

XXV.—*The Amide, Anilide, and o- and p-Toluidides of Glyceric Acid.*

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IN pursuing the systematic study of the effect on rotatory power produced by substitution in optically active compounds, we have recently been directing our attention to active amides and their substitution products.

The information at present available concerning the rotatory power of compounds of this class is summarised in the following table. In this table only such amides have been included as are derived from acids of which the rotatory power of several esters is also known, and the rotations of these esters are also given so that the relative rotatory effects of the amino- and alkyloxy-groups are rendered apparent. It will be seen that the existing material for such comparison is very scanty, being practically limited to the derivatives of malic, tartaric, and mandelic acids.

Mandelic acid (Walden, *Zeit. physikal. Chem.*, 1895, 17, 706).

		c.	$[\alpha]_D^{22}$.	$[M]_D$.
Free acid	Acetone.....	2.50	- 148.0°	- 225.0°
Methyl ester	„	3.33	- 110.2	- 182.9
Ethyl	„	5.81	- 90.6	- 163.1
„	„	1.16	- 87.1	- 156.8
Amide	„	2.50	- 66.6	- 100.6
„	„	1.50	- 66.7	- 100.7

Malic acid (Walden, *ibid.*, 248).

		<i>c.</i>	$[\alpha]_D^{20^\circ}$	$[M]_D$
Dimethyl ester	Liquid	—	-6.85°	-11.1°
Diethyl	"	—	-10.18	-19.3
Dipropyl	"	—	-11.62	-25.3
Diisopropyl	"	—	-10.41	-22.7
Diisobutyl	"	—	-11.14	-27.4
Diamide	Water	4.32	-37.6	-49.6
"	"	8.65	-38.0	-50.2
Dianilide	Glacial acetic acid	1.50	-60.66	-172.3
"	"	0.75	-58.66	-166.6
Di-o-toluidide	"	2.00	-65.0	-202.8
"	"	1.00	-66.5	-207.5
Di-p-toluidide	"	1.00	$[\alpha]_D^{30} - 70.0$	-218.4
β -Naphthimide	"	1.00	$[\alpha]_D^{20} - 51.5$	-124.1
Anil*	Water	0.2258	$[\alpha]_D - 33.95$	-59.4

d-Tartaric acid.

		<i>c.</i>	$[\alpha]_D^{20^\circ}$	$[M]_D$
Dimethyl ester	Liquid	—	+2.14°	+3.8°
Diethyl	"	—	+7.66	+15.8
Dipropyl	"	—	+12.44	+29.1
Diisopropyl	"	—	+14.89	+34.8
Diamide	Water	—	$[\alpha]_j + 133.9$	$[M]_j + 198.2$
Methyltartramide †	Water	7.31	$[\alpha]_D + 194.2$	$[M]_D + 281.6$
"	"	12.94	+192.6	+279.3
Ethyltartramide †	"	5.76	+164.9	+262.2
"	"	8.57	+166.2	+264.3

A glance at the table is sufficient to show that the rotatory effect of the NH_2 group is qualitatively similar to that of the alkyloxy-(OA) group, but quantitatively greater. Thus, in the case of mandelic acid, the replacement of OH by OA has the effect of diminishing the levorotation (the ethoxy- having a greater effect in this respect than the methoxy-group), the replacement by NH_2 leading to a still greater depression of the latter.

In the case of malic acid, the alkyloxy-groups successively raise the

* Bischoff and Walden, *Stereochemie*, 855.

† Ladenburg, *Ber.*, 1896, 29, 2710.

lævorotation, the latter being very greatly further elevated by the replacement of OA by NH_2 .

Again, in the case of *d*-tartaric acid, the effect is exactly similar, only that here it is the dextrorotation which is raised by these substitutions.

On substituting the hydrogen in the amino-group by phenyl or tolyl, it is seen that the rotatory effect of the group is still further increased. Again, if the amino-group becomes an imino-group leading to the formation of a ring compound, the rotatory effect is also increased, as in the cases of malic β -naphthimide and of methyl and ethyl tartrides.

The present paper deals with the preparation and properties of the amide, anilide, *o*-toluidide, and *p*-toluidide of glyceric acid. With the exception of the *o*-toluidide, these compounds have had their rotation determined in the liquid state, whilst the rotation of all of them has also been taken in methyl alcohol solution. So far as we are aware, these are the only amides which have hitherto had their rotation determined in the fused or liquid condition.

