CCLXVI.—*The Influence of Solvents and other Factors on the Rotation and the Rotation-Dispersion of Optically Active Compounds. Part XXVII. Derivatives of Lactic Acid.*

By T. S. PATTERSON and ALEXANDER LAWSON.

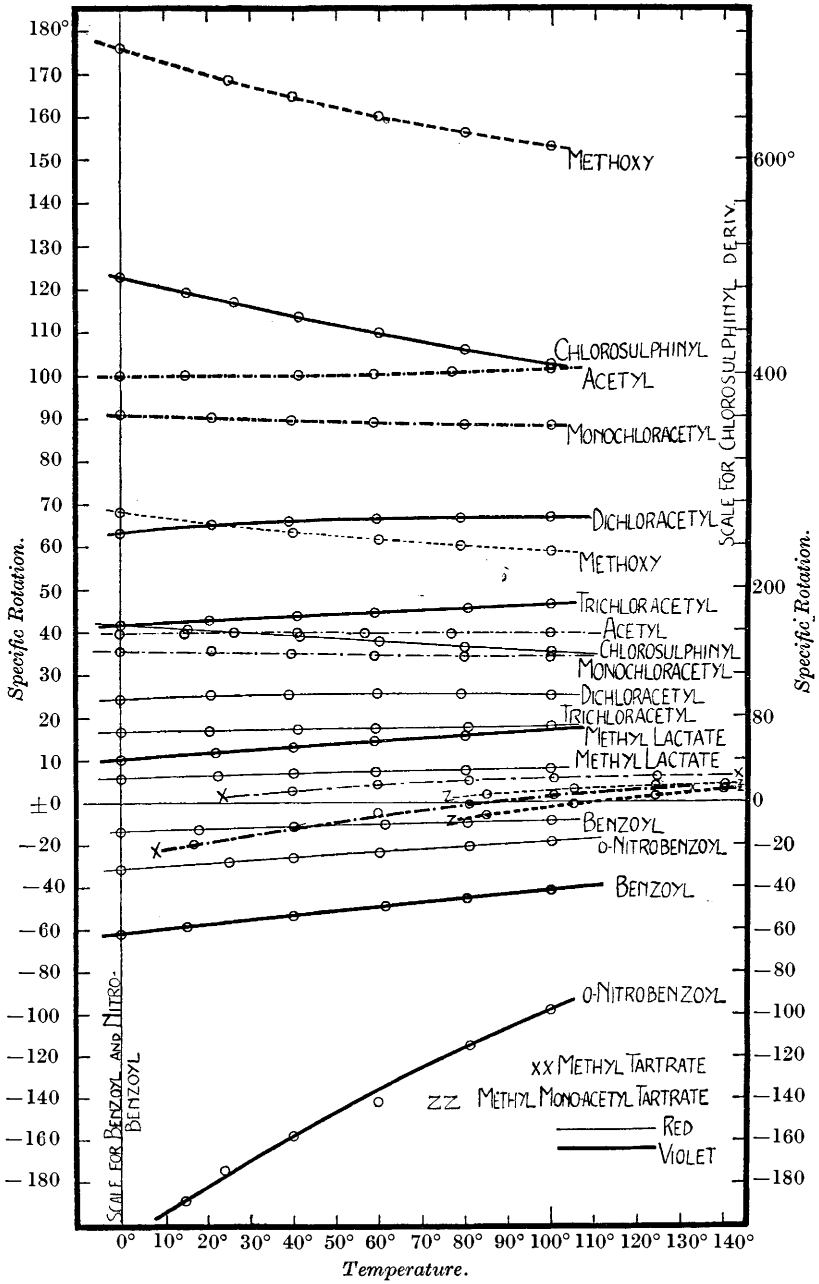
IN a paper published some years ago (J., 1913, **103**, 2263) one of us (with Forsyth) described the optical behaviour of a number of derivatives of lactic acid as regards influence of solvents and temperature change. At that time, unfortunately, light of one colour only was available, but, on account of the interest of derivatives of lactic acid in regard to rotation dispersion, it was thought worth while to repeat some of this work with light of other colours, and to include additional derivatives of lactic acid.

The procedure formerly described for obtaining lactic acid was slightly modified (see p. 2045), and from a sample of the acid having a moderately high lævorotation, methyl lactate was prepared. From this, the methyl esters of α-acetoxy-, α-methoxy-, α-benzoyloxy-, α-mono-, -di-, and -tri-chloroacetoxy-, α-*o*-nitrobenzoyloxy-, and α-chlorosulphinyl-propionic acid were obtained, and their rotations were examined for six different colours of light over a considerable range of temperature.

