XV.—*Studies in Optical Superposition. Part IV.*
1-Menthylamine Tartrates and 1-Amyl Dimethoxy-
succinates.

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THE so-called principle of optical superposition, which is due to van't Hoff, asserts that if in a molecule containing several asymmetric carbon atoms the part of the total rotation due to any one of these be $+\alpha^\circ$, then on replacing that atom by its mirror image the latter should be responsible for $-\alpha^\circ$ of the rotation of the new compound. The validity of this assumption is of some importance because if the assumption be true, the rotation of, for example, *d-sec.*-butyl *dl*-tartrate must be that of the active butyl radicle when in combination with either the *d*- or the *l*-tartaryl radicle, whilst that of *dl-sec.*-butyl *d*-tartrate must be the rotation of the active tartaryl radicle in combination with either the *d*- or the *l-sec.*-butyl group. It would therefore be possible to resolve the rotation of *d-sec.*-butyl *d*-tartrate into two parts, one being the rotation of the butyl radicle and the other that of the tartaryl radicle. By a procedure something like this Walden and Guye sought to establish the truth of van't Hoff's assumption, but as was shown in previous parts of this investigation (T., 1905, **87**, 33; 1906, **89**, 1884; 1907, **91**, 705) their method of proof completely eliminated the influence they wished to study, and it is easy to show that the experimental results which they arrived at would be obtained even if the principle were quite false.* It

* See also Guye and Gautier, *Zeitsch. physikal. Chem.*, 1907, **58**, 659. These authors appear to justify the proof of the principle of optical superposition by what they call the method of partially racemic esters, a method which is entirely fallacious, and they refer also to a second proof of the principle, which consists in determining the rotation of such a substance as *l*-amyl *l*-valerate and comparing

seems strange that van't Hoff, to whom more perhaps than to anyone else we are indebted for the idea that the spatial arrangement of the atoms of a molecule is a very important factor in conditioning its properties, should have been reluctant to admit the probability of the rotations of these superimposed radicles being mutually affected owing to different relative position, in the compound molecule, of the groups composing them. ("Die Lagerung der Atome im Raume," 3te. Auf., 1908, pp. 6, 7, 19, 95.) Maleic acid and fumaric acid differ in melting point and other properties simply because of the different relative arrangement of the atoms of their molecules. The melting point of *d*-tartaric acid (170°) differs from that of *i*-tartaric acid (143°) for just the same reason, but in the latter case two of the carbon atoms are asymmetric, so that optical superposition is directly involved in this difference in melting point. It therefore seems reasonable to

suppose that a *d*-tartaryl group, $\text{H}-\overset{\overset{\text{CO}_2\text{H}}{|}}{\underset{|}{\text{C}}}-\text{OH}$, would have different rotatory values according as it is in combination with a *d*-tartaryl or an *l*-tartaryl radicle.

In connexion with this matter van't Hoff (*loc. cit.*, p. 97) lays some stress on the fact that in certain cases active derivatives of isomeric radicles show comparatively little difference in rotation, as in the case of propyl and *sec*-propyl glycerates with specific rotations of -12.9° and -11.8° respectively, and he expressed the opinion that a compound in which the asymmetry depended on the difference between a propyl and a *sec*-propyl group, such as propyl *sec*-propylacetic acid, should show "nur

this with the sum of the rotations of two other esters, one containing the *l*-amyl radicle attached to an acid radicle of approximately the same weight as the valeryl radicle but inactive, *n*-valeryl, for example, and the other containing the active valeryl radicle together with an inactive alkyl radicle such as *i*-isoamyl. The sum of the rotations of the two latter esters is 5.34 , almost identical with that of the first, namely 5.32° ($l=0.5$ dcm. in each case), on which account they say that the principle of optical superposition is established. These considerations, they remark, have at the present time all the greater applicability especially when one remembers that substitution remote from the asymmetric atom has only a slight influence on rotation. Now it is of course true that this regularity is observed in many cases, as was pointed out first by P. F. Frankland and MacGregor (T., 1896, 69, 121), and especially will it be true in the case of amyl alcohol, the rotation of which is comparatively little subject to change in any case. Guye and Gautier's considerations are, however, no proof of the principle of optical superposition, since it is obviously illegitimate to test a general proposition by means of a particular case, where, a priori, the effect sought for is likely to be so small as to fall within the limits of experimental error. The moral to be drawn from this consideration is rather that in testing the principle of optical superposition compounds should be chosen in which a maximum, not a minimum, effect is likely to be found.

