XIX.—*Stereoisomeric $\alpha\alpha'$ -Dimethylpimelic acids.*

By F. STANLEY KIPPING, Ph.D., D.Sc.

$\alpha\alpha'$ -DIMETHYLPIMELIC acid was first described by the author and Mackenzie (Trans., 1891, **59**, 569), by whom it was obtained as a bye-product in the course of some experiments on the preparation of diacetylheptane, $\text{CH}_3\cdot\text{CHAc}\cdot[\text{CH}_2]_3\cdot\text{CHAc}\cdot\text{CH}_3$; this diketone being required in considerable quantities for the purpose of examining its behaviour on reduction (Kipping, Trans., 1893, **63**, 111), an alcoholic solution of trimethylene bromide was treated with ethylic sodio-methylacetoacetate, and the product—ethylic dimethyldiacetyl-pimelate—was hydrolysed with alcoholic potash. As is usual in such cases, the ethereal salt underwent both ketonic and acid hydrolysis, so that, in addition to diacetylheptane, $\alpha\alpha'$ -dimethylpimelic acid and $\alpha\alpha'$ -dimethyl- α' -acetylcaproic acid were formed, in accordance with the equations

* Prepared and analysed by Mr. Lander.

These two acids could not be satisfactorily separated by fractional distillation under reduced pressure, or by any of the ordinary methods, but, by taking advantage of the fact that the ammonium salt of dimethylacetylcaproic acid undergoes dissociation in boiling aqueous solution, whereas the neutral ammonium salt of dimethylpimelic acid is converted into the ammonium hydrogen salt, their separation was easily accomplished; for this purpose, it was only necessary to dissolve the mixture in ammonia, boil the solution until ammonia ceased to be evolved, and then extract the dimethylacetylcaproic acid with ether. The aqueous solution of ammonium hydrogen dimethylpimelate was then acidified, and the organic acid extracted by again shaking with ether; the yellow, or brown, oily dimethylpimelic acid which remained on evaporating the ethereal solution was further purified by fractional distillation under reduced pressure, and finally by recrystallisation.

Dimethylpimelic acid was also obtained, in a somewhat different manner, by the author and Mackenzie, namely, by the hydrolysis of its ethylic salt, a compound which was directly produced in large quantities when the alcohol employed in the preparation of ethylic dimethyldiacetylpmelate was not sufficiently free from water; the crude acid, obtained in this manner, was less impure than that separated from the dimethylacetylcaproic acid, and solidified more readily and completely, but not until it had been fractionally distilled under reduced pressure.

The crystalline dimethylpimelic acid, prepared by these methods, did not melt at all sharply, and very great difficulty was experienced in recrystallising it, as it was almost invariably deposited from solvents in an oily condition; ultimately, however, it was obtained in transparent crystals, melting sharply at $80-81^\circ$.

A few months after the publication of these observations, a paper by Perkin and Prentice, containing an account of pimelic acid and its homologues—and amongst them $\alpha\alpha'$ -dimethylpimelic acid—was communicated to the Society (Trans., 1891, 59, 818). These acids were prepared by treating ethylic pentanetetracarboxylate with sodium ethoxide and an alkyl iodide in alcoholic solution,

hydrolysing the products, and then decomposing the resulting tetracarboxylic acids by heating them at 200—220°,

The $\alpha\alpha'$ -dimethylpimelic acid which they thus obtained should obviously have been structurally identical with the acid described by the author and Mackenzie, and, as a matter of fact, in most respects, the properties of the two preparations appeared to be very similar; the boiling point of the ethylic dimethylpimelate prepared by Perkin and Prentice was also practically the same as that of the ethylic salt which had been described by the author and Mackenzie. In one important point, however, there was disagreement as regards the properties of the acid, inasmuch as Perkin and Prentice found its melting point to be 74—76°, and, in spite of repeated recrystallisation, they were unable to observe any alteration or any further approximation to the melting point (80—81°) given by the author and Mackenzie.

The two papers already referred to were closely followed by a third, in which an account of $\alpha\alpha'$ -dimethylpimelic acid was given by Zelinsky (*Ber.*, 1891, **24**, 3997), who, apparently, was unaware of the results which had been published by the author and Mackenzie. Zelinsky prepared $\alpha\alpha'$ -dimethylpimelic acid by treating ethylic α -cyanopropionate with sodium ethoxide and trimethylene bromide,

hydrolysing the product with potash, and warming the tetracarboxylic acid with concentrated sulphuric acid until it was converted into $\alpha\alpha'$ -dimethylpimelic acid; this compound was separated from accompanying oil, and the melting point, “*der vollständig gereinigten Krystalle*,” was found to be 71—73°. The oily mother liquor from these crystals did not solidify, and, on analysis, gave the same results as the crystalline acid; Zelinsky suggested, therefore, that the oil might be a stereoisomeride of the compound melting at 71—73°, but, owing to lack of material, he was unable to support this view by any further evidence.