The results appear to show, in agreement with those of other recent workers (Freudenberg, *Ber.*, 1914, **47**, 2027, etc.; Clough, J., 1918, **113**, 528; Wood and Nicholas, J., 1928, 1712), that the lactic acid, which itself, in the homogeneous condition, is dextrorotatory, but forms a lævorotatory lactide, is configuratively related to the *l*-tartrates and therefore ought to be called *l*-lactic acid.* Formerly it was referred to as *d*-lactic acid. The lactic acid with which Patterson and Forsyth worked should, therefore, be called *d*-lactic acid. Although, in the experiments now recorded *l*-lactic acid was used, the sign of rotation has been inverted in the diagrams to make the results comparable with those for the *d*-tartrates.

* The nomenclature "*l*(+) lactic acid" suggested by Wohl and Freudenberg (*Ber.*, 1923, **56**, 309) is open to the objection of ambiguity, unless the conditions of the positive rotation are more definitely specified. It refers in this case to the homogeneous condition at *ca.* 25° for sodium light, but, at other temperatures and for other colours of light, the rotation might possibly be negative. The symbol "*d*(+) tartaric acid" refers to a different condition of the active substance, *viz.*, to aqueous solutions at the ordinary temperature. In the homogeneous condition at about room temperature ordinary tartaric acid would probably be lævorotatory, at least for certain colours of light (J., 1913, **103**, 167). Something more definite would therefore be necessary, such as "$l\left(\overset{t^\circ}{\underset{\lambda}{+\text{homog.}}}\right)$ lactic acid," which, if precise, is also a little clumsy.

FIG. 1.


180°
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
±0
−20
−40
−60
−80
−100
−120
−140
−160
−180
Specific Rotation.
600°
400
200
80
0
−20
−40
−60
−80
−100
−120
−140
−160
−180
Specific Rotation.
SCALE FOR CHLOROSULPHINYL DERIV.
SCALE FOR BENZOYL AND NITRO-BENZOYL
METHOXY
CHLOROSULPHINYL
ACETYL
MONOCHLORACETYL
DICHLORACETYL
METHOXY
TRICHLORACETYL
ACETYL
CHLOROSULPHINYL
MONOCHLORACETYL
DICHLORACETYL
TRICHLORACETYL
METHYL LACTATE
METHYL LACTATE
X
Z
Z
X
X
Z
BENZOYL
O-NITROBENZOYL
BENZOYL
O-NITROBENZOYL
XX METHYL TARTRATE
ZZ METHYL MONOACETYL TARTRATE
RED
VIOLET
0°
10°
20°
30°
40°
50°
60°
70°
80°
90°
100°
110°
120°
130°
140°
Temperature.

In Fig. 1 are shown temperature–rotation curves for two colours of light, red ($\lambda = 6716$ Å.U.) and violet ($\lambda = 4358$ Å.U.), the curves for the latter being heavily drawn and those for the former lightly; each set of curves may therefore be taken by itself. Curves for other colours are unnecessary since, in all cases examined, they are distributed fairly evenly between the two extremes shown. In the diagram are also included curves for methyl tartrate and its mono-acetyl derivative, for the same colours of light, taken from a recent paper by Wood and Nicholas (J., 1928, 1692), in order to facilitate the comparison between the curves for the tartrates and the lactates. Further, it should be noted that there are three different scales on the diagram. That on the left margin above the zero line applies to all the curves in the upper part of the diagram (including the curves for methyl tartrate and acetyltartrate, both above and below the zero line), whilst the scale for the chlorosulphinyl derivative is given on the right margin. The scale given on the part of the diagram below the zero line applies to the benzoyl and nitrobenzoyl derivatives only.

The general impression produced by the curves of Fig. 1 is that they resemble fairly closely those for the corresponding tartrates; the curves for methyl lactate itself show the same type of curvature as do those for the tartrates, *i.e.*, they apparently tend towards maximum values at a high temperature. It is to be noticed that, whereas the methyl tartrate curve for violet light lies below the corresponding curve for red light, the opposite is the case for methyl lactate. It will be observed, however, that these two curves for methyl tartrate tend to intersect at a high temperature, whilst the two curves for methyl lactate tend to intersect at a low temperature. In other words, the region of anomalous dispersion for the simple tartaric esters occurs at a high temperature, and that for the simple lactic esters, if it exists, would be found at a low temperature.

