XXVII.—*The Effect of Contiguous Unsaturated Groups on Optical Rotatory Power. Part VI. The Influence of the Carbonyl Group on Optical Rotatory Power. Part VII. The Relative Influences of Aromatic and Hydroaromatic Nuclei on Optical Rotatory Power. Part VIII. The Influence on Optical Activity of Two Contiguous Unsaturated Groups in Comparison with that of One Unsaturated Group at Varying Distances from the Optically Active Complex.*

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PART VI.—*The Influence of the Carbonyl Group on Optical Rotatory Power.*

THE work of Walden (*Zeitsch. physikal. Chem.*, 1896, **20**, 569), Rupe (*Annalen*, 1903, **327**, 157), Hartwall (*Diss.*, Helsingfors, 1904), and the author (*Trans.*, 1908, **93**, 1, 700) has demonstrated that in general optically active esters and salts of acids containing an ethenoid group adjacent to the carboxyl group possess a greater degree of rotatory power than similar derivatives of the corresponding saturated acids. The present communication deals with an analogous series of compounds derived from ketonic acids, thus containing carbonyl in place of an ethenoid group in the above series.

The compounds chosen for the purposes of this investigation were the following:

Menthyl esters and brucine salts of glyoxylic, pyruvic, acetoacetic, and lævulic acids.

Brucine salts of mesoxalic, oxalacetic, and acetonedicarboxylic acids.

Brucine salts of certain aromatic ketonic acids.

The measurements of rotatory power were carried out in dry chloroform solution and in general at two dilutions, 5 grams per 100 c.c. and 2.5 grams per 100 c.c. of solution respectively. The length of solution used was 2-dm., and the temperature was maintained throughout at 20°. In the succeeding tables of results, there is given, in addition to the usual specific and molecular rotatory power, the "anomaly" $[D]_D$ based on the difference between the molecular rotatory power of the compound in question and the

"normal value," that is, the mean molecular rotatory power of the esters or salts of the higher normal fatty acids with menthol or brucine, as the case may be (compare *Trans.*, 1909, **95**, 1571).

I.—*Menthyl Esters of the Pyruvic Acid Series.*

	C : 5.			C : 2.5.		
	[α] _D .	[M] _D .	[D] _D .	[α] _D .	[M] _D .	[D] _D .
Menthyl pyruvate	-83.40	-188.5	+28.0	-82.00	-185.3	+24.1
„ acetoacetate { at once	—	—	—	68.36	164.1	2.9
„ { after 15	—	—	—	67.04	160.9	-0.3
„ { hours.	—	—	—	67.60	171.7	+10.5
„ lævulate	67.62	171.8	11.3			

Menthyl pyruvate and lævulinate showed no appreciable mutation.

II.—*Brucine Salts of the Pyruvic Acid Series.*

	C : 5.			C : 2.5.		
	[α] _D .	[M] _D .	[D] _D .	[α] _D .	[M] _D .	[D] _D .
Brucine glyoxylate	-12.50	-60.7	+186.7	-12.62	-61.3	+190.7
„ pyruvate	17.63	85.2	162.2	17.88	86.2	165.8
„ acetoacetate	11.02	54.7	192.7	10.82	53.7	198.3
„ lævulate	34.40	175.5	71.9	34.88	177.9	74.1

III.—*Dibrucine Salts of the Mesoxalic Acid Series.*

Dibrucine mesoxalate ...	-20.46	-189.1	+152.9	-20.70	-191.9	+156.1
„ oxalacetate ...	39.40	362.4	66.2	38.80	357.0	73.5
„ acetonedicarboxylate	45.84	428.2	33.3	45.84	428.2	37.9

IV.—*Brucine Salts of Aromatic Ketonic Acids.*

Brucine benzoate	-25.40	-131.1	+116.3	-25.00	-129.0	+123.0
„ phenylglyoxylate	6.00	32.6	214.8	6.14	33.4	218.6
„ phenylpyruvate.	+3.66	+20.4	267.8	+3.32	+18.5	270.5
„ benzoylacetate...	-32.26	-180.0	67.4	-33.83	-188.8	63.2
„ benzylpyruvate..	9.59*	54.9*	192.5	9.61*	55.5*	196.5
„ β -benzoylpropionate	32.18	184.1	63.3	31.88	182.4	69.6
„ benzoylpyruvate	+10.26	+60.1	307.5	+11.28	+66.1	318.1

* C : 4.32 and 2.16 respectively.