unwesentliche Drehung." It has since been shown, however, as a result of his suggestion, that propyl *sec.*-propylcyanoacetic acid has $[\alpha]_D^{20} + 11.3^\circ$ in toluene ($p: 10$) (Fischer and Flatau, *Ber.*, 1909, **42**, 2981), and that, although propyl *sec.*-propylacetic acid could not be resolved, *n*-butyl *sec.*-butylacetic acid has $[\alpha]_D^{20} + 5.73^\circ$ (Fischer, Holtzapfel, and Gwinner, *Ber.*, 1912, **45**, 247), whilst Pickard and Kenyon in another connexion (T., 1912, **101**, 624) have found for propyl-*sec.*-propylcarbinol $[\alpha]_D^{20} + 21.25^\circ$. The influence of isomerism in these substances appears, therefore, to be considerably greater than van't Hoff had expected.

The problem of optical superposition is difficult to attack directly, so the work of the previous parts of this investigation was planned on what seemed to be the most suitable method, namely, comparison of the rotation constants of compounds obtained by combining with some other active radicle the three forms of a substance capable of existing in a *d*-, an *l*-, and an *i*-variety. The dimethyl esters of diacetyl-*d*-, *l*-, and *i*-tartaric acids were examined, when it was found that the mean of the rotations of the *d*- and *l*-compounds, instead of being equal to that of the *i*-compound, as van't Hoff's assumption would require, differed from it at 20° in the homogeneous condition by 33.5° (the difference becoming less as the temperature rises) and by 25.5° , 51° , and 52.5° at the same temperature in ethyl alcohol ($p: 0.455$), benzene ($p: 5$), and nitrobenzene ($p: 5$) respectively. These results thus agreed with an observation previously made by Walden in a different connexion, who found that the molecular rotation of di-*l*-amyl *i*-tartrate exceeded that of di-*l*-amyl *dl*-tartrate by 4.06° (*Zeitsch. physikal. Chem.*, 1896, **20**, 377). Unless these differences are due to experimental error they are sufficient to disprove the principle of optical superposition.

More recently some work on this subject has been carried out by Tschugaev and Glebko (*Ber.*, 1907, **46**, 2752) by the same method as was adopted by Patterson, Taylor, and Kaye. These authors found that the *l*-menthylurethane derived from the ethyl ester of *i*-tartaric acid by the action of *l*-menthylcarbimide differs by only 2 per cent. of its rotation from the mean of the rotations of the urethanes derived from the esters of the *d*- and the *l*-acids, whilst in the case of the *D*-*l*-fenchylurethanes the percentage difference is about twice as great. They conclude that their results agree with the demands of the principle of optical superposition, at least as a first approximation. The really important question, however, is whether the differences are greater or less than the experimental error. If they are greater van't Hoff's assumption is disproved, but—and this is a point that has not previously been

put forward, and upon which we wish to lay particular stress—the converse is not necessarily true. It is carefully to be noticed that even if the mean value for the *d*- and the *l*-compounds were identical with the value for the rotation of the *i*-compound, the fact would not necessarily be a proof of the principle of optical superposition. It may, in fact, well be that in a series of compounds containing two or more asymmetric centres the mutual influence of the active groups in the several cases might, when studied by this method, be such as to mask the effect. This will perhaps be rendered most clear by according imaginary values to a set of compounds such as the *l*-amyl esters of *d*-, *l*-, and *i*-tartaric acids, on the assumption that the principle of optical superposition does not hold.

$\begin{array}{c} \text{R} \\ \\ \text{H}-\text{C}-\text{OH} \\ \\ \text{HO}-\text{C}-\text{H} \\ \\ \text{R} \end{array}$	$(+10^\circ)$ $(+15^\circ)$ $(+15^\circ)$ $(+10^\circ)$	$\begin{array}{c} \text{R} \\ \\ \text{HO}-\text{C}-\text{H} \\ \\ \text{H}-\text{C}-\text{OH} \\ \\ \text{R} \end{array}$	$(+20^\circ)$ (-18°) (-18°) $(+20^\circ)$	$\begin{array}{c} \text{R} \\ \\ \text{H}-\text{C}-\text{OH} \\ \\ \text{H}-\text{C}-\text{OH} \\ \\ \text{R} \end{array}$	$(+13^\circ)$ $(+14^\circ)$ (-16°) $(+17^\circ)$
<i>l</i> -Amyl <i>d</i> -tartrate.		<i>l</i> -Amyl <i>l</i> -tartrate.		<i>l</i> -Amyl <i>i</i> -tartrate.	
(I.)		(II.)		(III.)	

