The Configuration of the $\alpha\alpha'$ -Dimethylpimelic Acids

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The diastereomeric $\alpha\alpha'$ -dimethylpimelic acids melting at 81–81.5° and 76–76.5° have been investigated by several authors. They have been designated as the *para*- and *anti*-form, respectively, but no attempts to determine the configuration have been reported^{1,2,3}. The present authors have found that the *low-melting* acid can be resolved into optically active forms using strychnine. On the other hand, the *high-melting* form gives a strychnine salt, from which the inactive compound can be regenerated with unchanged m. p. This indicates that the latter acid is the pure *meso*-form.

The separation of the diastereomeric acids is rather tedious and time-consuming. Kipping has performed it through the anilides³, and in spite of extensive experiments no better method could be found. Owing to lack of material, the optical antipodes have not yet been prepared in a state of purity. The acid from the first crystallisation of the strychnine salt had $[\alpha]_D^{25} = -20^\circ$ (abs. ethanol). In the same solvent, dimethylglutaric and dimethyladipic acid show 36.5° and 30.3°⁴, respectively. The maximum activity of the dimethylpimelic acid can be assumed to be somewhat lower, probably near 25°. The strychnine salt thus gives a fairly good resolution.

Experimental. The inactive acids were prepared according to Kipping³.

0.250 g of the *low-melting* acid and 0.445 g of strychnine were dissolved together in hot dilute ethanol. After standing for several days, the salt was filtered off and the acid liberated. M. p. of the crude acid 67–68°. 0.0235 g dissolved in abs. ethanol to 10.00 ml: $2\alpha_D^{25} = -0.09^\circ$. $[\alpha]_D^{25} = -20^\circ$.

The mother liquor from the strychnine salt was evaporated to dryness and the acid liberated. 0.0293 g dissolved in abs. ethanol to 10.00 ml: $2\alpha_D^{25} = +0.105^\circ$. $[\alpha]_D^{25} = +18^\circ$.

Levorotatory $\alpha\alpha'$ -dimethylglutaric acid was prepared according to Möller⁵. 0.4586 g

dissolved in abs. ethanol to 10.00 ml: $2\alpha_D^{25} = -3.345^\circ$. $[\alpha]_D^{25} = -36.5^\circ$.

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Iron Transport through the Lymph Stream

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In the course of one hour about 30 μg of iron leaves the circulation of the rabbit. Most of this iron is ultimately utilized in the formation of hemoglobin, but a fraction before doing so is lead into the "depots" and utilized at a later stage only.

The iron circulating in the plasma is bound to β_1 -globulin and has prior to passing the capillary wall to be split off from that compound¹.

The writer found the thoracic lymph of the rabbit to contain 73 $\mu\text{g}/100$ ml of iron (range 40–115 $\mu\text{g}/100$ ml, S.D. 27 $\mu\text{g}/100$ ml), all this iron being bound to β_1 -globulin. It is probable that the same is the case for the iron of the whole extracellular fluid. The iron of the depots and that of the extracellular fluid has to enter the vascular bed prior to reaching the hemopoietic organs, and thus the problem occurs in which way these fractions reach the circulation.

Thirty minutes after injecting intraperitoneally or subcutaneously labelled iron- β_1 -globulin to the rabbit, 1 ml of thoracic lymph was found by the writer to contain more than 150 times as much labelled iron than does 1 ml of plasma. This observation suggests that much of the iron of the interspaces and thus also the iron released from the depots, as far it is bound to β_1 -globulin, is transported into the circulation with the lymph stream.

To test this conclusion, the influx of a large part of the lymph stream into the

Table 1. Change of iron content of the plasma of rabbits with ligated thoracic duct and of sham operated rabbits.

		Iron content, $\mu\text{g} / 100 \text{ ml}$	
		Time 0	after 4 h
Seven rabbits with ligated thoracic duct	<div> <div>mean</div> <div>range</div> <div>S. D.</div> </div>	<div> <div>$196 \pm 17^*$</div> <div>115—260</div> <div>45</div> </div>	<div> <div>$151 \pm 12^*$</div> <div>95—197</div> <div>32</div> </div>
Seven sham operated rabbits	<div> <div>mean</div> <div>range</div> <div>S. D.</div> </div>	<div> <div>$178 \pm 10^*$</div> <div>145—210</div> <div>27</div> </div>	<div> <div>$159 \pm 13^*$</div> <div>112—208</div> <div>35</div> </div>

* Standard deviation of the mean.

circulation was obstructed by ligating the thoracic duct and the *truncus jugularis sinister*. The effect of this obstruction on the iron content of the plasma of operated and of sham operated rabbits was then determined. The results of these experiments are seen in Table 1. They show a significant decrease of the iron content of the plasma following obstruction of much of the lymph flow.

Thus ligation of much of the lymph stream reduces the influx of iron into the plasma by $3.8 \mu\text{g}/\text{h}$. The total iron loss by the plasma amounts to $30 \mu\text{g}/\text{h}$. Thus $1/8$ of the total iron loss by the plasma is compensated by iron lead into the circulation by the lymph stream. The share of iron carried by the lymph stream in the iron replacement is, however, much larger, if we consider the amount of iron lead from the depots into the circulation alone. This amounts to $4.5 \mu\text{g}/\text{h}$. Thus the amount of iron lead into the plasma by the lymph stream makes out a very appreciable part of the iron carried from the depots into the circulation.

From the decrease of the plasma iron content due to obstruction of the lymph flow and from the iron content of the lymph we can calculate the volume of lymph lead hourly into the circulation. We arrive at a volume of up to $5.2 \text{ ml}/\text{kg}$ body weight. This compares with the values of 1.4 – $6.8 \text{ ml}/\text{kg}/\text{h}$ found by Forker *et al.*² for the rat, and 0.2 – $3.0 \text{ ml}/\text{kg}/\text{h}$ measured by Paine *et al.*³ in the dog.

As the lymph iron is bound to β_1 -globulin we have to expect that a corresponding amount of β_1 -globulin, making out 2.8% of the total plasma content, will reach the circulation with the lymph stream as well. This is about in the case of the rat (2.8% / h) and of the dog (2% / h)^{2,4}. Forker *et al.*² found, that at least about half of the plasma proteins of the dog are daily replaced by the lymph proteins. A result which suggests, among other things, that about 2.8% of the plasma iron passes the capillary wall without being dissociated.

Three experiments carried out with growing pigs also brought out the fact, that ligation of the thoracic duct appreciably depresses the plasma iron level.

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