As regards the other curves, it will be noticed that whereas the derivatives having considerable negative rotations show a rapid increase of rotation—*i.e.*, become less negative—with rise of temperature, apparently tending towards maximum values at a high temperature, those with intermediate rotations, such as methyl lactate itself, show comparatively small changes of rotation on heating, and would presumably reach maxima at temperatures in the region of 150°, whilst the derivatives with high rotations, such as the methoxypropionate and the chlorosulphinyl derivative * (the curve for the latter being on a reduced scale), have rotations which rapidly diminish as the temperature rises. The curves on the diagram,

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* A referee points out that methyl α-chlorosulphinylpropionate should contain an asymmetric sulphur atom (Phillips, J., 1925, **127**, 2552; Harrison, Kenyon, and Phillips, J., 1926, 2079), which might influence the rotation.

therefore, show a behaviour in general agreement with that of the *d*-tartrates, and it is for this reason that we consider them to be analogous to those for the derivatives of *d*-tartaric acid, and therefore, that this particular set are those of *d*-lactic acid.

Taking into consideration all these curves, it would appear that the general temperature–rotation curves (see J., 1916, **109**, 1141) for the lactates are very similar to those for the tartrates: at a low temperature the rotations should have high negative values; with continuously increasing temperature these values should increase, pass through a region at which the curves intersect one another, pass through maximum values, and ultimately tend again towards minimum values.

The region of visibly anomalous dispersion was not actually reached in any of these cases, but it has been shown by Clough (J., 1918, **113**, 552) to exist in solutions of methyl lactate in water. Now, it might be expected from the appearance of these curves that the intersection of the violet and the red curve for methyl lactate, which would occur at a low temperature in the homogeneous ester, should come into the region of ordinary temperatures in a solvent which depresses the rotation of the ester. Ethylene dibromide depresses the rotation of ethyl tartrate considerably, and therefore we examined a solution of methyl lactate in this solvent; the data obtained afforded evidence of visibly anomalous dispersion, thus confirming our expectation.

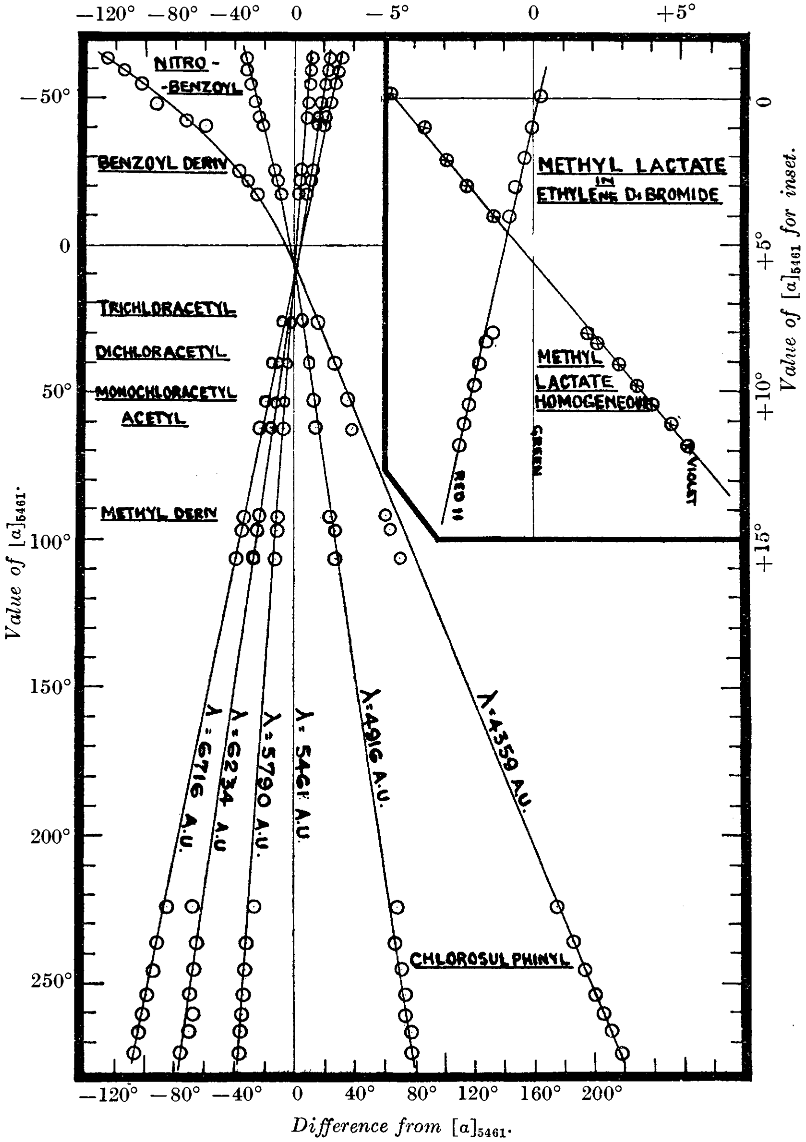
Fig. 2 shows a characteristic diagram drawn, after inversion of sign, from the data which we have collected. On the whole, the data perhaps do not lie quite so well upon straight lines as has been found for many other compounds. The line for violet light notably, but also that for blue, requires a decided curvature in order to fit approximately the experimental points. The scale of the main part of Fig. 2 is much too small for the data for methyl lactate, either in the homogeneous condition or in solution in ethylene dibromide, to be represented, and therefore a small characteristic diagram for these two conditions is inset; from this it will be seen that the region of visibly anomalous dispersion, which is not quite reached in the homogeneous ester, is reached in its solution. It appears from this diagram that by cooling homogeneous methyl *d*-lactate the rotation for green and violet would become identical at the rotational value + 5·5°, which would be the rational zero for these two colours.

