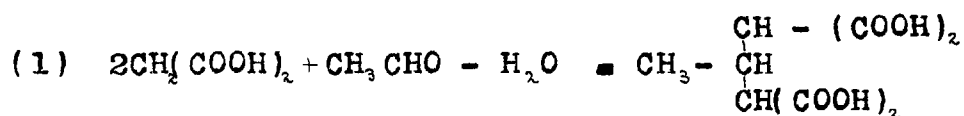
The di-methyl glutaric acid ( $\text{COOH} - \underset{\text{CH}_3}{\text{CH}} - \text{CH}_2 - \underset{\text{CH}_3}{\text{CH}} - \text{COOH}$ ) exists in two modifications, one easily soluble with a low melting point, the other difficultly soluble with a higher melting point. The "Umwandlungs" conditions are just the opposite as to what they are in the succinic acid series; the difficultly soluble acid is converted into the easily soluble one, by heating with hydrochloric acid to  $200^\circ$ . Both acids yield the same anhydride, from which, upon hydralizing, the difficultly soluble one is obtained.

As to the power of conducting electricity, the homologues of glutaric acid excel glutaric acid itself; an exception to this is trimethyl glutaric acid, whose dissociation constant is smaller than the same for glu-

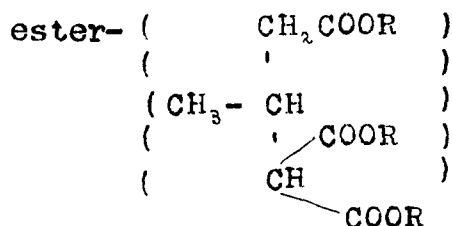
taric acid. Perhaps the constitution of the acid is not yet correctly established.

The alkyl homologues which have been studied in regard to their melting points, dissociation constants and as to their anhydrides, are - A-methyl, B-methyl, B-ethyl, B-Propyl, and B-butyl glutaric acids.

The study of the non-alkyl derivatives of glutaric acid has been confined principally to the B-derivatives, as until quite recently, only one A-derivative, ( $\alpha$ -methyl glutaric acid) was known. The principal aliphatic B-derivative that had been made and studied previous to 1896 are B-methyl, B-ethyl, B-isopropyl, and B-isobutyl glutaric acid. Of these B-methyl glutaric acid was first made by Kommenos by warming for several days a mixture of 100 grms. malonic acid, 88 grms. par-aldehyde and 100 grms. of acetic anhydride upon the water bath. The reaction goes as follows:-



It is interesting to note that in the synthesis of aromatic glutaric acids a condensation analogous to that of Komnenos does not take place. On the other hand, cinnamic ester deports itself in a manner similar to crotonic ester, which was used in preparing B-methyl glutaric acid, by Auwers(1), K bner, and Meyerburg in the following manner. The crotonic ester ( $\text{C}_3\text{H}_5\text{COOR}$ ) was condensed with sodium malonic ester, gave A-methyl-propene tricarboxylic



(1) Ber.xxiv. 2888