In the compound I, let the *l*-amyl radicles contribute each $+10^\circ$ to the rotation, and each of the asymmetric centres of the acid contribute 15° , whereas in the compound II, each *l*-amyl radicle contributes 20° and each *l*-tartaryl radicle -18° . In the compound III it would perhaps be most natural to expect the rotatory power of these different centres to lie more or less intermediate between the values in the compounds I and II. Half the rotation of the compound I gives the rotatory value of the group

$$\begin{array}{c} \text{R} \\ | \\ \text{H}-\text{C}-\text{OH} \\ | \\ \text{H}-\text{C}-\text{OH} \\ | \\ \text{R} \end{array}$$

when attached to an exactly similar group, whereas half the rotation of the compound II gives the rotatory power of the radicle $\text{H}-\text{C}-\text{OH}$ when combined with a group identical with itself.

The sum of these would be the rotation of the two groups in combination, assuming that they exert no influence on each other, whereas the rotation of the compound III is the sum of the rotations of these two groups plus any change of rotation due to the influence of optical superposition, and it will probably be clear that in certain cases a positive change in the rotation of the upper group might be masked by a negative change in the rotation of the lower group. Of course, in certain other cases the effect might be an enhancement. It will be clear, however, that the difference upon which we have to depend is merely a subsidiary or secondary

effect. In the imaginary example quoted above the mean of the rotations of I ($+50^\circ$) and II ($+4^\circ$) is 27° , whilst the rotation of the compound III is 28° , only one degree more. A slightly different choice of values would make this difference zero. Thus, even if the mutual influence of the different centres were very great indeed and the principle of optical superposition altogether violated, the mean of the rotations of two compounds of the type of I and II might, owing to a compensation of effects, be exactly equal to that of the compound III. It must carefully be noticed, therefore, that a negative result by our method may indicate, but is by no means necessarily a proof of, the correctness of this principle, whereas even a small positive result, provided, of course, it falls outside the limit of experimental error, may in reality indicate a wide departure from it, and is definitely a proof that van't Hoff's assumption is incorrect.

The present paper deals with two sets of three compounds each, similar to those referred to above, namely, the three di-*l*-menthylamine tartrates and the three di-*l*-amyl dimethoxysuccinates. The rotations of the three menthylamine tartrates were examined in methyl-alcoholic solution at a concentration of $c=1.311$ and at a temperature in the immediate neighbourhood of 22° , it having been found that a slight change of temperature of one or two degrees made no appreciable difference upon the rotations of the solutions. The numbers obtained were as follows:

l-Menthylamine Tartrates.

Methyl-alcoholic solution, $c=1.311$.

	$[\text{M}]_D^{20}$
<i>l</i> -Menthylamine <i>l</i> -tartrate	-193.2°
„ „ <i>d</i> -tartrate	-57.9
Mean	-125.5
<i>l</i> -Menthylamine <i>i</i> -tartrate	-147.5

The mean of the rotations of the *l*- and *d*-derivatives differs by 22° from the rotation of the corresponding *i*-tartrate, this agreeing roughly with Walden's results for the amyl tartrates, and with Patterson, Taylor, and Kaye's for the di-*l*-menthyl diacetyltartrates.

For our second series of compounds we thought it desirable to use an acid with as high a rotation as possible, and therefore chose dimethoxysuccinic acid, the different forms of which we have combined with *l*-amyl alcohol, and in the future intend to combine with other active alcohol-radicles.

The results obtained were as follows:

Di-l-amyl Esters of the Dimethoxysuccinic Acids.

	[M] _D .			
	20°.	60°.	100°.	140°.
<i>l</i> -Acid.....	-225.1°	-212.7°	-199.8°	-186.4°
<i>d</i> -Acid	+240.5	+230.3	+220.1	+209.2
Mean	+7.7	+8.8	+10.15	+11.4
<i>i</i> -Acid.....	+12.2	+11.86	+11.62	+11.46*

* Extrapolated.

