

CLXXIX.—*The Influence of Various Substituents on the Optical Activity of Tartramide. Part II.*

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IN a previous communication on the same subject, the optical activity of seventeen derivatives of tartramide has been described by one of us (P. F. Frankland and Slaton, *Trans.*, 1903, **83**, 1349), but amongst these only the methylamide and ethylamide were derivatives of tartaric acid with aliphatic amines. In the present communication we have confined our attention to the latter, having prepared and examined the normal and *isopropylamides*, the allylamide, the normal and *isobutylamides*, and the normal heptylamide. The rotation of these compounds has, as before, been determined in pyridine, and, when possible, also in methyl alcohol, and in water solution.

The amides described in the present paper were prepared by the interaction in the cold of the amine with an alcoholic solution of methyl tartrate, and all were obtained as crystalline bodies of high melting point (183—216°). Excepting in the case of the *isopropylamide*, of which only 23 per cent. of the theoretical quantity was obtained, the yields were excellent, and in the case of the *isopropylamide* also a better yield would no doubt have resulted if the alcohol had been evaporated off after completion of the reaction.

The results of our investigation are summarised in the following table :

Summary of Results :

	Melting point.	Pyridine.		Methyl alcohol.		Water.	
		<i>p.</i>	$[M]_D^{20^\circ}$.	<i>p.</i>	$[M]_D^{20^\circ}$.	<i>p.</i>	$[M]_D^{20^\circ}$.
Tartaric di-Amide.....	195°	—	—	0·0807	+208°	0·077	+160°
		—	—	0·1797	213	1·305	158
Methylamide.....	189	0·684	+274°	4·998	266	0·994	255
		7·679	279	4·986	262	10·350	242
Ethylamide	210—211	1·049	277	4·997	282	1·390	262
		5·030	279	5·001	281	7·468	256
<i>n</i> -Propylamide	216	2·196	289	2·019	290	1·808	264
		4·741	287	4·857	290	2·717	260
<i>iso</i> Propylamide	189	1·654	272	1·910	273	1·398	247
		4·665	272	4·867	272	4·682	247
Allylamide.....	183	2·528	251	2·900	273	2·392	247
		4·735	252	5·914	270	4·697	246
<i>n</i> -Butylamide.....	193	1·899	286	0·907	298	0·258	280
		4·801	288	4·416	291	—	—
<i>iso</i> Butylamide	183·5	1·753	295	1·007	306	0·549	275
		5·064	294	5·432	305	—	—
<i>n</i> -Heptylamide	183	1·621	304	0·9951	303	—	—
		3·579	305	—	—	—	—

With the above may be compared the previously-determined rotations of the following substitution derivatives of tartramide:

Tartaric di-	$[M]_D^{20^\circ}$.		
	Pyridine.	Methyl alcohol.	Water.
Piperidide *	$\pm 0^\circ$	—	—
Phenylhydrazide	< +80	—	—
Diacetyl[tartaric]- <i>o</i> -toluidide	+80	—	—
Hydrazide	—	—	+170°
<i>ac</i> -Tetrahydro- β -naphthylamide *	+240	—	—
Tartranil.....	+272	+268°	+216
Benzylamide	+300	—	—
Furfurylamide	+307	—	—
Tartaric- <i>p</i> -toluid	+366	+280	—
Acetophenone-hydrazone	+397	—	—
α -Naphthylamide	+400	—	—
Benzylidene-hydrazide	+554	—	—
<i>o</i> -Toluidide	+667	—	—
<i>m</i> -Toluidide	+730	—	—
Furfurylidene-hydrazide	+736	—	—
Anilide	+739	—	—
<i>p</i> -Toluidide.....	+793	—	—
<i>ar</i> -Tetrahydro- β -naphthylamide *	+840	—	—
β -Naphthylamide	+1160	—	—
Methyltartramide †	—	—	+281·6
Ethyltartramide †	—	—	+264·3

* Frankland and Ormerod, Trans., 1903, **83**, 1342.

† Ladenburg, Ber., 1896, **29**, 2710.

