

166. *Studies in Optical Superposition. Part IX. 1-Menthyl Esters of Mucic and Tetrahydroxyadipic [1. 2. 3. 4.]⁰* Acids.*

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By the action of acetic anhydride and a little sulphuric acid on *dl*-talmucic acid (Fischer's "*allomucic*" acid), tetra-acetylmucic acid and tetra-acetoxiadipic acid were produced. These were converted into the *l*-menthyl esters, the rotations of which have been compared. The rotations differ considerably, those of the latter ester being nearly 50% the higher. The results are therefore quite opposed to the requirements of van 't Hoff's principle of optical superposition.

IN Part VIII (J., 1927, 50) one of us with Fulton described some work in which salts of mucic acid and of so called "*allomucic*" acid, with active bases, were examined in connection with the problem of optical superposition.

Since then, Posternak (*Helv. Chim. Acta*, 1935, **18**, 1283), by oxidising *d*-allonolactone prepared from the *d*-allonic acid of Austin and Hummoller (*J. Amer. Chem. Soc.*, 1934, **56**, 1153), has shown that the compound prepared by Fischer (*Ber.*, 1891, **24**, 2136) from mucic acid, and by him named *allomucic* acid (m. p. 172°), does not have the structure which he assigned to it. Fischer's method of epimerising mucic acid affects, it would appear, mainly, or only, one of the two carbon atoms about which rearrangement might be expected to take place, and therefore gives an inactive mixture of *d*- and *l*-talmucic acids (I and II), which, separately, were prepared by him, although he did not deliberately make this *dl*-mixture from the two separate acids.

On account of this error in regard to "*allomucic*" acid the results described in Part VIII of this series do not have real bearing on the problem of optical superposition.

The present authors have, however, now prepared a number of derivatives of mucic

* For nomenclature, see A., 1909, i, 208.

acid and of tetrahydroxyadipic [1.2.3.4.^{0.}] acid, and have been able, in the case of the *l*-menthyl tetra-acetyl esters, to institute a direct comparison of rotation values.

It was necessary, before we succeeded in obtaining a suitable analogous pair of compounds, to prepare a number of derivatives of each acid. We here confine our remarks to the essential points regarding that suitable pair. The other compounds examined will be dealt with in the experimental part.

Mucic acid melts at 212°, its ethyl ester at 169°, and the tetra-acetyl derivative of this, at 189°. Tetra-acetylmucic acid itself melts at 242°, and tetra-acetylmucyl dichloride at 189°. *l*-Menthyl tetra-acetylmucate prepared from the last named by heating with menthol melts at 153°.