It will be seen that this system—carbonyl-carboxyl—follows in its main outlines the same rule as the other conjugated structures examined, the anomalies, prominent in those members containing the unsaturated residues adjacent to each other, rapidly declining as the latter are separated. One or two points, however, require special remark:

(a) One cannot always be certain that the carbonyl group is always present as such, since there frequently exists the possibility of an enolic structure in this part of the molecule.

(b) The carbonyl groups in glyoxylic and mesoxalic acids are modified by the addition of a molecule of water, thus lessening the total amount of residual affinity and to a certain extent invalidating the comparison. Consequently, if it be granted from the other examples that the carbonyl-carboxyl grouping enhances optical activity, the true anomalies in these two cases would be somewhat higher.

The series of aromatic ketonic acid salts is especially instructive, for in addition to confirming the general results arrived at from the aliphatic keto-acids, it further demonstrates that:

(a) The carbonyl group alone, when adjacent to the carboxyl group, creates an effect almost as pronounced as that of the benzoyl radicle (phenylpyruvic, benzylpyruvic acids).

(b) The benzoyl system, when separated by methylene groups from the asymmetric part of the molecule, ceases to a great extent to influence the activity (benzoylacetic and β -benzoylpropionic acids).

(c) The benzoyl system, accompanied in the same molecule by a conjugate carbonyl-carboxyl group, produces the maximum effect.

It therefore appears that the carbonyl group, like various other unsaturated groups, causes anomalies in molecular rotatory power; quantitatively speaking, the polarimetric effect of the carbonyl group is probably somewhat less than that of an ethenoid residue under similar conditions. On the other hand, adjacent carbonyl and carboxyl groups together exert an influence on optical activity comparable to that displayed by a benzoyl radicle—a system possessed of considerable residual affinity.

Finally, either by separating the adjacent unsaturated groups or by removing the conjugated system en bloc away from the optically active complex, the anomaly in optical rotatory power may be much diminished or even caused to disappear.

PART VII.—*The Relative Influences of Aromatic and Hydroaromatic Nuclei on Optical Rotatory Power.*

Although no fresh physical evidence as to the absolute structural condition of the "benzene ring" is yet available from the rotatory power of optically active aromatic compounds, one may conclude from the values given by Rupe and his students (*loc. cit.*) for certain menthyl esters of hydroaromatic acids that the successive

introduction of ethylene bonds, culminating finally in an aromatic nucleus, progressively increases optical activity:

	$[M]_D$	$[D]_D$
Menthyl cyclohexanecarboxylate	-157.2	-3.3
„ Δ^1 -cyclohexenecarboxylate	197.0	+36.5
„ benzoate.....	217.2	56.7
„ Δ^1 -ac-tetrahydro- α -naphthoate ...	-215.6	+55.1
„ α -naphthoate	245.3	84.8

There is, however, nothing to show whether the maximum influence of the phenyl group is due to three conjugated ethylenic bonds or to the residual affinity of the radicle as a whole, and accordingly for the purpose of the present paper the benzenoid residue is regarded as a single unsaturated group.

Some experiments, which incidentally illustrate the conditions under which ring-formation affects optical activity, have been carried out by the author to determine the nature of the influence of the aromatic residue from the rotatory powers of salts of various corresponding aromatic and hydroaromatic bases with some optically active acids.

The solutions designed for measurement in the polariscope were made up from the accurately weighed requisite amounts of the base and acid concerned, and the salts formed were subsequently recovered for analysis, etc.

The acids chosen were *d*-camphoric, *d*-camphor- π -sulphonic, and *d*-tartaric; the use of chloroform as a solvent, which is particularly desirable in the case of salts owing to its non-hydroxylic nature, was precluded in the salts of camphoric and tartaric acids by reason of insolubility. Consequently it was necessary to use alcohol for the camphorates, and water for the tartrates. The presence of an ionising solvent introduces a conflicting influence—the constant “molecular” rotation of ions (Oudemans-Landolt law); nevertheless, probably in consequence of incomplete dissociation, differences were found of the same qualitative nature as those manifested in the case of the camphor- π -sulphonates.