The foregoing figures show that all the substituted tartramides, excepting the phenylhydrazide and piperidide, have a higher dextro-

rotation than tartramide itself, and that substitution by aromatic radicles leads to a dextrorotation of a much higher order than that resulting from substitution by aliphatic groups. The piperidide is inactive, at any rate in pyridine and in aniline solutions, which were the only ones in which it was examined. The benzylamide and furfurylamide have about the same rotation in pyridine as the *n*-heptylamide, whilst the *ac*-tetrahydro- β -naphthylamide has even a lower dextrorotation in pyridine than any of the alkyl-substituted tartramides.

Taking the derivatives with the aliphatic amines of the normal series, it appears that the value of $[M]_D$ does not show any evidence of having reached a maximum within the range of the series of compounds prepared, for the *n*-heptylamide has a higher molecular rotation than any of the lower homologues. The *isopropyl*amide has a lower rotation than the *n*-propylamide, whilst the rotation of the *isobutyl*amide is greater (excepting in water solution) than that of the *n*-butylamide.

The rotation of the allylamide as compared with that of the *n*-propylamide is particularly interesting, for it is now generally believed that the presence of a double bond in a carbon-chain leads to an increase in the optical activity (see P. Frankland and Slaton, *Trans.*, 1903, 83, 1351, where numerous references to this relationship are given). In the present case, however, the substitution of *n*-propyl by allyl is attended by a marked diminution in the rotation, and the same exceptional relationship will be shown by one of us (P. Frankland and Done) to be exhibited in the case of the *n*-propylamide and allylamide of malic acid.

The piperidide is the only secondary amide hitherto examined, and, as indicated in the above table, it was found to be practically inactive; this result naturally suggests that racemisation of the tartaric acid had taken place in the process of preparation, but it may also be due to the dextrorotation being depressed to about zero by the introduction of the piperidine group, and that this is perhaps the case is rendered less remotely possible since it has been found by one of us that in the malic series the piperidide has a much lower rotation than the unsubstituted malamide in pyridine and methyl alcohol solutions, whilst in glacial acetic acid solution the sign of the rotation is actually reversed.

EXPERIMENTAL.

Tartaric Di-n-propylamide.

An excess of *n*-propylamine was added to a concentrated solution of methyl tartrate in absolute ethyl alcohol in the cold. The separation of amide commenced in the course of a few minutes; the crystals

formed, after standing for two days, were filtered off, and a further crop was obtained by evaporating part of the alcohol. The yield was about 80 per cent. The product was purified by recrystallising from a mixture of equal parts of ethyl alcohol and ethyl acetate.

0.0946 gave 10.0 c.c. moist nitrogen at 16.5° and 761 mm. $N = 12.30$.

$C_{10}H_{20}O_4N_2$ requires $N = 12.07$ per cent.

Tartaric di-n-propylamide crystallises in colourless, flat, elongated plates, or flat needles, melting at 216° with slight decomposition. It is easily soluble in pyridine, or hot alcohol, less so in ethyl acetate, whilst in cold water the strongest obtainable solution was about 2.4 per cent.

Rotation of Tartaric Di-n-propylamide.

$v.$	$d\ 20^\circ/4^\circ.$	$l.$	$\alpha_D^{20^\circ}.$	$[\alpha]_D^{20^\circ}.$	$[M]_D^{20^\circ}.$
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Pyridine Solution.

4.741	0.9867	0.999	+5.79°	+123.9°	+287.4°
2.196	0.9817	1.998	5.37	124.7	289.2

Methyl Alcohol Solution.

4.857	0.8083	1.998	+9.79°	+124.8°	+289.5°
2.019	0.7991	1.998	4.03	124.9	289.7

Water Solution.

2.717	1.0029	0.999	+3.05°	+112.1°	+260.0°
1.808	1.0014	1.998	4.11	113.6	263.6

Tartaric Diisopropylamide.