It will be noticed that here again at a temperature of 20° the mean value of the rotations of the derivatives of the *d*- and the *l*-acid, namely, +7.7°, differs from the value obtained for the rotation of the derivative of the *i*-acid, +12.2°, by some 5°, which, considering that the rotation of the derivatives of the *d*- and the *l*-acid extend over a range of some 500°, does not seem very much, but which compared with the rotation of *l*-amyl alcohol is not inconsiderable. It is thus merely a question whether this difference is greater or less than the experimental error, and the experimental error could only be determined in this case by repeating the whole investigation. That, however, as we had only a small supply of *l*-amyl alcohol, was impracticable, but attention may be directed to an interesting point which appears to bear upon this question. It will be noticed that as the temperature rises the mean value for the rotations of the derivatives of the *d*- and the *l*-acid gradually increases from +7.7° at 20° to +8.8° at 60°, to 10.15° at 100° and to 11.4° at 140°, whereas the rotation of the derivative of the *i*-acid gradually diminishes with increase of temperature, reaching the values +11.86° at 60°, 11.62° at 100°, and 11.46° at 140°. In other words, that at 140° the mean value of the *d*- and the *l*-derivatives is almost identical with that of the *i*-derivative. Now it must also be noticed, as is rendered most clear by plotting these two series of numbers on a diagram, that this is not a case in which two curves approach a common value asymptotically, but that the graphs would intersect in the immediate neighbourhood of 140°, and then separate again. Now if the principle of optical superposition were true it would surely be expected that these two values should be identical at all temperatures, or that they should differ at different temperatures only to a slight extent and in an irregular manner. The fact that this is not the case seems to us a strong indication, in the first place that these differences are not due to experimental error, and, in the second place, that the mutual effect of the different asymmetric centres varies with change of temperature, so that at 140° there is realised in this series of compounds the state of affairs referred to above (p. 146), where in spite of the assumed falsity of the principle of optical

superposition the various effects balance one another in such a way as to give a result identical with that which should be obtained if this principle were in fact true.

It would therefore seem that all the work theoretically sound which has been carried out on this subject by Walden, by Tschugaev and Glebko, by Patterson, Taylor, and Kaye, and by ourselves is decidedly out of agreement with the requirements of the principle of optical superposition. It ought, however, to be mentioned that our present results also contain a slight element of uncertainty since the *l*-amyl alcohol used in the investigation had α_D^{20} (100 mm.) -4.58° , whereas the purest obtained by Marckwald (*Ber.*, 1901, **34**, 485) had $[\alpha]_D^{20} -5.90^\circ$, which since $D_4^{20} = 0.816$ would give for the observed rotation $\alpha_D^{20} -4.812^\circ$, 0.232° higher than ours. Since the impurity contained in the alcohol is an inactive substance it is not likely to affect the results to any great extent. Nevertheless, the objection does exist.

It is of some interest to notice that the density of *l*-amyl *l*-dimethoxysuccinate is greater than that of *l*-amyl *d*-dimethoxysuccinate only by one or two units in the fourth place, whilst the density of *l*-amyl *i*-dimethoxysuccinate is greater at 20° than that of the other two by about four units in the third place. This difference diminishes, however, as the temperature rises, in such a way that in the neighbourhood of 130° the densities of all three would be the same. At higher temperatures, presumably, the density of the *i*-derivative would be less than that of either of the other two.

We wish particularly to direct attention to a slightly improved method for the preparation of alkyloxy-esters. The *d*- and the *l*-dimethoxysuccinic esters used by us were prepared exactly according to the method of Purdie and Irvine (*T.*, 1901, **79**, 957), but during the course of our work it occurred to us that the process might be improved. On the one hand it has been shown by J. W. Walker (*T.*, 1895, **67**, 914) that in the esterification of a hydroxy-acid by the silver salt method a product is obtained having a much higher rotation than the ester which has been prepared from the acid and the alcohol (see also Purdie and Williamson, *T.*, 1896, **69**, 821, *passim.*), and it was shown by Purdie and Lander (*T.*, 1898, **73**, 288) that this is due to the formation of some alkyloxy-derivative. Then, on the other hand, Purdie and Pitkeathly (*T.*, 1899, **75**, 160) state that when tartaric acid is alkylated directly with ethyl iodide and silver oxide a fairly good yield of ethyl diethoxysuccinate is obtained. It would therefore appear that the simplest and quickest way of preparing the alkyloxy-derivative of an ester would be to produce the simple ester from the silver salt

of the acid by the action of alkyl iodide and simultaneously to convert this into the alkyloxy-compound by means of further alkyl iodide and silver oxide. Thus to prepare dimethyl dimethoxysuccinate, silver oxide and methyl iodide are heated in a flask under reflux to the boiling point of the iodide, silver tartrate being then added from time to time in portions of 5 or 6 grams. This method gives practically a quantitative yield. Its special advantage lies in the fact that it is generally much easier and quicker to make the silver salt of an acid than to make the methyl ester. In addition