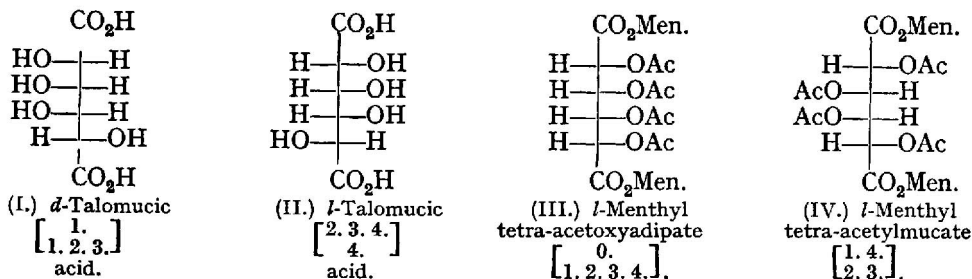
For comparison with these derivatives of mucic acid, we prepared corresponding derivatives of tetrahydroxyadipic acid. Epimerisation of mucic acid was carried out mainly as described by Butler and Cretcher (*J. Amer. Chem. Soc.*, 1929, 51, 2168), who however were under the impression that their product had the constitution assigned to it by Fischer. This yielded a product of m. p. 172° (taken slowly), as stated by Butler and Cretcher, but of 176—178° as described by Posternak, when the m. p. was taken rapidly. This product, according to Posternak, is the racemic form of Fischer's talomucic acid. From it we prepared the ethyl ester and found it to have m. p. 137—138° as reported by Butler and Cretcher. According to Posternak, only *d*- and *l*-talomucic acid are produced in this epimerisation, and tetrahydroxyadipic acid not at all, or only in minimal quantity. If tetrahydroxyadipic acid were produced in small quantity, one would expect to find it in the mother-liquors, after the separation of the *dl*-talomucic acid, but we thought that instead of attempting to obtain it in that way, it might be better to acetylate the whole of the *dl*-talomucic acid, obtained in any given preparation, and then to separate the tetra-acetyl derivative of the tetrahydroxyadipic acid from any tetra-acetyl-*dl*-talomucic acid which might have been formed. In contrast to mucic acid, however, from numerous experiments which we have made, *dl*-talomucic acid, apparently like saccharic acid, mannosaccharic acid and idosaccharic acid, appears to react very little with acetic anhydride in the presence of a little sulphuric acid. But on working up the residue from such acetylations a small quantity of a substance was obtained which consisted of a mixture of needles and plates. After mechanical separation, the needles (the more soluble portion) were found to melt at 242°, the melting point of tetra-acetylmucic acid, to which substance the needles bore a close resemblance. This was definitely shown to be tetra-acetylmucic acid by hydrolysis and identification of the mucic acid formed (m. p. 212°). The plates, on the other hand, melted at 220°, and gave on analysis the same figure as for tetra-acetylmucic acid. This substance, on hydrolysis gave a tetrahydroxyadipic acid melting at 199—200°, which was therefore different from mucic acid (212°) on the one hand, and from *dl*-talomucic acid (176—178°) on the other.

The tetrahydroxyadipic acid (m. p. 199—200°) itself treated with ethyl alcohol and hydrogen chloride gave an ethyl ester melting at 155°, which on analysis gave data corresponding to those for ethyl tetrahydroxyadipate. Samples of the tetrahydroxyadipic acid (m. p. 199—200°), and this ester (m. p. 155°) were submitted to Professor Posternak in Geneva, who was good enough to compare them with his own products, and found them to be identical. We have pleasure in expressing our thanks to him for his kind assistance. It thus appeared that Posternak's tetrahydroxyadipic acid *can* be obtained from the product of epimerisation of mucic acid, and this might be due either to the fact that a small amount of this acid was formed directly in the epimerisation, or that perhaps *dl*-talomucic acid treated with acetic anhydride may be partly epimerised to mucic acid on the one hand and tetrahydroxyadipic acid on the other, although we know of no other case in which epimerisation takes place under these conditions.

To test the latter explanation further, we treated carefully purified *dl*-talomucic acid with acetic anhydride, removed any acetylated products, repurified the residual *dl*-talomucic acid, and acetylated this again. Tetra-acetylmucate and tetra-acetoxyadipate were both formed, and from the residual *dl*-talomucic acid this process was again repeated with the same result; *dl*-talomucic acid always seemed to yield both tetra-acetylmucic acid and tetra-acetoxyadipic acid. By the action of thionyl chloride on this tetra-acetoxyadipic

acid, we prepared the corresponding *chloride*, m. p. 165°, and from it the *ethyl ester*, m. p. 136°, and finally also the *l-menthyl ester*, m. p. 135—136°.

We had thus obtained two compounds (III and IV) differing only in the arrangement, in pairs, of radicals about four asymmetric carbon atoms.



According to van 't Hoff's principle of optical superposition the rotations of these (III and IV) ought to be the same.