These later determinations of the melting point of dimethylpimelic acid not only differed from one another, but also from that given by the author and Mackenzie, and to such an extent that the discrepancies could hardly be assigned to the slight and almost unavoidable differences in observation; at the same time, the differences were not large enough, and there was altogether insufficient evidence of any kind, to warrant the conclusion that the three preparations in question were not identical.

142 KIPPING: STEREOISOMERIC $\alpha\alpha'$ -DIMETHYLPIMELIC ACIDS.

Under these circumstances, a more exhaustive investigation of $\alpha\alpha'$ -dimethylpimelic acid was eminently desirable, firstly, in order to confirm or disprove the accuracy of previous observations, and, secondly, in order to ascertain whether this acid, like all the lower substituted acids of the same series, exists in stereoisomeric forms.

The results arrived at may be summarised as follows.

$\alpha\alpha'$ -Dimethylpimelic acid exists in two stereoisomeric modifications melting at $81-81.5^\circ$ and $76-76.5^\circ$ respectively, and the crude crystalline acid obtained by hydrolysing ethylic dimethyldiacetylpyemlate is a mixture of these stereoisomerides. The acid of higher melting point—which may be termed the *para*-acid—is easily obtained from this mixture in a pure condition by fractional crystallisation, but the *anti*-acid—the modification of lower melting point—cannot be directly isolated, at any rate when operating with moderately small quantities.

The two modifications are most conveniently separated with the aid of their anilides; the anilide of the *para*-acid melts at $183-184^\circ$, that of the *anti*-acid at $154-155^\circ$, and, on hydrolysis with dilute alcoholic hydrochloric acid, each is reconverted into the modification from which it is derived.

The two acids differ in crystalline form and in solubility, but, on the whole, they are very similar in all ordinary properties, and they have the same electrical conductivity. The difference in melting point is remarkably small, very much smaller in fact than in the case of the two stereoisomeric forms exhibited by other acids of this series having a similar constitution, as will be seen from the following table.

	Para.	Anti.	Diff.
Dimethylsuccinic acid....	$192-194^\circ$	$120-123^\circ$	72°
Dimethylglutaric acid...	128	103	25
Dimethyladipic acid.....	142	$70-72$	71
Dimethylpimelic acid....	$81-81.5$	$76-76.5$	5

Now, since dimethylpimelic acid is the highest member of this particular dimethyl-series, and its two modifications show the smallest difference in melting point, it might be expected that, for this and other reasons, the two modifications of such acids would show a continually diminishing difference with increasing molecular weight; so far, however, there is little evidence of any such regularity, at any rate in melting point, as the two modifications of dimethylglutaric acid differ by only 25° , those of dimethyladipic acid by as much as 71° .

As regards electrical conductivity, on the other hand, there is a marked regularity on passing up the series, and the two modifications

of dimethylpimelic acid, like those of the next two lower members, have the same dissociation constant.

	Dimethylsuccinic acid.	Dimethylglutaric acid.	Dimethyladipic acid.	Dimethylpimelic acid.
Para. K =	0.0190	0.0055	0.0042	0.00343
Anti. K =	0.0122	0.0055	0.0042	0.00344

Both modifications of $\alpha\alpha'$ -dimethylpimelic acid, the anti-form more especially, have a very great tendency to remain in the liquid condition unless they are in a state of great purity; the pure compounds, however, may be recrystallised without difficulty, and, under suitable conditions, may be obtained in forms which allow of goniometrical measurement. The crystallographic examination was kindly undertaken by Mr. W. J. Pope, and the results, which are given below, afford a valuable, and by no means superfluous, proof of the non-identity of these, otherwise so similar, modifications.