EXPERIMENTAL.

From a sample of syrupy lactic acid having α_{5461} (100 mm.) − 3·47° active zinc ammonium lactate was prepared as follows. To 900 c.c. of

FIG. 2.

Characteristic Diagram for Derivatives of d-*Lactic Acid.*



boiling water were added, with stirring, 750 c.c. of the syrup, followed slowly by 426 g. of zinc oxide, and the solution was boiled till neutral in reaction (about 8 hours). On cooling, inactive zinc lactate separated and was filtered off, and on concentration of the filtrate, active zinc lactate crystallised out. The inactive salt was boiled with several 2-litre portions of water till the extracts showed no appreciable rotation. The product obtained from these extracts was added to the main bulk of active zinc lactate. In this way about 278 g. of active and 900 g. of inactive zinc lactate were obtained, so that the original lactic acid syrup must have been composed of about 62% of the lævo- and 38% of the dextro-form. The purest sample of zinc lactate obtained had $\alpha_{5461}^{17^\circ}$ − 0·39° ($c = 2{\cdot}5$; $l = 200$ mm.).

Of this zinc lactate, 100 g. were dissolved in 500 c.c. of water, 40 g. of ammonium carbonate in 180 c.c. of cold water were added, and the precipitated zinc carbonate was filtered off. To this solution of ammonium lactate 160 g.* of active zinc lactate in 750 c.c. of water were added. The zinc ammonium *l*-lactate obtained on evaporation and cooling was recrystallised from dilute ammonia solution until it showed $\alpha_{5461}^{25^\circ}$ (200 mm.) = — 1·90° for a solution of 1·6 g. in 20 c.c. of dilute ammonia (300 c.c. of concentrated ammonia and 1000 c.c. of distilled water; Patterson and Forsyth, *loc. cit.*). From 2 litres of lactic acid syrup, 400—450 g. of pure zinc ammonium *l*-lactate could be obtained.

Methyl l-*Lactate*.—The ester was prepared by the methods of Purdie and Irvine (J., 1899, **75**, 484) and Patterson and Forsyth (*loc. cit.*), the zinc ammonium lactate having previously been carefully dried in an air-oven until it had lost a weight equivalent to slightly more than 2 mols. of water of crystallisation. The methyl alcohol had been purified by standing over quick-lime, and by distillation. The ester boiled at 47°/15 mm.