In order to obtain a basis for the approximate numerical estimation of anomalies, it was desirable to ascertain the molecular rotatory power of salts of these acids with the normal aliphatic amines.

Since the volatility of the lowest members of the fatty amines rendered them difficult to manipulate in these experiments, whilst the higher members are difficult to obtain, the molecular rotatory power of the *n*-butylamine salts of the acids employed was accepted as an approximate series constant (Tschugaeff, *Ber.*, 1898, **31**, 360,

1775; Hilditch, Trans., 1909, **95**, 1571), and the following values were thus obtained:

	Solvent.	C : 5 per cent.		C : 5 per cent.	
		$[\alpha]_D$	$[M]_D$	$[\alpha]_D$	$[M]_D$
Camphoric acid.....	Alcohol	+48.02	+96.0	+47.72	+95.4
Di- <i>n</i> -butylamine camphorate...	,,	+10.96	+37.9	+11.16	+38.6
Camphor- π -sulphonic acid.....	Chloroform	+24.82	+57.6	+24.04	+55.8
<i>n</i> -Butylamine camphor- π -sulphonate	,,	+20.36	+62.1	+20.44	+62.3
Tartaric acid.....	Water	+14.02	+21.0	+14.44	+21.7
Di- <i>n</i> -butylamine tartrate	,,	+17.86	+52.9	+17.40	+51.5

The following tables show the polarimetric results derived from the various salts studied:

I.—Neutral Camphorates in Alcohol.

Base.	C : 5 per cent.			C : 2.5 per cent.		
	$[\alpha]_D$	$[M]_D$	$[D]_D$	$[\alpha]_D$	$[M]_D$	$[D]_D$
Aniline	+32.50	+125.4	+87.5	+31.84	+122.9	+84.3
Pyridine	25.90	92.7	54.8	27.12	97.1	58.5
Piperidine	14.24	52.7	14.8	14.36	53.1	14.5
Quinoline	+19.16	+87.7	+49.8	+18.76	+85.9	+47.3
Tetrahydroquinoline	17.56	81.8	44.9	17.28	80.5	41.9
α -Naphthylamine	+18.12	+88.1	+50.2	+18.00	+87.5	+48.9
<i>ar</i> -Tetrahydro- α -naphthylamine	16.92	83.6	45.7	16.76	82.8	44.2
β -Naphthylamine	+18.64	+90.6	+52.7	+18.72	+91.0	+52.4
<i>ac</i> -Tetrahydro- β -naphthylamine	14.38	71.0	33.1	14.32	70.7	32.1

II.—Camphor- π -sulphonates in Chloroform.

Base.	C : 5 per cent.			C : 2.5 per cent.		
	$[\alpha]_D$	$[M]_D$	$[D]_D$	$[\alpha]_D$	$[M]_D$	$[D]_D$
Aniline	+23.28	+75.7	+13.6	+23.32	+75.8	+13.5
Pyridine	31.42	97.7	35.6	31.72	98.7	36.4
Piperidine	22.94	72.7	10.6	21.40	67.8	5.5
Quinoline	+27.90	+100.7	+38.6	+26.96	+97.3	+35.0
Tetrahydroquinoline	25.98	94.8	32.7	25.36	92.6	30.3
α -Naphthylamine	+21.38	+80.2	+18.1	+20.92	+78.4	+16.1
<i>ar</i> -Tetrahydro- α -naphthylamine	19.92	75.5	13.4	19.80	75.0	12.7
β -Naphthylamine	+21.54	+80.8	+18.7	+20.80	+78.0	+15.7
<i>ac</i> -Tetrahydro- β -naphthylamine	17.36	65.8	3.7	17.36	65.8	3.5

III.—*Neutral Tartrates in Water.*

Base.	C : 5 per cent.			C : 2·5 per cent.		
	[α] _D .	[M] _D .	[D] _D .	[α] _D .	[M] _D .	[D] _D .
Aniline	+16·58	+55·7	+2·8	+16·12	+54·2	+2·7
Pyridine	19·30	59·5	6·6	18·72	57·7	6·2
Piperidine	17·12	54·8	1·9	16·80	53·8	2·3
Quinoline	+13·22	+54·0	+1·2	+12·80	+52·2	+0·7
Tetrahydroquinoline	13·42	55·8	2·9	12·80	53·3	1·8

The anomalies in the diquinoline tartrate group are not outside the limits of experimental error, and it was impossible to employ the naphthylamine tartrates on account of their sparing solubility.