A comparison of the properties of anti-dimethylpimelic acid (m. p. $76-76.5^\circ$) with those of the dimethylpimelic acid (m. p. $74-76^\circ$), described by Perkin and Prentice, leaves little doubt as to the identity of these two compounds, and since this particular modification is by far the more readily soluble of the two, it is highly improbable that the para-acid could have been present in Perkin and Prentice's preparation and yet have escaped notice; this conclusion, moreover, is borne out by the fact that only one modification was obtained by them in the case of all the substituted pimelic acids prepared in a similar manner. That two methods of preparation, namely, that of Perkin and Prentice on the one hand, and that of the author on the other, should lead to such different results is at first sight remarkable, because in both cases the acid was obtained by substituting hydrogen for a group X in an ethereal salt of the constitution

yet, when $\text{X} = -\text{COOEt}$, only the anti-acid was formed, whereas, when $\text{X} = -\text{CO}\cdot\text{CH}_3$, both modifications were produced. The explanation of this difference probably lies in the fact that the two asymmetric carbon atoms, upon which the existence of the two stereoisomerides is assumed to depend, originated under very different conditions; in one case, asymmetry was not established until two of the carboxyl groups of the tetracarboxylic acid were displaced by two hydrogen atoms—a change which was accomplished by heating at $200-220^\circ$; in the other the asymmetric carbon atoms originated in alcoholic solution at a comparatively low temperature. There is

144 KIPPING: STEREOISOMERIC $\alpha\alpha'$ -DIMETHYLPIMELIC ACIDS.

also this further difference between the two modes of preparation, that whereas Perkin and Prentice obtained their acid directly from a compound which could not itself exhibit stereoisomerism, the mixture of the anti- and para-acids was produced from a substance which should itself exist in stereoisomeric forms. Arguments of this kind may not perhaps be generally applicable, but they certainly show that in this particular case the two methods of preparation are really not so similar as they appear to be, and do not, therefore, necessarily yield identical products. Such considerations may also be of value in elucidating the nature of the two isomerides in question, because, as the acid melting at $76-76.5^\circ$ is the one which is produced by changes occurring at a high temperature, it is probably the internally compensated, and not the racemic modification.

On comparing Zelinsky's method of preparation with that employed by the author, it is evident that the conditions under which the asymmetric carbon atoms of the dimethylpimelic acid originated are practically identical, the main difference between the two pro-

cesses being, in fact, that, whereas the conversion of the $\text{CH}_3-\text{C}-$ groups of ethylic dimethyldiacetylpimelate into $\text{CH}_3-\text{C}-$ groups

was accomplished in boiling alcoholic solution, the substitution of

hydrogen for the cyanogen radicles in the groups $\text{CH}_3-\text{C}-$ was effected by Zelinsky by heating the ethylic salt with alcoholic

potash, and then warming with sulphuric acid (at a temperature not stated). It seems probable, therefore, that identical products should have been obtained by the two methods, and that Zelinsky's acid (m. p. $71-73^\circ$) was in reality a mixture of the two stereoisomerides; this conclusion is borne out by the fact that in the case of $\alpha\alpha'$ -dimethylglutaric acid (Zelinsky, *Ber.*, 1889, **22**, 2823) and of $\alpha\alpha'$ -dimethyladipic acid (Zelinsky, *Ber.*, 1891, **24**, 3997)—both of which were prepared by methods essentially identical with that used in the case of $\alpha\alpha'$ -dimethylpimelic acid—mixtures of the two modifications were obtained. It is not impossible that the acid prepared from ethylic dimethyldiacetylpimelate may have undergone change on distillation under reduced pressure, the one modification having been partially converted into the other; such an assumption would doubtless explain away the difficulties, but it has no basis in fact, and is

not warranted by the results of experiments described below ; nevertheless, it cannot be dismissed as impossible.

Isolation of Para-dimethylpimelic acid.

The dimethylpimelic acid employed in these experiments was prepared by the hydrolysis of ethylic dimethyldiacetylpmelate (Kipping and Mackenzie, *loc. cit.*), and was separated from the dimethylacetylcaproic acid by the method already mentioned. The crude acid was dark brown, and as it showed no signs of crystallising, even on keeping for a long time over sulphuric acid, it was distilled under reduced pressure. The two principal fractions were those collected between 245° and 250° and between 250° and 255° (50 mm.), but a considerable quantity passed over below 245° , and a small quantity of a tar-like oil remained in the distilling flask.

Those fractions which deposited crystals were filtered with the aid of the pump, and the residue spread on porous earthenware, on which it was left until it became quite hard and could be readily reduced to a fine powder without caking ; the oily filtrate was again placed over sulphuric acid, but only a trace of a crystalline deposit was formed even after several months had elapsed.