The rotation of the preparation was then examined as shown below. In the sequel, for convenience and to save space, letters will be used to indicate the colour of light as follows :

	r_1.	r_2.	y.	g.	b.	v.
λ, Å.U.	6716	6234	5790	5461	4916	4358

t	17·6°	22·3°	40·4°	79·6°	100°
d	1·096	1·091	1·071	1·025	1·002

t.	$[\alpha]_{r_1}$.	$[\alpha]_{r_2}$.	$[\alpha]_{y}$.	$[\alpha]_{g}$.	$[\alpha]_{b}$.	$[\alpha]_{v}$.
−7·5°	−5·76°	−6·53°	−7·32°*	−7·95°†	−9·15°	−9·705°†
0	5·88	6·68	7·58	8·29	9·47	10·40
22·3	6·39	7·20‡	8·22‖	9·04‖	10·48‡	11·93‖
39·9	6·695	7·69	8·79	9·70	11·36	13·17
58·7	7·13	8·17	9·36	10·35	12·25	14·42
80·05	7·57	8·68	10·02	11·08	13·11	15·73
100	7·95	9·16	10·53	11·69	13·97	16·86

* At −9°. † At −10°. ‡ At 22°. ‖ At 21·9°.

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[*] This is 40 g. less than is required to convert all the ammonium lactate into double salt. Crystallisation of the product thus took place from a solution containing excess of ammonium lactate.

Methyl l-α-*Acetoxypropionate*.—This was prepared from methyl lactate and acetyl chloride and purified by fractionation with a column; b. p. 68°/13 mm.

t	18·8°	20·4°	39·6°	67°	80°	100°
d	1·089	1·0866	1·0677	1·0350	1·0204	0·9983

t.	$[\alpha]_{r_1}$.	$[\alpha]_{r_2}$.	$[\alpha]_{y}$.	$[\alpha]_{g}$.	$[\alpha]_{b}$.	$[\alpha]_{v}$.
0°	−40·025°	−46·64°	−54·56°	−61·78°	−76·62°	−100·03°
15	39·83	46·41	54·47*	61·72*	76·27	100·02*
41·3	39·74	46·33	54·21	61·47	76·65	100·47
58·8	39·71	46·13	54·21	61·54	76·83	100·06
76·8	39·49	46·16	54·06	61·48	77·10	100·78
100	39·505	46·275	54·11	61·50	77·21	101·35

* At 15·4°.

Methyl l-α-*Chloroacetoxypropionate*.—This ester, prepared from methyl lactate and chloroacetyl chloride (b. p. 105—106°, obtained from the acid and thionyl chloride) and purified by fractionation with a column, had b. p. 110°/15 mm. (Found : Cl, 19·65. Calc. : Cl, 19·77%).

Densities determined :

t	20·5°	40·5°	41·5°	59·2°	80°	100°
d	1·2521	1·2287	1·2284	1·2064	1·1830	1·1598

t.	$[\alpha]_{r_1}$.	$[\alpha]_{r_2}$.	$[\alpha]_{y}$.	$[\alpha]_{g}$.	$[\alpha]_{b}$.	$[\alpha]_{v}$.
0°	−35·91°	−41·95°	−49·145°	−55·69°	−69·56°	−91·04°
21·3	35·99	41·58	48·70	55·19	68·98	90·48
39·75	35·065	40·98	48·02	54·50	68·37	89·97
59·0	34·58	40·45	47·60	53·955	67·51	89·47
80·0	34·09	39·84	46·86	53·18	66·58	88·29
100·0	34·35	39·715	46·42	52·87	66·08	88·04

Methyl l-α-*Dichloroacetoxypropionate*.—This was prepared from methyl lactate and dichloroacetyl chloride (b. p. 107—108°); it had b. p. 115°/15 mm. (Found : Cl, 33·27. Calc. : Cl, 33·03%).

Densities determined :

t	22·0°	39·0°	60·5°	81·5°	100°
d	1·3315	1·3105	1·2842	1·2582	1·2359

t.	$[\alpha]_{r_1}$.	$[\alpha]_{r_2}$.	$[\alpha]_{y}$.	$[\alpha]_{g}$.	$[\alpha]_{b}$.	$[\alpha]_{v}$.
0°	−24·94°	−29·13°	−34·18°	−38·82°	−48·18°	−63·36°
21	25·46	29·82	35·07	39·79	49·64	65·41
39	25·53	29·97	35·11	39·95	49·96	66·345
59·5	25·575	29·925	35·175	40·05	50·14	66·78
79	25·43	29·86	35·105	39·91	50·41	66·71
100	25·19	29·67	34·965	39·76	49·87	66·77

Methyl l-α-*Trichloroacetoxypropionate*.—When prepared from methyl lactate and trichloroacetyl chloride (b. p. 117—118°; from the acid and thionyl chloride) and purified by fractional distillation under reduced pressure, the ester had b. p. 116°/13 mm. (Found : Cl, 42·40. Calc. : Cl, 42·69%).