Analysing these results (which, it must be conceded, are, for optical activity, remarkably consistent), we have:

Base.	Constitution.	Anomaly shown in rotatory power.
(a) Aniline.	Benzenoid conjugated with aminic-group.	Well defined.
Pyridine.	Benzenoid group.	Well defined.
Piperidine.	Alicyclic group.	Relatively small.
(b) Quinoline.	Two conjugated aromatic nuclei.	Well defined.
Tetrahydroquinoline.	Aromatic system + alicyclic amine, the former being also adjacent to the secondary amino-group.	Almost as pronounced as that due to quinoline.
(c) α -Naphthylamine.	Amino-group adjacent to two conjugated aromatic nuclei.	Well defined.
<i>ar</i> -Tetrahydro- α -naphthylamine.	Alicyclic + benzenoid systems, the latter still contiguous to the amino-group.	Slightly less than with α -naphthylamine.
(d) β -Naphthylamine.	Similar to α -naphthylamine.	Much the same as α -naphthylamine.
<i>ac</i> -Tetrahydro- β -naphthylamine.	Alicyclic + benzenoid systems, the latter separated by the former from the amino-group.	Relatively small.

The whole series therefore shows very clearly the enhancing effect of an aromatic group as contrasted with the very small effect of a hydroaromatic nucleus. The only other instance of reduced naphthylamine derivatives (which are obviously exceptionally suited for this comparison) is exactly parallel (Frankland and Ormerod, *Trans.*, 1903, **83**, 1342):

	[M] _D .
Tartarodi- β -naphthylamide	+1163
Tartarodi- <i>ar</i> -tetrahydro- β -naphthylamide	840
Tartarodi- <i>ac</i> -tetrahydro- β -naphthylamide.....	240

These results show that a benzenoid group, when united to another unsaturated group, enhances optical activity, and that the preponderating factor is its unsaturated nature, its ring-structure having very little to do with its influence on rotatory power.

It is frequently stated that ring-formation usually profoundly alters the rotation of a substance, but a brief examination of the literature will reveal that, while this is very true when the asymmetric atoms themselves take part in the formation of the ring system, in all other cases corresponding open- and closed-chain compounds show only small and indefinite changes.

By way of example, and in addition to the results above, we may quote those of Rupe (*loc. cit.*):

	[M] _D .	[M] _D .	
Menthyl cyclopropanecarboxylate.....	-153.5	-164.7	Menthyl <i>n</i> -butyrate.
„ cyclobutanecarboxylate	164.4	165.7	„ <i>n</i> -valerate.
„ cyclopentanecarboxylate.....	171.3	164.7	„ <i>n</i> -hexoate.
„ cyclohexanecarboxylate	157.2	165.9	„ <i>n</i> -heptoate.

PART VIII.—*The Influence on Optical Activity of Two Contiguous Unsaturated Groups in Comparison with that of One Unsaturated Group at Varying Distances from the Optically Active Complex.*

Attention was drawn by Tschugaëff (*loc. cit.*) to the rotatory power of the first three members of menthyl esters of the homologous phenyl aliphatic acids and to those of the corresponding amyl esters (Guye and Chavanne, *Bull. Soc. chim.*, 1896, [iii], 15, 177), pointing out that the value in both, abnormally large in the benzoates, decreased to almost the average value of esters of a normal aliphatic acid when the third member was reached:

Ester.	Amyl.		Menthyl.	
	[M] _D .	[D] _D .	[M] _D .	[D] _D .
Mean value of fatty acid ester	+4.33	—	-157.8	—
Benzoate	+9.52	+5.19	-236.3	+78.5
Phenylacetate	7.91	3.58	190.7	32.9
β-Phenylpropionate	4.73	0.40	161.9	4.1

The brucine and cinchonine salts of the same acids, more recently examined by the author (*Trans.*, 1908, 93, 1388), show the same gradation in optical anomaly.

Tschugaëff concluded that the power of an unsaturated group to affect optical activity rapidly declined as it was separated from the asymmetric system, and Guye (*Proc.*, 1901, 17, 48) adopted these examples as particular cases of his more general conclusion that substitution at a point sufficiently removed from the asymmetric atom creates little optical effect.