The first point which required attention was, whether dimethylpimelic acid melted at $80-81^{\circ}$, as previously stated by the author and Mackenzie. A portion of the fine powder was therefore recrystallised from light petroleum (b. p. $50-60^{\circ}$) containing a very small proportion of benzene, the addition of which tended to prevent the separation of the acid in an oily condition ; the first crystallisation gave a deposit melting at $58-63^{\circ}$, but after numerous operations, which extended over several weeks, the melting point of the most sparingly soluble portion rose to $72-73^{\circ}$; at this stage, the substance was obtained in what seemed to be definite crystals, but, on further recrystallisation from light petroleum, its melting point rose about 1° with each operation, and finally reached 81° . This preparation was then successively recrystallised from cold water, petroleum, cold water, and a mixture of petroleum with benzene, but the last, and most sparingly soluble, fraction melted, as before, at $81-81.5^{\circ}$.

A sample of this compound was then analysed.

0.1519 gave 0.3212 CO_2 and 0.1177 H_2O . $\text{C} = 57.63$; $\text{H} = 8.61$.
 $\text{C}_8\text{H}_{16}\text{O}_4$ requires $\text{C} = 57.44$; $\text{H} = 8.51$ per cent.

A portion of the same sample was titrated against alkali.

0.0938 gram neutralised 9.65 c.c. of sodium carbonate solution, 1 c.c. of which was equivalent to 0.009675 gram of dimethylpimelic acid ; quantity found = 0.0934.

These analyses, and the method of preparation of the compound,

show it to be $\alpha\alpha'$ -dimethylpimelic acid, and the melting point previously given is therefore confirmed; the properties of this acid are described later.

Examination of Mother Liquors.—The crystals deposited from the various portions of the mother liquors, from which the acid melting at 81 — 81.5° had separated, were now examined in order, if possible, to isolate an isomeride, but all attempts in this direction were unsuccessful; although fractions melting as low as 58 — 64° and as high as 75 — 77° could be separated without much difficulty, the melting point invariably altered on recrystallising, and finally the portions became so small that it was of little use continuing the process.

Attempts were then made to effect a separation by fractional crystallisation from cold water, and in this way a considerable quantity of a substance melting fairly sharply at 74 — 76° was finally obtained from the more readily soluble portions; it is probable that this preparation consisted essentially of the anti-acid, but as the melting point of this isomeride was at that time unknown, the fraction in question was thought to be a mixture and the experiments were discontinued.

The appearance and behaviour of the numerous samples of acid obtained in the above operations certainly led to the conclusion that the original substance was a mixture of stereoisomerides, but before proceeding further in the attempts to isolate the unknown modification some preliminary evidence of its existence was desirable. For this reason, a portion of the crystalline powder melting at 56 — 60° was dissolved in light petroleum, the filtered solution evaporated, and the residue kept for two days over sulphuric acid under reduced pressure; an analysis and a titration of this substance—a colourless oil—gave practically the same results as those obtained with a sample of the pure para-acid. This fact clearly indicated the presence of an isomeride of the latter, as it was improbable that any other substance could be present in sufficient quantity to lower the melting point from 81° to 60° , and yet have no effect on the results of the analyses.

On this assumption, the experiments were continued, and in the first place various salts were prepared from the crude mixture of acids; in all cases, however, these salts were badly characterised, and quite unsuitable for the end in view.

The conversion of one of the modifications of acids of this kind into the other may, as is well known, be frequently brought about by heating with hydrochloric acid, and apparently the intermediate formation of an anhydride is by no means a necessary step in the process, since this treatment has been found to be applicable in the case of dimethyladipic acid (Zelinsky, *Ber.*, 1891, **24**, 3997); if then one of the dimethylpimelic acids in the mixture could be thus

transformed into the other modification, the product might be the unknown anti-acid.

A portion of the oil, which had been separated from the crystalline acid as described above, was heated with about 20 parts of moderately concentrated hydrochloric acid at 200–220° for about 10 hours; there was slight pressure on opening the tube, and the acid had charred, yielding decomposition products which had an odour of petroleum. The solution was extracted with ether, and the brown oil, obtained on evaporating the extract, was placed in a desiccator, where it gradually solidified; after freeing the crystalline mass from oil with the aid of porous earthenware, it was first dissolved in benzene and treated with animal charcoal, and then recrystallised from light petroleum. The several fractions obtained in this way melted at very different temperatures, ranging from about 60° to about 76°, but it was found to be impossible to isolate any definite substance with the quantity at disposal; it would seem, therefore, that a complete conversion of one isomeride into the other had not taken place, although apparently this change had occurred to some extent, as the mixture solidified so much more readily after the treatment than before. A portion of the oily mixture was also heated alone at 190–200° for about six hours, but this experiment was equally unsuccessful, as the product could not be got to crystallise.

Preparation and Separation of Stereoisomeric Anilides.