The theoretical quantity of *isopropylamine* was added to a solution of methyl tartrate in absolute ethyl alcohol. After standing two days the liquid became viscid and yellow; the amide separated from this on cooling with ice or adding a crystal as nucleus. After standing two more days the crystals were filtered off, but only a 23 per cent. yield was obtained. The product was recrystallised from ethyl acetate to which a little alcohol had been added.

0.1130 gave 12.1 c.c. moist nitrogen at 17° and 737 mm. $N = 12.03$.

$C_{10}H_{20}O_4N_2$ requires $N = 12.07$ per cent.

Tartaric di-isopropylamide crystallises in slightly flattened needles, melting at 189° without decomposition. Its solubility in the ordinary solvents is rather greater than that of the normal propylamide.

Rotation of Tartaric Diisopropylamide.

<i>p.</i>	<i>d</i> 20°/4°.	<i>l.</i>	$\alpha_D^{20^\circ}$.	$[\alpha]_D^{20^\circ}$.	$[M]_D^{20^\circ}$.
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Pyridine Solution.

1·654	0·9806	1·998	+3·80°	+117·3°	+272·0°
4·665	0·9858	0·999	5·38	117·1	271·7

Methyl Alcohol Solution.

1·910	0·7970	1·998	+3·59°	+117·8°	+273·3°
4·867	0·8058	0·999	4·60	117·4	272·4

Water Solution.

1·398	1·0003	1·998	+2·98°	+106·7°	+247·4°
4·682	1·0059	0·999	5·00	106·3	246·6

Tartaric Diallylamide.

This was similarly prepared by mixture of theoretical proportions of allylamine and methyl tartrate in alcoholic solution. The amide already began to separate after an hour, and by filtering off the crystals after twenty-four hours' contact, a yield of 62 per cent. was obtained. The product was purified by recrystallisation from a mixture of equal parts of ethyl alcohol and ethyl acetate.

0·0997 gave 10·84 c.c. moist nitrogen at 15° and 745 mm. $N = 12·48$.

$C_{10}H_{16}O_4N_2$ requires $N = 12·28$ per cent.

Tartaric diallylamide crystallises in flat, thin, colourless plates melting at 183° to a pale yellow liquid. Its solubility in the common solvents is about the same as that of the *n*-propylamide.

Rotation of Tartaric Diallylamide.

<i>p.</i>	<i>d</i> 20°/4°.	<i>l.</i>	$\alpha_D^{20^\circ}$.	$[\alpha]_D^{20^\circ}$.	$[M]_D^{20^\circ}$.
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Pyridine Solution.

2·528	0·9838	1·998	+5·48°	+110·3°	+251·4°
4·735	0·9896	0·999	5·18	110·7	252·3

Methyl Alcohol Solution.

2·900	0·8023	1·998	+5·57°	+119·8°	+273·2°
5·914	0·8092	0·999	5·66	118·4	269·9

Water Solution.

2·392	1·0036	1·998	+5·19°	+108·2°	+246·7°
4·697	1·0086	0·999	5·10	107·8	245·7

Tartaric Di-n-butylamide.

Butylamine was added in theoretical quantity to a cooled solution of methyl tartrate in ethyl alcohol. The separated amide was filtered off after the mixture had stood for about thirteen hours, a 75 per cent. yield being obtained. The product was purified by recrystallisation from a mixture of two parts of ethyl acetate to one of ethyl alcohol.

0.1482 gave 14.0 c.c. moist nitrogen at 17° and 737 mm. $N = 10.84$.

$C_{12}H_{24}O_4N_2$ requires $N = 10.77$ per cent.

Tartaric di-n-butylamide crystallises in beautiful, long, flat, needles melting at 193° without decomposition. Like the other amides described above, it is very soluble in pyridine or alcohol; its solubility in water is, however, very small (only 0.3 per cent.).

Rotation of Tartaric Di-n-butylamide.