Rupe (*loc. cit.*) elaborated the question by his work on isomeric pentenoic and hexenoic menthyl esters, and suggested that the size

of the anomaly produced by unsaturation is determined mainly by the proximity of the unsaturated group to the asymmetric system :

		[M] _D .
Menthyl	$\Delta^{\alpha\beta}$ -pentoate	- 177.1
"	$\Delta^{\beta\gamma}$ -pentoate	172.5
"	$\Delta^{\gamma\delta}$ -pentoate	160.2
"	$\Delta^{\alpha\beta}$ -hexenoate	- 172.4
"	$\Delta^{\beta\gamma}$ -hexenoate	164.1
"	$\Delta^{\gamma\delta}$ -hexenoate	153.5
"	$\Delta^{\delta\epsilon}$ -hexenoate	154.4

The author has in previous papers (Trans., 1909, **95**, 336, 1570, etc.) attributed many cases of abnormal rotatory power to the presence of adjacent or "conjugated" unsaturated systems in the molecules in question, and it appears well to discuss in detail those cases which are at first sight equally well covered either by the latter or by the Tschugaeff-Rupe explanation. For it must be observed that in the examples from which these authors' deductions are made, a carboxyl residue always intervenes between the phenyl and asymmetric radicles, and thus, simultaneously with increasing distance of the phenyl group from the asymmetric system, the contiguity of the unsaturated phenyl and carboxyl residues is automatically destroyed.

It is interesting in this connexion to notice that in the case of some neutral aniline and benzylamine salts of optically active acids, in which the benzenoid and carboxyl residues are separated by a (saturated) quinquivalent nitrogen atom, the decrease in optical activity is not always so marked as in the former instances of simple aromatic esters and salts. These examples, which were observed under the same conditions as the similar salts described on a preceding page, are collected in the next table.

Acid.	Solvent.	Percentage concentra- tion.	Aniline salt.			Benzylamine salt.		
			[α] _D .	[M] _D .	[D] _D .	[α] _D .	[M] _D .	[D] _D .
Camphoric	Alcohol	5.0	+ 32.50	+ 125.4	+ 87.5	+ 16.92	+ 70.0	+ 32.1
"	"	2.5	31.84	122.9	84.3	17.16	71.0	32.4
Camphor- π -sulphonic	Chloroform	5.0	+ 23.28	+ 75.7	+ 13.6	+ 22.00	+ 74.6	+ 12.5
Camphor- π -sulphonic	"	2.5	23.32	75.8	13.5	21.36	72.4	10.1
Tartaric	Water	5.0	+ 16.58	+ 55.7	+ 2.8	+ 18.28	+ 66.5	+ 13.7
"	"	2.5	16.12	54.2	2.7	17.40	63.3	11.8

If, on the other hand, compounds are selected in which it is possible, while maintaining the same relative positions of unsaturated groups to asymmetric system, to alter the amount of residual affinity (and therefore of any effect due to conjugation) by changing the character of one of the unsaturated radicles, the results obtained are very different. In some cases, for example,

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one can compare corresponding benzyl and benzoyl derivatives of an active substance, when, whilst the phenyl group is left at the same distance from the active complex, there is in one case a single phenyl group and in the other a conjugated (phenyl+carbonyl) system.

We may thus compare some ethers of menthol described by Tschugaeff (*J. Russ. Phys. Chem. Soc.*, 1902, **34**, 606) with the esters to which reference has already been made:

	[M] _D	Difference.
Menthyl ethyl ether, $\text{CH}_3\cdot\text{CH}_2\cdot\text{O}\cdot\text{C}_{10}\text{H}_{19}$	-179.0	53.7
Menthyl benzyl ether, $\text{C}_6\text{H}_5\cdot\text{CH}_2\cdot\text{O}\cdot\text{C}_{10}\text{H}_{19}$	-232.7	
Menthyl acetate, $\text{CH}_3\cdot\text{CO}\cdot\text{O}\cdot\text{C}_{10}\text{H}_{19}$	-157.3	79.0
Menthyl benzoate, $\text{C}_6\text{H}_5\cdot\text{CO}\cdot\text{O}\cdot\text{C}_{10}\text{H}_{19}$	-236.3	