Densities determined :

t	21·5°	40°	59°	81·5°	100°
d	1·3919	1·3678	1·3416	1·3129	1·2893

t.	$[\alpha]_{r_1}$.	$[\alpha]_{r_2}$.	$[\alpha]_{y}$.	$[\alpha]_{g}$.	$[\alpha]_{b}$.	$[\alpha]_{v}$.
0°	−16·64°	−19·48°	−22·81°	−25·88°	−32·13°	−41·68°
20·5	16·97	19·83	23·26	26·39	32·84	42·995
41	17·13	20·12	23·63	26·79	33·575	43·73*
59	17·305	20·33	23·885	27·12	33·99	44·66
80·5	17·52	20·57	24·27	27·54	34·52	45·51
100	17·73	20·79	24·445	27·79	34·93	46·20

* At 40°.

Methyl l-α-*Methoxypropionate.*—The ester, prepared exactly by the method of Purdie and Irvine (J., 1899, **75**, 485) and purified by fractionation with a column under diminished pressure, boiled at 38°/13 mm.

Densities determined :

t......	15°	24·5°	42·0°	49·5°	61·5°	73·5°	89·0°
d......	1·0039	0·9953	0·9765	0·96775	0·9555	0·9408	0·9225

t.	$[\alpha]_{r_1}$.	$[\alpha]_{r_2}$.	$[\alpha]_{y}$.	$[\alpha]_{g}$.	$[\alpha]_{b}$.	$[\alpha]_{v}$.
0°	−68·135°	−79·46°	−93·42°	−106·12°	−133·14°	−176·24°
25	64·96	75·88	89·40	101·57	126·39	168·7
40	63·51	74·55	87·41	99·41	124·38	165·36
60	62·29	72·54	85·09	96·445	122·06	160·51
79	60·37	71·22	82·53*	93·87*	117·92	156·57*
100	58·82	69·42	80·93	92·19	115·88	153·35

* At 80°.

Methyl l-α-*Benzoyloxypropionate.*—Prepared by boiling methyl lactate with excess of benzoyl chloride for about 3 hours under reflux, and fractionated under reduced pressure till of constant rotation, this ester had b. p. 145°/13 mm.

Densities determined :

t	16·5°	20·25°	40·0°	60·0°	80·25°	98°
d	1·1474	1·1443	1·1260	1·1068	1·0872	1·0703

t.	$[\alpha]_{r_1}$.	$[\alpha]_{r_2}$.	$[\alpha]_{y}$.	$[\alpha]_{g}$.	$[\alpha]_{b}$.	$[\alpha]_{v}$.
0°	13·36°	16·57°	21·06°	25·76°	37·53°	61·65°
18	12·59	15·73	20·14*	24·64*	35·92*	58·44*
40	11·69	14·485	18·57	22·60	32·97	53·55
61·5	10·68	13·35	16·98	20·63	30·02	48·94
80·5	9·84	12·25	15·59	19·01	27·72	44·85
100	9·095	11·26	14·33	17·48	25·46	41·45

* At 15·5°.

Methyl l-α-o-*Nitrobenzoyloxypropionate.*—*o*-Nitrobenzoyl chloride (7 g.) and methyl lactate (8 g.) were boiled gently in a flask fitted to an air condenser for 8 hours, and the unchanged methyl lactate was distilled off under reduced pressure. The residue, which distilled at 140—200°/6 mm., was dissolved in ether and shaken with sodium carbonate solution. The purified ester had b. p. 175—180°/6 mm., and solidified on standing. When crystallised several times from light petroleum, it had m. p. 36—37° (Found : N, 5·67. Calc. : N, 5·53%).

Densities determined :

t	25·5°	42°	60°	82°	100°
d	1·2692	1·2537	1·2367	1·2177	1·2009

t.	$[\alpha]_{r_1}$.	$[\alpha]_{r_2}$.	$[\alpha]_y$.	$[\alpha]_g$.	$[\alpha]_b$.	$[\alpha]_v$.
14°	31·14°	39·755°	51·34°	63·57°	95·52°	189·39°
25	29·47	37·185*	48·26*	59·80*	91·06*	174·22*
40	27·08	34·20	43·74	54·74	83·35	158·07
60	24·08	30·34	39·14	48·62	74·92	141·79
81·25	20·90	26·47	34·30	42·60	65·50	114·55
100	18·69	23·66	30·87	40·57	59·02	97·92

* At 24°.