Three different specimens of this menthyl tetra-acetoxyadipate were prepared and examined polarimetrically for comparison with menthyl tetra-acetylmucate. Solutions of approximately $p = 5$ in benzene were used. Fuller data are given further on. The results at 20° for mercury green light ($\lambda = 5461$) were as follows :

<i>l</i> -Menthyl tetra-acetylmucate	49.9°	50.8°	49.9°
<i>l</i> -Menthyl tetra-acetoxyadipate	74.2°	72.9°	71.1°

It will be observed that there is a considerable difference in the rotations of these two substances, and that, therefore, our results are not at all in agreement with van 't Hoff's principle of optical superposition, as has now been found in a number of somewhat similar cases. It is especially to be noticed that the tetra-acetoxyadipate has the higher rotation value. If the adipate were a mixture of mucate with some impurity, it is more likely that its rotation should have the lower value.

We also prepared, incidentally, *l*-menthyl dehydromucate by the action of hydrogen chloride on a mixture of menthol and mucic acid at 165°, as well as *d*-*sec*-*octyl tetra-acetylmucate* (m. p. 114—115°) and examined their rotations. We were unable to obtain *d*-*sec*-*octyl tetra-acetoxyadipate* in a sufficiently pure condition for comparison with the corresponding mucate.

The table below gives a list of corresponding compounds in the three series. It may be useful for reference.

	Mucic.	<i>dl</i> -Talomucic.	Tetrahydroxyadipic.
Acid	212°	172°	199—200°
Ethyl ester	169	137—138	155
Ethyl tetra-acetyl ester	189	108—109	136
Tetra-acetyl acid	242		220
Tetra-acetyl acid chloride	189		165
<i>l</i> -Menthyl tetra-acetyl ester	153—154		135—136
<i>dl</i> - <i>sec</i> - <i>Octyl tetra-acetyl ester</i>	102—103		
<i>d</i> - <i>sec</i> - <i>Octyl tetra-acetyl ester</i>	114—115		

EXPERIMENTAL.

Epimerisation of Mucic Acid.—Mucic acid (200 g.) was heated with pyridine (200 g.) and water (2 l.) for 48 hrs. at 135—140° on an oil-bath. *dl*-Talomucic acid was isolated through its barium salt, and crystallised from hot water. Yield 44 g., m. p. 172°.

Treatment of dl-Talomucic Acid with Acetic Anhydride.—*dl*-Talomucic acid (25 g., once crystallised from water) was heated gently with acetic anhydride (65 c.c.) and a trace of sulphuric acid. After the initial reaction the solution was refluxed for 1 hour, cooled, and poured into ice-water. The crystalline solid was recrystallised from 30% alcohol. A mixture of plates and needles separated, m. p. 215°; yield 5.2 g. This was heated with 30% alcohol (60—70 c.c.) nearly to boiling and filtered. The residue consisted almost entirely of plates, which on recrystallisation had m. p. 218—220°. The filtrate gave a mixture of needles and plates. By repeating this operation several times an almost complete separation was achieved into plates (1.1 g.), m. p. 220° and needles, m. p. 240° (Found for the plates: C, 40.7; H, 5.4; H₂O, 8.7. Calc. for C₁₄H₁₈O₁₂, 2H₂O: C, 40.6; H, 5.4; H₂O, 8.2%).

Tetrahydroxyadipic Acid.—Tetra-acetoxyadipic acid (plates, 200 mg.) was heated for 3 hours with 3% hydrochloric acid (10 c.c.). The solution in 3 days gave a crystalline acid (100 mg.), m. p. 198—200°, mixed m. p. with mucic acid (212°) 203—204° (Found: C, 34.3; H, 4.9. Calc. for $C_8H_{10}O_8$: C, 34.3; H, 4.8%).

Ethyl Tetrahydroxyadipate (Posternak, *loc. cit.*).—The acid (100 mg.) was heated for 1 hour in alcohol with 2% of hydrogen chloride. White brilliant plates were obtained from alcohol; m. p. 155°, mixed m. p. with ethyl mucate (169°) 145—146° (Found: C, 45.3; H, 6.6. Calc. for $C_{10}H_{18}O_8$: C, 45.1; H, 6.8%).