The great difficulty experienced in the attempts to separate the two acids by fractional crystallisation was due almost entirely to the fact that the mixture was so frequently deposited from its solution as an oil, even when evaporation took place very slowly at the ordinary temperature; as the separation of the corresponding anilides would probably be free from this difficulty, a portion of the crystalline mixture and a portion of the oil were separately treated with a slight excess of the theoretical quantity of phosphorus pentachloride. The oils thus produced were heated for some time at about 100° in a stream of dry air, in order to expel most of the phosphorus oxychloride, and were then slowly poured into excess of dry aniline; the pasty products were heated for a short time on the water bath to complete the action, and then extracted with warm dilute hydrochloric acid to remove the excess of aniline; the solid residues were finally submitted to fractional crystallisation from hot dilute alcohol and ethylic acetate.

The first product which was isolated melted at about 208°, and proved to be a phosphorus compound—probably the anilide of phosphoric acid, $\text{PO}(\text{NH}\cdot\text{C}_6\text{H}_5)_3$, which melts at 208°—produced from the phosphorus oxychloride which was not completely expelled, but on

148 KIPPING: STEREOISOMERIC $\alpha\alpha'$ -DIMETHYLPIMELIC ACIDS.

further crystallisation a crystalline anilide free from phosphorus was obtained. This compound melted at 183 — 184° , and gave, on analysis, results agreeing well with those required by the anilide of dimethylpimelic acid.

0.1614 gave 0.4400 CO_2 and 0.1170 H_2O . $\text{C} = 74.35$; $\text{H} = 8.05$.

$\text{C}_{21}\text{H}_{26}\text{N}_2\text{O}_2$ requires $\text{C} = 74.56$; $\text{H} = 7.69$ per cent.

The mother liquors from this anilide, on further treatment, yielded fractions of much lower melting point, and also a considerable quantity of a brown oil, which solidified only very slowly; from these portions, but only after repeated recrystallisation from various solvents, a substance melting at 154 — 155° was isolated.

This compound, which proved to be isomeric with the anilide melting at 183 — 184° , gave the following result on analysis.

0.1310 gave 0.3579 and 0.0951 . $\text{C} = 74.51$; $\text{H} = 8.06$.

$\text{C}_{21}\text{H}_{26}\text{N}_2\text{O}_2$ requires $\text{C} = 74.56$; $\text{H} = 7.69$ per cent.

After separating these compounds as completely as possible, crystalline deposits were obtained, some of which, though quite colourless and free from oil, melted as low as 130 — 135° ; these fractions doubtless consisted in the main of the anilide melting at 154 — 155° , but, although free from any phosphorus compound, and apparently also from the anilide melting at 183 — 184° , they contained some other substance the nature of which could not be determined; it was the presence of this unknown substance which rendered the isolation of the second anilide a matter of some difficulty, a mixture consisting only of the anilides of the two dimethylpimelic acids being very readily resolved into its components by fractional crystallisation from hot dilute alcohol.

Both the samples of crude anilides, prepared from the crystalline and oily acids respectively, were found to be mixtures, but that obtained from the crystalline acid contained a relatively larger proportion of the anilide melting at 183 — 184° .

Reconversion of the Anilides into the Acids.

Having obtained the two anilides in a state of purity they were separately reconverted into the corresponding acids, firstly in order to ascertain which was the derivative of the para-acid, and secondly in order to obtain the stereoisomeric anti-acid.

The pure anilide melting at 154 — 155° was dissolved in a little hot dilute methylic alcohol, a small quantity of concentrated hydrochloric acid added, and the solution heated to boiling in a reflux apparatus until the addition of water produced no perceptible turbidity; this operation occupied about 20 hours. The solution was then repeatedly evaporated on the water bath until free from hydrochloric acid, the

residue dissolved in a small quantity of water, the solution filtered from traces of a brown oil (probably slightly impure acid), and the colourless filtrate evaporated to dryness. The pasty residue was then dried at 100° , extracted with boiling light petroleum, and the filtered extract evaporated. The crystalline powder insoluble in petroleum was proved to be aniline hydrochloride by the usual tests, thus affording further evidence that the substance melting at 154 – 155° was an anilide.

The oily acid obtained on evaporating the light petroleum extract was dissolved in water, and the solution left at the ordinary temperature; oily drops separated in the course of a few days, but on rubbing with a glass rod they gradually solidified, and on further evaporation over sulphuric acid the rest of the acid was deposited in colourless crystals; these melted at 73 – 75° , but on recrystallisation from water their melting point rose to, and became constant at, 76 – 76.5° .

