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The Absolute Configuration of α,α′-Diethylsuccinic Acid and α-Methyl-α′-ethylsuccinic Acid

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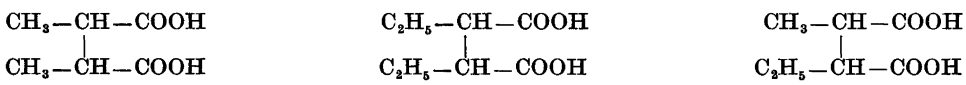
The absolute configuration of α,α′-diethylsuccinic acid has been determined by correlation to α,α′-dimethylsuccinic acid by the quasi-racemate method, using *threo*-α-methyl-α′-ethylsuccinic acid as an auxiliary substance. The dextrorotatory forms have analogous configurations expressed by the stereoformulas Ia—IIIa.

The configuration of alkylsubstituted succinic acids is of considerable interest, since they often result from oxidative degradation of various natural products. The configurational relations between monosubstituted succinic acids have been investigated by Fredga, Matell [1] and others. Some years ago, Carnmalm elucidated the configuration of α,α′-dimethylsuccinic acid (I) by degradation to methyl-ethyl-acetic acid.[2] McCasland and Proskow [3] reached the same conclusion by theoretical considerations: both methods show that the dextrorotatory acid has D-configuration as expressed by stereoformula Ia (Fischer convention) or α(R),α′(R) configuration (according to the convention of Cahn, Ingold and Prelog [4]).

The α,α′-diethylsuccinic acid (II) can be obtained from some synthetic oestrogenic hormones by ozonolysis and was therefore of special interest to one of us (L. T.). We also learnt that Professor H. Schmid, Zürich, had obtained this compound during his work on the absolute configuration of strychnine.



I II III

By agreement with Professor Schmid we started the investigation of acid II by the quasi-racemate method, which has previously proved to be of great value in correlating succinic acid configurations.[5]

Preliminary experiments were carried out with α,α′-dimethylsuccinic acid and α-ethylsuccinic acid, whose configurations are known [2,6] but no quasi-

racemic compounds were found. We therefore turned to *threo*-α-methyl-α'-ethylsuccinic acid (III), described by Berner *et al.*[7] This acid gave positive results with both I and II (Figs. 1—4). The diagrams were, however, a little difficult to interpret, partly due to the fact that the acid III melts much lower than I and II. In such cases the quasi-racemic compound may melt incongruently, the maximum being more or less overlapped by the descending curve branch.[8]

It is well known that X-ray analysis is a standard method for phase studies, and this method has also been successfully utilised for the detection of quasi-racemic compounds.[8-10] X-Ray analysis was therefore carried out with mixtures of the optically active acids as a complement to the melting-point investigation.

The acid couple (+)I,(+)III (Fig. 1) gives a diagram characteristic of a system forming solid solutions. The X-ray powder photogram also indicates solid solutions but it is difficult to say which compound is solvent and which is solute.

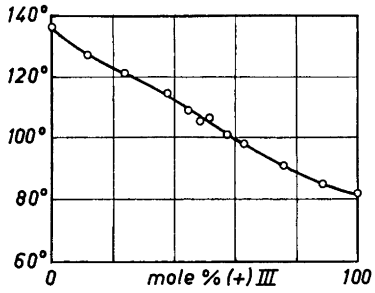


Fig. 1. (+)I and (+)III.

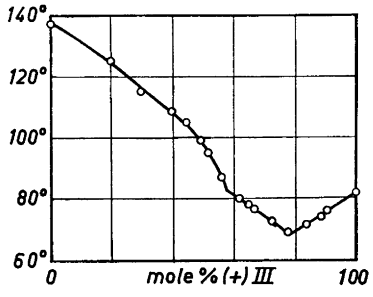


Fig. 2. (−)I and (+)III.

The couple (−)I,(+)III (Fig. 2) shows a new phase, probably a quasi-racemate, but the molecular compound melts incongruently. The X-ray photograms of the components are rather similar but the photogram of the mixture indicates a new phase.

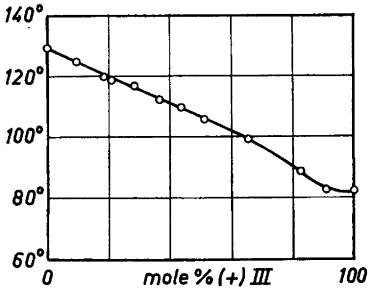


Fig. 3. (+)II and (+)III.

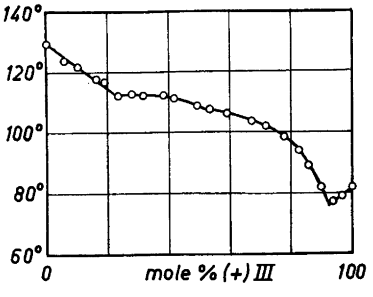
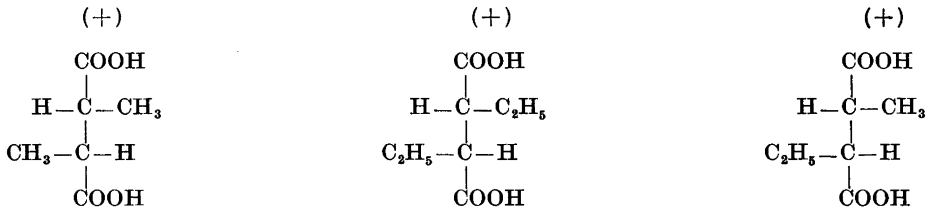


Fig. 4. (−)II and (+)III.

The system (+)II,(+)III gives a diagram indicating solid solutions (Fig. 3). In the region 90—100 % (+)III there is an indication of restricted solubility. This is confirmed by the X-ray photogram, which shows solubility of (+)III in (+)II, except at high amounts of (+)III, where the diffraction lines of this compound appear.

Compounds (−)II and (+)III show a very evident quasi-racemate from the X-ray photogram. The melting-point curve (Fig. 4) indicates a second molecular compound beside the 1:1 compound. It is suggested that it is formed in the molar ratio 1:3.

Summing up, the phase studies permit the conclusion that the acids with opposite modes of rotations also have opposite configurations. The configuration for the three dextrorotatory acids will then be α(R),α'(R) (Cahn-Ingold-Prelog convention) or according to formulas Ia—IIIa (Fischer convention).



Ia IIa IIIa

During his work, Professor Schmid reached the same conclusion by correlating diethylsuccinic acid by double homologisation to β,β'-diethyladipic acid.[11] The configuration of the latter is reported to be known.[12]

EXPERIMENTAL

α,α'-Dimethylsuccinic acid (I). The acid was prepared and resolved into the optical antipodes by the method of Berner and Leonardsen.[7]

α,α'-Diethylsuccinic acid (II). The dextro and laevo forms were kindly submitted by Professor Schmid.

threo-*α-Methyl-α'-ethylsuccinic acid.* Part of the material was kindly submitted by Professor Berner and the rest was synthesised and resolved according to his method.[7] The laevorotatory form is very difficult to obtain in a pure state, and therefore only the dextro form was prepared.

Melting point diagrams. The mixtures were prepared by dissolving weighed quantities of the components in a few drops of ether. After evaporating and drying, the mixtures were thoroughly powdered. The melting points were recorded using a Kofler hot stage microscope.[13]

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