Rotation of dimethyl d-dimethoxysuccinate in the homogeneous condition and in solution in nitrobenzene and in ethylene bromide.

the whole course of the reaction is smoother and simpler than by the method of Purdie and Irvine (see p. 154).

We have also taken the present opportunity to examine the rotation of dimethyl *d*-dimethoxysuccinate over a considerable range of temperature both in the homogeneous condition and in solution in nitrobenzene and in ethylene bromide, two solvents which, on ethyl tartrate at least, exert quite opposite effects.

The results are shown graphically in the diagram. The rotation of the homogeneous ester diminishes with rise of temperature

almost linearly, but we are inclined to think that there is probably a point of inflexion in the neighbourhood of 100° , and that below this temperature the rotation tends towards a maximum, and above it towards a minimum value.

Ethylene bromide diminishes the rotation of the ester, and the appearance of the curve in this solvent would suggest the existence of a maximum rotation in the neighbourhood of zero. Nitrobenzene, on the other hand, at ordinary temperatures raises the rotation of the ester to a very considerable extent. In this solvent the temperature-coefficient is large, and the rotation diminishes very much more rapidly on heating than does that of the homogeneous ester. It is interesting to notice that there is here no point of inflexion apparent, and that the temperature-rotation curve cuts that for the homogeneous ester. The behaviour of these two solvents on the rotation of this ester is thus similar to their influence on the rotation of ethyl tartrate, and suggests that here also a maximum rotation occurs at the ordinary temperature in the solvent producing the lowest rotation; that in the homogeneous ester this maximum moves towards a higher value at a lower temperature; whilst in nitrobenzene a much greater maximum rotation would be found at a still lower temperature (see T., 1913, 103, 157).

EXPERIMENTAL.

Di-l-menthylamine d-Tartrate, $M=460$.—This salt, which was prepared by adding two molecular proportions of *l*-menthylamine to a concentrated aqueous solution of tartaric acid, was purified by solution in ethyl alcohol and precipitation with ether. On heating, slight traces of liquid appeared on the walls of the containing tube at about 90° , darkening in colour occurred at 190° , and the salt melted fairly sharply at 198° :

0.3988 gave 21.6 c.c. N_2 (moist) at 15° and 752.6 mm. $N=6.29$.

$C_{24}H_{42}O_6$ requires $N=6.08$ per cent.

0.3448 of this specimen, made up to 26.3 c.c. ($c=1.3111$) with ordinary pure methyl alcohol (acetone-free), gave $\alpha_D^{22.6}$ [$l=400$ mm.] -0.66° , whence $[\alpha]_D^{22.6} -12.585^{\circ}$, and $[M]_D^{22.6} -57.89^{\circ}$.

Di-l-menthylamine l-tartrate was prepared from *l*-tartaric acid, 2.463 grams of which, made up to 26.3 c.c. with water, gave $\alpha_D^{19.5}$ [$l=400$ mm.] -5.387° , whence $[\alpha]_D^{19.5} -13.4^{\circ}$. A specimen of ordinary laboratory tartaric acid gave, under the same conditions, α_D^{19} [$l=400$ mm.] $+5.34^{\circ}$. One gram of this acid, mixed with 2.12 grams of *l*-menthylamine and 8 c.c. of water, gave, on keeping overnight, large, flat crystals, readily soluble in methyl or ethyl

alcohol. The specimen used was purified by solution in ethyl alcohol and precipitation by ether. On heating it showed traces of liquid on the walls of the containing tube at about 120°, and melted fairly sharply at 194°:

0.4 gave 20.7 c.c. N₂ (moist) at 19° and 776.3 mm. $N = 6.08$.

C₂₄H₄₂O₆ requires $N = 6.08$ per cent.