Tetra-acetoxyadipyl Dichloride.—The tetra-acetyl acid (4 g.) and thionyl chloride (60 c.c.) were heated together in toluene (40 c.c.) for 6 hours. When the mixture was vacuum-distilled to 20 c.c., the *dichloride* crystallised in fine needles, m. p. 155—160°. Recrystallised from petroleum (b. p. 120°), it had m. p. 165°; yield, 2.7 g. (Found: C, 40.4; H, 3.85. $C_{14}H_{16}O_{10}Cl_2$ requires C, 40.5; H, 3.85%).

Ethyl Tetra-acetoxyadipate.—The tetra-acetyl dichloride (50 mg.) was heated with alcohol (0.5 c.c.) in benzene (5 c.c.) for 1 hour. When the solvent was driven off, and the residue crystallised from alcohol, plates, m. p. 136°, were obtained (Found: C, 49.0; H, 5.8. $C_{18}H_{26}O_{12}$ requires C, 49.8; H, 6.0%).

Ethyl Tetra-acetyl-dl-talomucate.—Ethyl *dl*-talomucate (5 g.) reacted readily with acetic anhydride (21 c.c.). After 1½ hours' refluxing, the mixture was poured into ice-water. A solid product was obtained, m. p. 106°, which after recrystallisation from aqueous alcohol yielded needles (6.5 g.), m. p. 108—109° (Found: C, 49.5; H, 5.7. $C_{18}H_{26}O_{12}$ requires C, 49.8; H, 6.0%).

l-Menthyl Tetra-acetylmucate.—Tetra-acetylmucyl dichloride (500 mg.) and *l*-menthol (500 mg.) were heated together at 125° until evolution of hydrogen chloride ceased. A poor yield was obtained, of a product which, crystallised from methyl alcohol, had m. p. 153°. Methods employing various solvents gave no better results. This agrees with the results of Karijone and Morotomi (*Chem. Abstr.*, 1929, 4193).

l-Menthyl Tetra-acetoxyadipate.—Tetra-acetoxyadipyl dichloride (2.7 g.) was added slowly to *l*-menthol (3 g.) and heated at 125—130° until the evolution of hydrogen chloride ceased. On cooling, a solid was obtained which, crystallised from methyl alcohol, had m. p. 135—136° (Found: C, 62.3; H, 8.3. $C_{24}H_{54}O_{12}$ requires C, 62.4; H, 8.3%).

dl-sec-Octyl Tetra-acetylmucate.—Tetra-acetylmucyl dichloride (1 g.) was heated in benzene (10 c.c.) with *dl-sec*-octyl alcohol (0.6 c.c.) for 8 hours. On evaporation of the benzene a semi-crystalline mass was obtained. Crystallised from methyl alcohol, it gave plates, m. p. 102—103° (Found: C, 59.4; H, 8.4. $C_{30}H_{50}O_{12}$ requires C, 59.8; H, 8.3%).

d-sec-Octyl Tetra-acetylmucate.—Prepared as for the *dl*-compound, *d-sec*-octyl alcohol ($[\alpha]_{5461}^{20} + 11.7^\circ$) being used, this *ester*, after six crystallisations from methyl alcohol, formed plates, m. p. 114—115° (Found: C, 59.8; H, 8.5. $C_{30}H_{50}O_{12}$ requires C, 59.8; H, 8.3%).

We were unable to isolate *l-sec*-octyl tetra-acetoxyadipate in a crystallisable condition.

Rotation Data.—Colours of light used:

r_1	r_2	y	g	b	v
6716	6234	5790	5461	4916	4359

l-Menthyl tetra-acetylmucate in benzene.