The rotations of these new compounds should be compared with those of the esters of *d*-glyceric acid given below (P. Frankland and Price, Trans., 1897, 71, 270) :

Methyl glycerate.....	$[\alpha]_D^{15} - 4.80^\circ$	$[M]_D^{15} - 5.76^\circ$
Ethyl ,, 	- 9.18	- 12.30
Propyl ,, 	- 12.94	- 19.15
<i>iso</i> Propyl ,, 	- 11.82	- 17.49
Butyl ,, 	- 13.19	- 21.37
<i>iso</i> Butyl ,, 	- 14.23	- 23.05
Amyl ,, 	- 14.12	- 24.85
Heptyl ,, 	- 11.30	- 23.05
Octyl ,, 	- 10.22	- 22.28

The rotation of glycerylamine is much greater, $[M]_D^{100} = -41.98^\circ$, of glycerylamine still greater, $[M]_D^{100} = -72.36^\circ$, whilst that of glyceryl-*p*-toluidide is intermediate between that of the two latter, $[M]_D^{95} = -67.65^\circ$. The lævorotation of the *o*-toluidide in the fused state is doubtless lower than that of the para-compound, as in methyl alcohol solution it is very much lower than that of the latter; indeed, it is about the same as that of glycerylamine in the same solvent at the same concentration.

The lævorotation of the amide, anilide, and *p*-toluidide is very considerably greater in methyl alcohol solution than in the liquid state; the *o*-toluidide, as already mentioned, could only be optically examined in solution, but it may safely be assumed that its rotation is similarly affected by this solvent.

It is further noteworthy that the rotation of the amide, anilide, and *p*-toluidide in each case diminishes with rise of temperature; in methyl alcohol solution, increase of concentration diminishes the rotation of the amide and anilide, whilst it increases that of the *o*-toluidide. The rotation of the *p*-toluidide is almost independent of the concentration within the limits examined, there being, however, a very slight diminution with increase of concentration.

The corresponding compounds of inactive glyceric acid were also prepared, and their melting points compared with those of the active substances :

	Melting point.	
	Active.	Inactive.
Glycerylamide.....	99.5—100°	91.5—92°
Glycerylanilide	113 —113.5	91
Glyceryl- <i>o</i> -toluidide...	89 —89.5	129 —129.5
Glyceryl- <i>p</i> -toluidide ..	131 —131.5	120 —120.5

Thus, in all cases, excepting that of the *o*-toluidide, the melting point of the active is higher than that of the corresponding inactive compound.

We are continuing the investigation of the effect produced by these and similar substitutions.

EXPERIMENTAL.

I. *Glycerylamide (Inactive).*

Dry ammonia was passed into inactive ethyl glycerate surrounded with a freezing mixture of ice and salt. The saturated liquid was allowed to stand for 24 hours, the excess of ammonia and alcohol being then taken off under reduced pressure at the ordinary temperature of the air. When nearly the whole of the ammonia had been removed, the residue crystallised out. It was recrystallised from methyl alcohol; the prismatic crystals melt at 91.5—92°.

0.0411 gave 0.0054 nitrogen. $N = 13.14$.

$C_3H_7O_3N$ requires $N = 13.33$ per cent.

Glycerylamide (Active).

This was prepared in exactly the same way from active ethyl glycerate.* It forms large plates or prisms melting at 99.5—100°.

0.0402 gave 0.0052545 nitrogen. $N = 13.07$.

0.0409 „ 0.005397 „ „ $N = 13.20$.

$C_3H_7O_3N$ requires $N = 13.33$ per cent.

$d_{130^\circ/4^\circ} = 1.3099$. $d_{140^\circ/4^\circ} = 1.3016$. $d_{150^\circ/4^\circ} = 1.2932$.

* $\alpha_D = -11.35^\circ$; $l = 1$.

Rotation of glycerylamide.

Temp.	Length of tube.	$d\ t^{\circ}/4^{\circ}$.	α_D .	$[\alpha]_D$.	$[M$
100°	44 mm.	1.3347	-23.47°	-39.98°	-41.98°
109.5	,,	1.3268	-23.06	-39.50	-41.48
136	,,	1.3048	-21.88	-38.11	-40.02
182	,,	1.2666	-19.91	-35.73*	-37.52
[20° calculated from rotations at 100° and 136° above				-44.14	-46.35]

II. Glycerylanilide (Inactive).

Ten grams of inactive ethyl glycerate were heated with 8 grams of aniline (7 grams is the theoretical quantity required) for 4 hours at 140°. The temperature was then gradually raised to 160° and maintained there for 4 hours more. On cooling, the mixture solidified to a brown, pasty mass. The colour was removed by boiling in alcoholic solution with animal charcoal, and crystallisation was then effected from chloroform, small plates melting at 91° being obtained.

0.1745 gave 12.2 c.c. moist nitrogen at 12° and 729 mm. $N = 7.95$.

0.1584 „ 11.0 c.c. „ „ 12.5 „, 725.5 mm. $N = 7.85$.

$C_9H_{11}O_3N$ requires $N = 7.73$ per cent.

Glycerylanilide (Active).