0.2448 of this substance, made up to 26.3 c.c. ($c = 1.3111$) with ordinary pure methyl alcohol (acetone-free), gave $\alpha_D^{20.7}$ [$l = 400$ mm.] -2.203° , whence $[\alpha]_D^{20.7}$ 42.005° and $[M]_D^{20.7}$ -193.2° .

Di-l-menthylamine i-Tartrate.—The *i*-tartaric acid used in this investigation was prepared by the method worked out by Winther (*Zeitsch. physikal. Chem.*, 1906, **56**, 507). On shaking an aqueous solution of the acid with the calculated quantity of *l*-menthylamine the salt separates at once. After two crystallisations from absolute ethyl alcohol it melted at 218°. It was decidedly more readily soluble in methyl alcohol. The specimen used was purified by solution in absolute ethyl alcohol and precipitation by ether:

0.4014 gave 21.5 c.c. N₂ (moist) at 19° and 750.6 mm. $N = 6.17$.

C₂₄H₄₂O₆ requires $N = 6.08$ per cent.

0.3448 of this salt, made up to 26.3 c.c. ($c = 1.3111$) with ordinary pure methyl alcohol (acetone-free), gave α_D^{22} [$l = 400$ mm.] -1.682° , whence $[\alpha]_D^{22}$ -32.07° and $[M]_D^{22}$ -147.5° .

Dimethyl d-dimethoxysuccinate was prepared from methyl *d*-tartrate exactly according to Purdie and Irvine (T., 1901, **79**, 957). It boiled at 135°/16 mm., and melted at about 49°.

Rotation of Dimethyl d-Dimethoxysuccinate.

t	15°	16°	55.9°	60.5°	73.2°	100°	150°	182°
α_D^t (100 mm.) [*] + 101.6°		101.35°	93.56°	92.64°	90.26°	85.66°	77.99°	72.81°
d	1.178	1.177	1.136	1.129	1.117	1.088	1.0355	0.998
$[\alpha]_D^t$	86.2°	86.1°	82.4°	82.1°	80.8°	78.7°	75.3°	73.00°
$[M]_D^t$...	177.7°	177.4°	169.7°	169.0°	166.4°	162.2°	155.2°	150.3°

Densities determined:

t	65.3°	69.6°	80.6°	99.8°	153°
d	1.1251	1.1204	1.1088	1.0881	1.0328

* The rotations were determined in a brass tube ($l = 30.48$ at 20°) and were corrected for expansion of the tube on heating and then calculated to a 100 mm. layer of the liquid at the temperature of the experiment.

Dimethyl d-Dimethoxysuccinate in Ethylene Bromide. $p = 9.016$.

t	14.9°	43.5°	57.8°	76.7°	106°
α_D^{20} (100 mm.)*	+13.576°	13.09°	12.74°	12.37°	11.85°
d	2.026	1.971	1.945	1.909	1.852
$[\alpha]_D^{20}$	74.3°	73.6°	72.7°	71.8°	71.00°
$[M]_D^{20}$	153.1°	151.6°	149.7°	148.0°	146.2°

Densities determined:

t	15.8°	44.9°	88.5°
d	2.0254	1.9690	1.8851

* In a glass tube.

Dimethyl d-Dimethoxysuccinate in Nitrobenzene. $p = 9.102$.

t	-10.6°	-8.8°	-3.2°	+18.4°	48.3°	81°	124.5°	159.5°
$[\alpha]_D^{20}$ (100 mm.)*	+12.82°	12.78°	12.35°	11.37°	10.07°	8.88°	7.77°	7.02°
d	1.2300	1.2280	1.2225	1.2010	1.1710	1.139	1.096	1.061
$[\alpha]_D^{20}$	114.5°	114.4°	111.0°	104.0°	94.4°	85.6°	77.9°	72.7°
$[M]_D^{20}$	235.9°	235.7°	228.7°	214.2°	196.5°	176.4°	160.4°	149.7°

Densities determined:

t	15.6°	43.0°	98.7°	150°
d	1.2041	1.1764	1.1212	1.0707

* Glass tube.

Dimethoxysuccinic acid was prepared exactly according to Purdie and Irvine (T., 1901, **79**, 959). The acid, when recrystallised from water, melted at 153°.