(I) $p = 5.6, t = 20.05^\circ, d^{20^\circ} = 0.8889.$

	$\alpha^{20^\circ} (l = 75 \text{ mm.}).$	$[\alpha]^{20^\circ}.$		$\alpha^{20^\circ} (l = 75 \text{ mm.}).$	$[\alpha]^{20^\circ}.$
r_1	-1.20°	-32.1°	g	-1.86°	-49.9°
r_2	-1.40	-37.5	b	-2.42	-64.9
y	-1.66	-45.5	v	-3.10	-83.1

(II) $p = 4.028, t = 20^\circ, d^{20^\circ} = 0.8898.$

	$\alpha^{20^\circ} (l = 100 \text{ mm.}).$	$[\alpha]^{20^\circ}.$		$\alpha^{20^\circ} (l = 100 \text{ mm.}).$	$[\alpha]^{20^\circ}.$
r_1	-1.23°	-34.3°	g	-1.82°	-50.79°
r_2	-1.40	-39.1	b	-2.36	-65.87
y	-1.60	-44.5			

(III) $p = 3.980, t = 20.05^\circ, d = 0.8890.$

	$\alpha^{20^\circ} (l = 100 \text{ mm.}).$	$[\alpha]^{20^\circ}.$		$\alpha^{20^\circ} (l = 100 \text{ mm.}).$	$[\alpha]^{20^\circ}.$
r_1	-1.10°	-31.2°	g	-1.76°	-49.95°
r_2	-1.30	-36.59	b	-2.25	-63.86
y	-1.50	-42.57	v	-2.93	-83.15

l-Menthyl tetra-acetoxyadipate in benzene.

(I) $p = 4.9114, t = 20.05^\circ, d^{20^\circ} = 0.8891.$

	$\alpha^{20^\circ} (l = 75 \text{ mm.}).$	$[\alpha]^{20^\circ}.$		$\alpha^{20^\circ} (l = 75 \text{ mm.}).$	$[\alpha]^{20^\circ}.$
r_1	-1.55°	-47.33°	g	-2.43°	-74.2°
r_2	-1.75	-53.44	b	-3.13	-95.6
y	-2.14	-65.34	v	-4.02	-122.8

(II) $p = 2.478, t = 20^\circ, d^{20^\circ} = 0.8861.$

	$\alpha^{20^\circ} (l = 100 \text{ mm.}).$	$[\alpha]^{20^\circ}.$		$\alpha^{20^\circ} (l = 100 \text{ mm.}).$	$[\alpha]^{20^\circ}.$
r_1	-1.04°	-47.3°	g	-1.60°	-72.8°
r_2	-1.18	-53.7	b	-2.04	-92.9
y	-1.41	-64.2	v	-2.74	-124.8

(III) $p = 4.9017, t = 20.05^\circ, d^{20^\circ} = 0.8967.$

	$\alpha^{20^\circ} (l = 100 \text{ mm.}).$	$[\alpha]^{20^\circ}.$		$\alpha^{20^\circ} (l = 100 \text{ mm.}).$	$[\alpha]^{20^\circ}.$
r_1	-1.23°	-45.61°	g	-1.82°	-71.0°
r_2	-1.40	-52.5	b	-2.36	-90.5
y	-1.60	-61.9	v	-3.36	-128.1

1-Menthyl dehydromucate in chloroform. $p = 3.49$.

<i>t.</i>	<i>d.</i>	<i>y.</i>		<i>g.</i>		<i>v.</i>	
		<i>a</i> (160 mm.).	[<i>a</i>].	<i>a.</i>	[<i>a</i>].	<i>a.</i>	[<i>a</i>].
0°	1.535	-5.43°	-65.05°	-6.20°	-74.3°	-10.24°	-122.7°
11.8	1.4692	5.34	64.87	6.09	74.05	10.05	122.2
21	1.466	5.18	63.75	5.99	73.26	9.73	120.8
30	1.451	5.19	64.44	5.90	73.26	9.73	120.8
40	1.431	5.08	63.82	5.80	72.86	9.53	119.2
50	1.4139	5.06	64.46	5.75	73.27	9.43	120.1

Thanks are tendered to the Carnegie Trustees for the Universities of Scotland and to the Chemical Society for grants defraying part of the cost of this investigation. One of us (R. W. L.) acknowledges also tenure of a Carnegie Scholarship, and, earlier, of the Mackay-Smith and the James Fleming Scholarships of Glasgow University.

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[Received, May 13th, 1940.]