This substance was prepared from active ethyl glycerate as described above for the inactive compound. It was first crystallised from alcohol, being obtained in long, flat blades. On subsequently crystallising from chloroform, in which it is but slightly soluble, it was obtained in small needles. On melting, these yielded a dark liquid, which could not be satisfactorily examined in the polarimeter; it was therefore boiled with animal charcoal in alcoholic solution, and finally crystallised from this solvent. The crystals melted at 113—113.5°, and yielded a clear and colourless liquid.

0.2288 gave 15.6 c.c. moist nitrogen at 14° and 736 mm. $N = 7.77$.

0.1993 „ 13.2 c.c. „ „ 12° „, 751.4 mm. $N = 7.77$.

$C_9H_{11}O_3N$ requires $N = 7.73$ per cent.

$d\ 120^{\circ}/4^{\circ} = 1.1914$. $d\ 140^{\circ}/4^{\circ} = 1.1744$.

* This value is somewhat doubtful, as the glycerylamide underwent partial decomposition during the polarimetric measurements at this temperature.

Rotation of glycerylanilide.

Temp.	Length of tube	$d \text{ } t^{\circ}/4^{\circ}$.	α_D .	$[\alpha]_D$.	$[M]_D$.
100°	49.85 mm.	1.2084	-24.09°	-39.98°	-72.36°
109	"	1.2008	-23.42	-39.12	-70.81
139	"	1.1752	-21.19	-36.16	-65.45
180	"	1.1404	-18.15	-31.93	-57.79
[20° calculated from rotations at 100° and 139° above.				-47.82	-86.55]

III. *Glyceryl-o-toluidide (Inactive).*

Ten grams of inactive methyl glycerate were heated with 15 grams of *o*-toluidine for 4 hours at 140°, the temperature being then raised slowly to 160°; finally the excess of toluidine was distilled off under 14 mm. pressure. On cooling, the contents of the flask nearly solidified to a dark brown mass. On crystallising from benzene, the substance was still much coloured, and it was therefore boiled with animal charcoal in alcoholic solution. It was then several times recrystallised from benzene until of constant melting point, and finally from chloroform by which the melting point was not altered. The crystals are colourless, have a somewhat silky appearance, and melt at 129—129.5°. The liquid obtained by melting the crystals does not colour in contact with air, and in this respect differs from the active compound (see below).

0.2000 gave 0.4499 CO₂ and 0.1219 H₂O. C=61.35; H=6.77.

0.1536 „ 9.4 c.c. moist nitrogen at 14.5° and 757.4 mm. N=7.15.

C₁₀H₁₃O₃N requires C=61.54; H=6.66; N=7.18 per cent.

Glyceryl-o-toluidide (Active).

This was prepared similarly to the inactive substance, 15 grams of active methyl glycerate * being heated with 22.5 grams of *o*-toluidine. Although the colour of the product was removed by boiling in alcoholic solution with animal charcoal, it reappeared during the exposure to air necessitated by the subsequent filtration. Thus pink crystals were obtained from benzene, but finally an almost perfectly colourless separation was obtained by using chloroform as the solvent and washing the crystals with ice-cold chloroform. The crystals had a constant melting point of 89—89.5°. On melting these crystals, however, the liquid obtained was of such a deep-red colour, when viewed by transmitted light, that it could not be used for polarimetric observation. The rotation could therefore only be determined in solution, and this

* $\alpha_D = -6.20^{\circ}$; $l=1$.

necessitated determining the rotatory power of all the other substances referred to in this paper in solution also. The values for the rotatory powers in solution are given later (see p. 273).

0.2002 gave 0.4509 CO₂ and 0.1213 H₂O. C = 61.42; H = 6.73.

0.2004 „ 0.4515 CO₂ „ 0.1219 H₂O. C = 61.44; H = 6.75.

0.2030 „ 12.6 c.c. moist nitrogen at 12° and 746.4 mm. N = 7.23.

C₁₀H₁₃O₃N requires C = 61.54; H = 6.66; N = 7.18 per cent.

IV. *Glyceryl-p-toluidide (Inactive).*

This was prepared from inactive ethyl glycerate and *p*-toluidine (m. p. 44.5°). After heating together as described in the case of the *o*-toluidide, the mixture became semi-solid on cooling. The brown mass was treated with benzene to extract the excess of base, and the residue then crystallised from chloroform, in which it is only very slightly soluble. Crystallisation was repeated from this solvent until the melting point was constant at 120—120.5°.

0.2009 gave 12.9 c.c. of moist nitrogen at 14° and 734 mm. N = 7.29.

0.2013 „ 12.6 „ „ „ 13° „ 744.5 mm. N = 7.24.

C₁₀H₁₃O₃N requires N = 7.18 per cent.

Glyceryl-p-toluidide (Active).