<i>p.</i>	<i>d</i> 20°/4°.	<i>l.</i>	$\alpha_D^{20^\circ}$.	$[\alpha]_D^{20^\circ}$.	$[M]_D^{20^\circ}$.
<i>Pyridine Solution.</i>					
1.899	0.9809	1.998	+4.10°	+110.2°	+286.4°
4.801	0.9849	0.999	5.23	110.7	287.8
<i>Methyl Alcohol Solution.</i>					
0.907	0.7949	3.899	+3.22°	+114.6°	+297.8°
4.416	0.8033	0.999	3.97	112.0	291.3
<i>Water Solution.</i>					
0.258	0.9989	3.899	+1.08°	+107.5°	+279.5°

Tartaric Diisobutylamide.

*iso*Butylamine was added in theoretical quantity to a cooled solution of methyl tartrate in ethyl alcohol. After standing twelve hours, the amide which had separated was filtered off, the yield being about 70 per cent., whilst more was obtainable by evaporating the mother liquor.

0.1227 gave 11.8 c.c. moist nitrogen at 19° and 756.5 mm. $N = 11.01$.

$C_{12}H_{24}O_4N_2$ requires $N = 10.77$ per cent.

Tartaric diisobutylamide crystallises in small rhombic plates melting at 183.5°. It is more soluble in the ordinary organic solvents than the normal butyl- and propyl-amides, resembling the *isopropylamide* in this respect, but it is only very slightly so in water (0.8 per cent.).

Rotation of Tartaric Diisobutylamide.

<i>p.</i>	<i>d</i> 20°/4°.	<i>l.</i>	α_D^{20} .	$[\alpha]_D^{20}$.	$[M]_D^{20}$.
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Pyridine Solution.

1.753	0.9805	1.998	+3.90°	+113.6°	+295.3°
5.064	0.9853	0.999	5.64	113.2	294.3

Methyl Alcohol Solution.

1.007	0.7949	3.899	+3.67°	+117.6°	+305.7°
5.432	0.8065	0.999	5.13	117.2	304.8

Water Solution.

0.549	0.9991	3.899	+2.26°	+105.6°	+274.6°
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Tartaric Di-n-heptylamide.

A theoretical quantity of *n*-heptylamine (Kahlbaum) was added to a cold solution of methyl tartrate in absolute alcohol. The mixture became a solid mass in the course of a few hours, and a theoretical yield of the amide was obtained. It was recrystallised from methylated spirit until of constant rotation. It forms elongated, flat plates melting at 183° without decomposition, and is much less soluble in most solvents than are the lower amides above mentioned. It is insoluble in water, slightly soluble in cold alcohol, and at the ordinary temperature gives only about a 4 per cent. solution in pyridine.

0.2680 gave 19.4 c.c. moist nitrogen at 12° and 728 mm. ; N = 8.22.

$C_{18}H_{36}O_4N_2$ requires N = 8.14 per cent.

Rotation of Tartaric Di-n-heptylamide.

<i>p.</i>	<i>d</i> 20°/4°.	<i>l.</i>	α_D^{20} .	$[\alpha]_D^{20}$.	$[M]_D^{20}$.
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Pyridine Solution.

1.621	0.9789	2.993	+4.19°	+88.24°	+303.5°
3.579	0.9805	0.999	3.11	88.72	305.2

Methyl Alcohol Solution.

0.9951	0.7955	3.899	+2.72°	+88.14°	+303.2°
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*Rotation of Tartaric Diphenylhydrazide.**Glacial Acetic Acid Solution.*

0.5672	1.052	3.899	+1.88°	+80.85°	+266.80°
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Rotation of Tartaric Dimethylamide.

<i>p.</i>	<i>d</i> 20°/4°.	<i>l.</i>	$\alpha_D^{20^\circ}$.	$[\alpha]_D^{20^\circ}$.	$[M]_D^{20^\circ}$.
<i>Methyl Alcohol Solution.</i>					
4.998	0.8147	3.899	+23.97°	+151.0°	+265.8°
4.986	0.8147	1.998	12.08	148.8	261.9

*Rotation of Tartaric Diethylamide.**Methyl Alcohol Solution.*

4.997	0.8117	1.998	+11.20°	+138.1°	+281.7°
5.001	0.8127	1.998	11.21	137.9	281.3

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