Methyl α-m-*Nitrobenzoyloxypropionate.*—Methyl lactate (8 g.) was boiled under reflux with *m*-nitrobenzoyl chloride (7 g.) until no more hydrogen chloride was evolved (about 6 hours). The excess of methyl lactate was distilled off under reduced pressure, and the residue distilled at 180—196°/8 mm. On fractionation of this product, the rotation gradually diminished, apparently on account of racemisation (Found : N, 5·85. Calc. : N, 5·53%).

It seems curious that the *m*-nitro-derivative should undergo racemisation whilst the corresponding *o*-compound seemed to be quite stable.

In an attempt to prepare methyl α-*p*-nitrobenzoyloxypropionate, methyl lactate and *p*-nitrobenzoyl chloride did not seem to react with one another at all.

Methyl l-α-*Chlorosulphinylpropionate* (see note, p. 2044).—This was prepared by Frankland and Garner's method for the ethyl derivative (J., 1914, **105**, 1101). The product, purified by fractional distillation through a column, boiled at 89°/13 mm. (Found : Cl, 18·13; S, 17·64. Calc. : Cl, 19·03; S, 17·20%).

Densities determined :

t	19·5°	40°	59·5°	80°	100°
d	1·3420	1·3165	1·2922	1·2645	1·2414

t.	$[\alpha]_{r_1}$.	$[\alpha]_{r_2}$.	$[\alpha]_y$.	$[\alpha]_g$.	$[\alpha]_b$.	$[\alpha]_v$.
0°	−166·84°	−198·26°	−236·72°	−272·86°	−351·68°	−491·59°
15·5	162·57*	196·08*	230·34	265·80	345·07*	477·77
26·5	159·70	192·73	225·86	260·36	334·40	468·84
41·5	155·91†	184·50†	219·80	253·41	328·17†	455·22†
60	150·83	178·47	212·43	244·80	316·60	439·97
80	144·46	171·70	204·84	235·96	304·59	422·92
100	139·94	165·80	197·81	223·96	292·70	408·71

* At 16°. † At 42°.

Methyl l-*Lactate in Ethylene Dibromide.*—$p = 2{\cdot}3043$.

t	20·5°	39°	59·5°	80·5°	100°
d	2·1193	2·0819	2·0402	1·9963	1·9577

t.	$[\alpha]_{r_2}$.	$[\alpha]_g$.	$[\alpha]_v$.
21°	−0·05°	+0·16°	+4·97°
30	−1·085	−0·14	+3·76
43	−1·31	−1·805	+0·955
49	−2·21	−2·05	+0·91
59·5	−2·21	−2·62	+1·21
70	−2·70	−2·98	−1·17
80·5	−2·40	−4·02	−2·65
90	−3·54	−4·06	−3·54
100	−3·535	−4·70	−4·67

The data for the characteristic diagram (based on $[\alpha]_g$) were taken from smoothed curves drawn from the above figures, and were as follows (before inversion, see p. 2042) :

$[\alpha]_{r_2}$	−0·05°	−0·95°	−1·7°	−2·4°	−3·15°
$[\alpha]_g$	+0·10	−1·0	−2·0	−3·0	−4·0
$[\alpha]_v$	+5·0	+2·60	+0·80	−0·95	−2·6

Summary.

1. The temperature–rotation data for a number of lactates appear to show that the derivatives of that form of lactic acid which, in the homogeneous condition at a temperature of 25°, is lævorotatory for sodium light, are configuratively related to the derivatives of *d*-tartaric acid. This form should therefore be designated *d*-lactic acid. Its lactide is strongly dextrorotatory. The configurational sign of the lactic acid contained in a sample of the commercial syrup (the rotation of which is mainly due to lactide) is nearly always that of the rotation of the syrup itself; in other words, a lævorotatory syrup contains *l*-lactic acid in excess.

2. The region of visibly anomalous rotation dispersion was realised in a 2·3043% solution of methyl *l*-lactate in ethylene dibromide.

3. From this and the data for homogeneous methyl *l*-lactate the rational zero for the colours $\lambda = 5461$ and $\lambda = 4358$ Å.U. is + 5·5° for the *d*-derivatives and − 5·5° for the *l*-derivatives.

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