This was similarly prepared and purified by crystallisation from chloroform. The constant melting point was 131—131.5°.

0.1001 gave 6.5 c.c. moist nitrogen at 23° and 754.8 mm. N = 7.27.

0.2009 „ 12.9 c.c. „ „ 14° „ 734 mm. N = 7.28.

C₁₀H₁₃O₃N requires N = 7.18 per cent.

$d_{140^\circ/4^\circ} = 1.1735$. $d_{150^\circ/4^\circ} = 1.1643$.

Rotation of Glyceryl-p-toluidide.

Temp.	Length of tube.	$d_{t/4^\circ}$.	α_n .	$[\alpha]_D$.	$[M]_D$.
179°	49.92 mm.	1.1376	-16.82°	-29.62°	-57.76
136	„	1.1772	-19.03	-32.38	-63.14
109	„	1.2020	-20.41	-34.02	-66.34
98	„	1.2121	-20.99	-34.69	-67.65
[20° calculated from rotations at 98° and					
136° above				-39.43	-76.89]

V. *Rotation of Glycerylanilide and of Glyceryl-o- and -p-toluidide in Methyl Alcohol Solution.*

Owing to the impossibility of taking the rotation of the fused glyceryl-*o*-toluidide, it was determined in solution, the rotation of the

p-compound and of the glycerylanilide and amide being also determined under the same conditions for the purpose of comparison.

The glycerylanilide is only soluble in methyl alcohol to the extent of a little more than 6 per cent., and the glyceryl-*p*-toluidide to the extent of 6.61 per cent., so the rotations were determined in solutions of about 2.5, 5, and 6 per cent. concentration respectively.

In benzene, glycerylanilide is only soluble to the extent of 0.15 per cent. Glycerylamide is even less soluble in methyl alcohol than the other compounds, and hence could only be optically examined in the two lower concentrations.

Rotation in methyl alcohol solution at 20° (l = 100.45 mm.).

Weight of solution, grams.	Weight of substance, grams.	Grams substance in 100 grams solution.	$d\ 20^\circ/4^\circ$.	$\alpha_D^{20^\circ}$.	$[\alpha]_D^{20^\circ}$.	$[M]_D^{20^\circ}$.
<i>Glycerylamide.*</i>						
8.1877	0.1997	2.4390	0.8022	-1.24°	-63.09°	-66.24°
7.7469	0.3689	4.7619	0.8122	-2.40	-61.77	-64.86

[Rotation in liquid state (calculated) $[\alpha]_D^{20^\circ} = -44.14^\circ$, $[M]_D^{20^\circ} = -46.35^\circ$].

Glycerylanilide.

10.2500	0.2500	2.4390	0.8035	-1.42°	-72.13°	-130.55°
10.5000	0.5000	4.7619	0.8118	-2.70	-69.53	-125.85
10.6000	0.6000	5.6604	0.8155	-3.12	-67.29	-121.79

[Rotation in liquid state (calculated) $[\alpha]_D^{20^\circ} = -47.82^\circ$, $[M]_D^{20^\circ} = -86.55^\circ$].

Glyceryl-p-toluidide.

10.2500	0.2500	2.4390	0.8039	-1.26°	-63.97°	-124.74°
10.5000	0.5000	4.7619	0.8108	-2.49	-63.95	-124.70
10.6000	0.6000	5.6604	0.8140	-2.95	-63.74	-124.29

[Rotation in liquid state (calculated) $[\alpha]_D^{20^\circ} = -39.43^\circ$, $[M]_D^{20^\circ} = -76.89^\circ$].

Glyceryl-o-toluidide.

10.2500	0.2500	2.4390	0.8025	-0.64°	-32.55°	-63.47°
10.5000	0.5000	4.7619	0.8117	-1.37	-35.41	-69.05
10.6000	0.6000	5.6604	0.8137	-1.72	-37.18	-72.50

* A 6 per cent. solution could not be prepared, owing to the limited solubility.

VI. *Molecular Volumes.*

In the following table, the experimental molecular volumes are compared with the values calculated by Traube's formula :

	Molecular volume at 15°.	
	Calculated.	Experimental.
Glycerylamide.....	85.1	$\frac{105}{1.4053} = 74.7$
Glycerylanilide	143.7	$\frac{181}{1.2806} = 141.3$
Glyceryl- <i>p</i> -toluidide ...	159.8	$\frac{195}{1.2885} = 151.3$

Constants used :

C = 9.9 ; H = 3.1 ; O (in CO) = 5.5 ; O (in OH) = 0.4 ; N''' = 1.5.

Co-volume = 25.9 ; deduction for benzene ring = 13.2.

Thus in the case of all three compounds the molecular volume points to association, which is greatest in that of the amide and least in that of the anilide.

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