Di-l-amyl d-Dimethoxysuccinate.—Ten grams of *d*-dimethoxysuccinic acid were placed in a Claisen flask along with 50 grams of *l*-amyl alcohol, the rotation of which was α_D^{20} [$l=100$ mm.] -4.58° . Dry hydrogen chloride was then passed into the mixture in the cold for about a day, after which the flask was heated on the water-bath to just below 100°, the passage of dry hydrogen chloride being continued for three or four days. The contents of the flask were then distilled under the ordinary pressure until the temperature rose to 140°, and then for a short time under diminished pressure. When all the amyl alcohol had been removed the *l*-amyl *d*-dimethoxysuccinate was distilled under a pressure of about 9 mm. A small first fraction was collected up to a temperature of about 170°; the main fraction boiled at 175–180°. The crude product had α_D^{17} [$l=30.48$ mm.] $+23.7^\circ$. It was then redistilled and boiled at about 170°/3 mm. It was divided into four fractions. The rotations of the last three at 15.9° in a tube of $l=30.48$ mm. were

II + 24.12°, III + 24.13°, IV + 23.82°. Fractions I and IV were then combined and redistilled, being collected in two portions. Fractions II and III were then similarly treated, and the second fractions from each distillation were combined and finally distilled. The boiling point lay at about 170°/5 mm. The rotation of this substance was then examined over a considerable range of temperature with the following results. A brass tube, gilt inside, was used, allowance being made for the expansion of the brass. The numbers quoted below for observed rotation are those for an actual thickness of 100 mm. at each temperature.

Di-l-amyl d-Dimethoxysuccinate [M=318].

<i>t</i>	15°	31°	51°	74°	110°	136°	17.2°*
α_D^{20} (100 mm.)	+78.95°	76.18°	73.25°	69.99°	64.43°	60.44°	78.52°
<i>d</i>	+1.0171	1.0035	0.9870	0.9677	0.9377	0.9157	1.0138
$[\alpha]_D^{20}$	+77.62°	75.92°	74.22°	72.33°	68.72°	66.01°	77.42°
[M] _D ...	+246.8°	241.4°	236.0°	230.0°	218.5°	209.9°	246.3°

Densities determined :

<i>t</i>	15.7°	29.0°	45.2°	69.3°	99.6°
<i>d</i>	1.0169	1.0057	0.9916	0.9706	0.9460

* After cooling.

Dimethyl *l*-tartrate was prepared from a pure specimen of sodium ammonium *l*-tartrate by the action of pure methyl alcohol and dry hydrogen chloride in the cold. The process was not altogether satisfactory, since the crude ester tended to decompose on distillation. The methyl *l*-tartrate ultimately obtained was induced to solidify by the introduction of a fragment of methyl *d*-tartrate into a few drops on a watch-glass. This brought about crystallisation of this portion, which in turn was used to induce crystallisation of the main portion. The setting up of crystallisation in an active substance by the introduction of a small quantity of the enantiomorph is a somewhat remarkable fact. Although the methyl *l*-tartrate crystallised, it formed in the end only a pasty mass showing no definite melting point.

Dimethyl l-dimethoxysuccinate was prepared from some of this methyl *l*-tartrate by treatment with methyl iodide and silver oxide. An ester was obtained boiling at 125—135°/9 mm., the rotation of which was found to be α_D^{20} [*l*=30.48] – 28.72°, and at a higher temperature α_D^{75} [*l*=30.48] – 25.16°, both values being about two degrees lower than the corresponding rotation values of the *d*-ester, this being doubtless due to some racemisation having occurred in the preparation of the methyl *l*-tartrate, which, as explained, had not been satisfactory. The dimethyl *l*-dimethoxysuccinate was therefore crystallised several times from a mixture of ether and

light petroleum until the melting point rose to 52° , and the rotation had reached the same value as was found for the *d*-ester, namely, $\alpha_D^{25} [l=30.48 \text{ mm.}] -28.255^{\circ}$. The ester was thus pure, and was hydrolysed with barium hydroxide as before, giving *l*-dimethoxysuccinic acid* (m. p. 154°), from 10 grams of which *l*-amyl *l*-dimethoxysuccinate was prepared in exactly the same way as was the *l*-amyl *d*-dimethoxysuccinate. The ester boiled at about $160-170^{\circ}/5 \text{ mm.}$, the yield being 14.8 grams. The crude product had $\alpha_D^{18.2} [l=25 \text{ mm.}] -18.16^{\circ}$. This was then redistilled, four fractions being collected, the rotations of which were, in a 25-mm. tube and at 19.5° : I -17.95° , II -18.33° , III -18.05° , IV -17.83° . Fractions II and III were then united, redistilled, and collected in two portions. The boiling point lay about $160^{\circ}/5 \text{ mm.}$ With the second fraction the following observations were made:

Di-l-amyl l-Dimethoxysuccinate [$M=318$].

t	17°	33.8°	50°	81.5°	95.5°	137°
$\alpha_D^{18.2}$ (100 mm.)	-72.31°	-69.65°	-67.11°	-62.3°	-60.09°	-53.96°
d	1.0155	1.0015	0.988	0.961	0.950	0.915
$[\alpha]_D^{18.2}$	-71.21°	-69.55°	-67.94°	-64.83°	-63.25°	-58.98°
$[M]_D^{18.2}$...	-226.4°	-221.2°	-216.0°	-206.1°	-201.1°	-187.55°

Densities determined:

t	16.3°	31.4°	50.5°	75.1°
d	1.0161	1.0036	0.9870	0.9663

Dimethyl i-dimethoxysuccinate was prepared as follows: Fifty grams of silver oxide were placed in a flask along with 205 grams of methyl iodide. The flask, fitted to an inverted condenser, was then heated on the water-bath until the methyl iodide boiled. Twenty-four grams of silver *i*-tartrate, which had been prepared by neutralising *i*-tartaric acid with sodium hydroxide and then precipitating with silver nitrate, washing by decantation with water several times, then with alcohol, and finally with ether, and drying on a porous plate overnight. The silver tartrate was added in portions in the course of half-an-hour. The excess of methyl iodide was then distilled off from the water-bath, the residual mass placed in a Soxhlet apparatus, and extracted with ether for about two hours. The crude dimethoxysuccinic ester weighed 13 grams, the yield being thus practically quantitative. The dimethyl *i*-dimethoxysuccinate was recrystallised from ether, in which it is readily soluble. It melts at 68° . The ester crystallises also from benzene in small, diamond-shaped crystals; it is very sparingly

* The whole preparation would doubtless have been much more satisfactory and simple had it been conducted in the same manner as was later that of the *i*-ester.

soluble in light petroleum, but can be recrystallised from it also. Twenty grams of this dimethyl *i*-dimethoxysuccinate were dissolved in about 100 c.c. of water, and hydrolysed by heating on the water-bath for three hours with a little more than the calculated quantity of sodium hydroxide solution. The excess of sodium hydroxide was then titrated exactly with hydrochloric acid, using litmus as an indicator. The solution was filtered and evaporated to dryness. The resulting salt after drying on the water-bath was broken into small pieces, placed in a Soxhlet apparatus, and extracted with ether for some hours. Crusts of small, well-formed crystals soon separated in the flask, and when the extraction was complete the ether was distilled off and the remaining *i*-dimethoxysuccinic acid recrystallised from water, in which, however, it is very readily soluble. It melts at 161°.

Di-l-amyl i-dimethoxysuccinate was prepared from 10 grams of *i*-dimethoxysuccinic acid (which softened a little about 157° and melted fairly sharply at 160—161°) and 50 grams of *l*-amyl alcohol in just the same way as the *d*- and *l*-compounds. The *l*-amyl *i*-dimethoxysuccinate was distilled under a pressure of about 3 mm. After a small first fraction had been collected at 155°, a second main fraction of 14 grams was collected between 153° and 175°, but chiefly at 155°/3 mm. It had α_D^{16} [$l=100$ mm.] +3.916°. This fraction was then redistilled under 3 mm. pressure, and a small first fraction removed. The second fraction boiled at 155°/3 mm.; it had α_D^{17} [$l=100$ mm.] 3.913°, practically identical with the previous value.

l-Amyl *i*-Dimethoxysuccinate [$M=318$].

t	17°	37.5°	60°	91.6°	20.4°
α_D^{16} (100 mm.)	+3.913°	3.780°	3.664°	3.487°	3.905°
d	1.0196	1.0017	0.9819	0.9544	1.0167
$[\alpha]_D^{16}$	+3.84°	3.77°	3.73°	3.65°	3.84°
$[M]_D^{16}$	+12.21°	12.00°	11.87°	11.62°	12.21°

Densities determined:

t	17.6°	42.35°	70.4°	99.2°
d ..	1.0193	0.9973	0.9726	0.9479

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