The anilide melting at 183 – 184° was also hydrolysed with dilute alcoholic hydrochloric acid exactly in the manner just described; it yielded aniline hydrochloride, and an acid which melted at 81 – 81.5° .

There are, therefore, two stereoisomeric $\alpha\alpha'$ -dimethylpimelic acids; the para-acid melts at 81 – 81.5° , and its anilide at 183 – 184° , whereas the anti-acid melts at 76 – 76.5° , and its anilide at 154 – 155° .

Properties of the Stereoisomeric Acids.

A short description of para-dimethylpimelic acid has been previously given (Kipping and Mackenzie, *loc. cit.*, p. 578), but several new facts have been established in the course of these experiments. The pure acid separates from tepid water in beautiful, fern-like crystals; and when crystallisation takes place slowly at the ordinary temperature it is deposited in aggregates of large opaque prisms, or in beautiful, highly lustrous and transparent, rhombic or six-sided plates (see below). It may also be recrystallised from light petroleum or from a mixture of light petroleum and benzene, but the crystals obtained under these conditions (compact prisms) are not very suitable for crystallographic examination.

The solubility of the para-acid in water was determined with the following results.

2.7630 grams of a solution, saturated at 15° , gave, on evaporation, 0.0315 gram of the acid; 100 parts of water at 15° dissolve, therefore, 1.15 parts of the acid.

5.5547 grams of a solution, saturated at 15° , gave, on evaporation, 0.0662 gram of acid; 100 parts of water at 15° dissolve, therefore, 1.19 grams of acid.

150 KIPPING: STEREOISOMERIC $\alpha\alpha'$ -DIMETHYLPIMELIC ACIDS.

Dr. J. Walker very kindly measured the electrical conductivity of the two stereoisomerides, and obtained the following results.

Para-dimethylpimelic acid (m. p. $81-81.5^\circ$).... $K = 0.00344$

Anti-dimethylpimelic acid (m. p. $76-76.5^\circ$).... $K = 0.00343$

Both specimens, Dr. Walker stated, gave excellent measurements, a fact which indicated a high state of purity.

The white, opaque prisms, usually obtained on evaporating a cold aqueous solution of the para-acid, are 4 or 5 mm. in length, and their edges and corners are quite transparent, the opacity of the mass being due to fern-like inclusions. The forms ordinarily shown are $c\{001\}$ and $m\{110\}$; more rarely the pinacoid $a\{100\}$ is present as a narrow strip. The acid condenses on volatilisation in tablets flattened in the direction of the c -axis; crystals of the same kind are sometimes obtained on crystallisation from water, and seem to consist of the forms $c\{001\}$, $p\{111\}$, and $q\{111\}$ (see Fig. 1). Through the basal pinacoid of these,

FIG. 1.

FIG. 2.

the extinction bisects the angles, and an optic axis is seen emerging in the plane $b\{010\}$; under a $\frac{1}{12}$ th oil immersion objective, the optic axis is seen emerging almost in the centre of the field. The double refraction and the dispersion are weak. These crystals do not lend themselves readily to measurement, the faces being extremely conchoidal in character, and giving multiple images on the goniometer. A few better-developed, transparent crystals, about $\frac{1}{2}$ mm. long and $\frac{1}{8}$ mm. broad, were obtained, by allowing the aqueous solution to evaporate spontaneously over sulphuric acid. These were rhombohedral in shape, showing the forms $c\{001\}$, $m\{110\}$, and sometimes $a\{100\}$ (see Fig. 2); one crystal which showed a face of the form $p\{111\}$ was found amongst these. The crystals belong to the monosymmetric system; the faces were all very conchoidal in character, and the measurements made on the crystals cannot be regarded as very accurate. The forms $c\{001\}$ and $m\{110\}$ are of about

the same size, whilst $a\{100\}$ is always very much smaller. The crystals have a quartz-like lustre, but no characteristic cleavage; the refractive index is about the same as that of cedar-wood oil. These crystals are of the same kind as those described above, the optic axis always being visible through the pinacoid c .

Crystalline System—Monosymmetric.

$$a : b : c = 1.263 : 1 : 1.062.$$

$$\beta = 43^\circ 23'.$$

Forms present :

a	$\{100\}$.
c	$\{001\}$.
p	$\{11\bar{1}\}$.
m	$\{110\}$.

Angle.	No.	Limits.	Mean.	Calc.
$mm = 110 : 1\bar{1}0$	21	$80^\circ 6' - 83^\circ 50'$	$81^\circ 53'$	—
$mm = 110 : \bar{1}10$	18	$95 10 - 100 48$	$98 32$	$98^\circ 7'$
$mc = 110 : 001$	15	$54 48 - 58 24$	$56 42$	—
$mc = 110 : 10\bar{1}$	11	$120 36 - 129 41$	$124 47$	$123 18$
$ac = 100 : 001$	4	$40 16 - 44 41$	$42 51$	$43 23$
$ac = 100 : 00\bar{1}$	5	$135 7 - 137 52$	$136 49$	$136 37$
$mp = 110 : 11\bar{1}$	1	—	$55 36$	$56 0$
$pc = 11\bar{1} : 00\bar{1}$	1	—	$67 18$	—

On melting the crystalline substance on a microscope slide, putting on a cover glass and allowing to cool, the acid crystallises readily from centres giving a transparent product which sometimes shows an optic axis. Tiny bubbles are seen in the mass along the lines of junction of the various individuals; the substance may be easily recognised by this peculiarity. The crystalline form of the solidified magma is the same as that of the crystals obtained from aqueous solution or by volatilisation.

Anti-dimethylpimelic acid, even when pure, frequently separates from cold water as an oil; if, however, a crystal is introduced as soon as oily drops are observed, and the solution is then left for some days, the acid separates in beautiful rosettes or clusters of concentrically grouped spear-shaped crystals, which float at the surface of the liquid with the points projecting downwards; this behaviour is very characteristic, and the crystals are quite different in appearance from those of the para-acid. All other ordinary solvents, with the exception of light petroleum, dissolve the anti-acid so readily that it cannot well be recrystallised from any of them.

The solubility of this acid was determined with the following result: 2.1389 grams of an aqueous solution, saturated at 15° , gave, on

152 KIPPING: STEREOISOMERIC $\alpha\alpha'$ -DIMETHYLPIMELIC ACIDS.

evaporation, 0.0472 gram of acid; 100 parts of water at 15° dissolve, therefore, 2.206 parts of acid.

This result is practically the same as that obtained by Perkin and Prentice with their dimethylpimelic acid (m. p. 74—76°), inasmuch as they found the solubility to be 2.19 parts in 100 of water at 13.5°; it affords, therefore, confirmatory evidence of the identity of the two compounds.

The metallic salts of anti-dimethylpimelic acid are apparently identical with those of the para-acid, as, on adding solutions of copper sulphate, ferric chloride, and mercuric chloride to a solution of the ammonium salt, precipitates identical in appearance with those obtained in the case of the para-acid (*loc. cit.*) were produced; barium chloride and lead acetate also gave no precipitate in moderately concentrated solutions of the anti-acid, just as with the para-acid.

The crystals of the anti-acid produced by slow evaporation of its pure aqueous solution over sulphuric acid are tiny, flattened, transparent needles about 0.5 mm. in length and 0.1 mm. in diameter.

FIG. 3.

These crystals belong to the orthorhombic system, and show the forms $m\{110\}$ and $p\{101\}$; the faces are much pitted by re-solution, and were only measured with difficulty. The faces of the form $m\{110\}$ are always much smaller than those of $p\{101\}$; the two faces of the latter give the crystal a wedge-shaped appearance, and meet in a rounded knife-edge, through which six or seven sets of interference-spectra are visible between crossed nicols. The crystals never show the two ends complete, as they always grow in rosettes of four or five individuals, and have to be detached for measurement; only two faces of the form $p\{101\}$ are found on

each crystal. On examining the crystal through the face (101), in convergent polarised light, under a $\frac{1}{2}$ th oil immersion objective, a well-defined orthorhombic interference figure of large axial angle is seen; the figure is not quite central owing to the fact that the plate is wedge-shaped. The axis a is the acute bisectrix, and the optic axial plane is parallel to the pinacoid b ; the double refraction is positive and moderately weak, whilst the dispersion is weak.

Crystalline System—Orthorhombic.

$$a : b : c = 0.8207 : 1 : 2.862.$$

Forms present :

$$\begin{array}{ll} m \dots \dots \dots & \{110\}. \\ p \dots \dots \dots & \{101\}. \end{array}$$

Angle.	No.	Limits.	Mean.	Calc.
<i>mm</i> = 110 : 110	16	99° 15'—103° 8'	101° 15'	101° 45'
<i>mm</i> = 110 : 110	16	75 20—81 37	78 40	—
<i>pp</i> = 101 : 101	12	143 16—152 31	148 0	—
<i>pp</i> = 101 : 101	7	30 24—37 19	33 12	32 0

On fusing a little of the acid on a microscope slide and subsequently cooling, it solidifies slowly, crystallisation proceeding from centres as in the case of the acid melting at 81°; no small bubbles are to be seen in the mass as in the preceding case, and on examining the product microscopically it is seen that the crystals are of the same kind as those obtained from water. The acute bisectrix is perpendicular to the slide, so that the bi-axial interference figure is seen through it in all parts of the plate. On volatilisation, the acid solidifies in rosettes or ill-defined plates which always show the characteristic bi-axial interference figure.

The fact that these two acids are different is proved beyond all doubt by the crystallographic evidence alone; the one acid is always obtained in monosymmetric crystals, whilst the other invariably crystallises in the orthorhombic system.

The remarkably small difference in melting point between the two stereoisomeric acids, and the fact that except as regards solubility the two modifications presented no well-marked points of difference, rendered further evidence of their non-identity desirable, particularly as their crystallographic character had not at the time been examined; it seemed not impossible that although the two acids had been prepared from what were certainly different anilides, the compound melting at 76—76·5° might be impure para-acid, formed during the hydrolysis of the anilide with alcoholic hydrochloric acid—a process which had been necessarily rather prolonged. This doubt was set at rest by the following experiment: An intimate mixture of approximately equal portions of the two acids melting at 76° and 81° respectively, was found to soften distinctly at 55° and to liquefy completely just below 70°; after having been kept for about two days, the liquid mixture had solidified, and, when re-heated, it sintered distinctly at about 52°, melting completely at 65°; such a result could not have been obtained had the acid melting at 76° been an impure preparation of the para-modification.

The conversion of one of the modifications of the acid into the other, although doubtless capable of being accomplished by some of the methods ordinarily employed in such cases, has, unfortunately, not been effected in the present instance, owing to lack of material, and only one experiment with this object in view was made. In order to settle the question previously raised, whether distillation under reduced pressure caused any change in the original acid pre-

154 KIPPING: STEREOISOMERIC $\alpha\alpha'$ -DIMETHYLPIMELIC ACIDS.

pared from ethylic dimethyldiacetylpimelate, small quantities of the two pure stereoisomerides were separately heated at about 250—260° for at least 10 minutes; that is to say, the two acids were heated under practically the same conditions as were employed in the original distillation. In both cases a certain amount of decomposition occurred, as was shown by the slight darkening in colour, and vapours were evolved in fairly large quantity causing the formation of a layer of oil on the cooler parts of each of the vessels; in both cases this oily layer very soon solidified to a mass of beautiful crystals. Those obtained from the para-acid consisted of six-sided or rhombic plates belonging to the monosymmetric system, and were found to be identical with the crystals of the para-acid deposited from aqueous solution; those produced from the anti-acid consisted of isolated clusters or rosettes of spear-shaped orthorhombic prisms identical with the crystals of the anti-acid obtained from aqueous solution; in both cases, moreover, the condensate appeared quite homogeneous, indicating that no change of one modification into the other had occurred. The whole of the two samples which had been thus treated were separately recrystallised from cold water; the para-acid then melted at 73—77°, the anti-acid at 68—72°, but this was apparently due to minute traces of their decomposition products and not to the presence of the isomeride, since the crystals were well defined, and appeared to be homogeneous under the microscope. Although, therefore, not quite conclusive, this experiment shows that even if one form is converted into the other at about 250°, the change takes place very slowly.

Properties of the Stereoisomeric Anilides.

The anilide of para-dimethylpimelic acid is much more sparingly soluble in dilute alcohol than the anilide of the anti-acid, and also differs from the latter in appearance, so that the two compounds are very easily separated. The para-anilide crystallises from ethylic acetate, alcohol, and acetone in long, flattened prisms or needles, which are colourless and opaque; it is only moderately soluble in cold ethylic acetate and in cold alcohol, but readily in hot alcohol and acetic acid.

The crystals obtained from solution melt sharply at 183—184°, but when the capillary tube is withdrawn and again placed in the hot acid the solidified substance does not melt until the temperature rises to 187—188°; this curious behaviour indicates the existence of two crystalline forms, but even after keeping for four days at the ordinary temperature, the specimens which had been once melted, liquefied again at 187—188°, and not at 183—184°.

The anilide of anti-dimethylpimelic acid is very readily soluble in

ethylic acetate, acetic acid, alcohol, and benzene, but rather sparingly in ether, and practically insoluble in cold light petroleum. It separates from cold dilute alcohol in curious, colourless, pear-shaped masses composed of extremely minute needles or prisms; these forms are highly characteristic, and totally different in appearance from the crystals of the para-anilide. The melting point of this anti-anilide is 154—155°.

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