A similar comparison of the corresponding amyl ethers and esters (Guye and Chavanne, *loc. cit.*) leads to the same result:

	[M] _D	Difference.
l-Amyl ethyl ether, $\text{CH}_3\cdot\text{CH}_2\cdot\text{O}\cdot\text{C}_5\text{H}_{11}$	+0.7	2.5
l-Amyl benzyl ether, $\text{C}_6\text{H}_5\cdot\text{CH}_2\cdot\text{O}\cdot\text{C}_5\text{H}_{11}$	+3.2	
l-Amyl acetate, $\text{CH}_3\cdot\text{CO}\cdot\text{O}\cdot\text{C}_5\text{H}_{11}$	+3.3	6.3
l-Amyl benzoate, $\text{C}_6\text{H}_5\cdot\text{CO}\cdot\text{O}\cdot\text{C}_5\text{H}_{11}$	+9.6	

Both these cases involve change of residual affinity without any relative change of molecular position, and all show differences in rotatory power quite as marked as in the first-mentioned series, which involve progressive removal of an unsaturated radicle. Moreover, the examples of menthyl and amyl ethers display unmistakably the peculiar anomaly produced by conjugation, apart from any question of relative position in space.

It has been remarked (Trans., 1908, **93**, 1618) that the sulphonic group SO_2 behaves as a relatively saturated group with reference to optical activity; use has been made of this fact to produce another series of comparisons bearing upon the present subject, in which, again without altering relative molecular positions, a conjugated system XY has been changed by replacing one member of the system ($\text{Y}\cdot\text{CO}$) by another of less residual affinity ($\text{Y}\cdot\text{SO}_2$), rather than by an almost completely saturated group ($\text{Y}\cdot\text{CH}_2$), as in the last examples. As the details given below demonstrate, in all cases the effect on optical activity is greatest in presence of the most unsaturated conjugated system, and when more than two systems are compared, the optical anomaly falls off in the same order as the residual affinities of the systems concerned.

The compounds studied in this way include, on the one hand, corresponding arylcarboxylic and arylsulphonic esters of menthol, and, on the other, the acetyl, benzoyl, and benzenesulphonyl derivatives of cinchonine and of cinchonidine.

The polarimetric measurements were carried out in chloroform solutions in a 2-dcm. tube maintained at a temperature of 13–14°.

Observations were made in the case of the menthyl esters with solutions containing 5 and 2·5 grams per 100 c.c. of solution respectively, and with solutions of 2 per cent. concentration of the alkaloidal derivatives. The results are summarised in the following tables :

I.—*Menthyl Esters.*

Ester.	C : 5.			C : 2·5.		
	$[\alpha]_D$.	$[M]_D$.	$[D]_D$.	$[\alpha]_D$.	$[M]_D$.	$[D]_D$.
Benzoate.....	-85·60	-222·6	+62·1	-86·04	-223·8	+62·6
Benzenesulphonate	72·68	215·1	54·6	73·20	216·7	55·5
<i>p</i> -Toluate	-95·22	-260·9	+100·5	-95·36	-261·3	+100·1
<i>p</i> -Toluenesulphonate.....	66·76	206·9	46·4	66·80	207·1	45·9
β -Naphthoate	-90·60	-280·9	+120·4	-91·12	-282·5	+121·3
Naphthalene- β -sulphonate.	56·50	195·4	34·9	57·12	197·6	36·4

II.—*Cinchonine Derivatives.*

Substituent.	C : 2.		
	$[\alpha]_D$.	$[M]_D$.	Difference.
Acetyl	+108·50	+364·6	—
Benzenesulphonyl	+62·15	+269·7	-94·9
Benzoyl	-27·80	-110·6	-475·2

III.—*Cinchonidine Derivatives.*

Acetyl	+12·90	+43·3	—
Benzenesulphonyl	+11·43	+49·6	+6·3
Benzoyl	+98·65	+392·6	+349·3

The conclusion is therefore reached that, in compounds where the influence of two or more given radicles on optical activity may be due either to their proximity to the asymmetric nucleus or to conjugated unsaturation, both causes contribute to the effect, but conjugation is evidently the predominating factor.

The series of brucine salts of aromatic ketonic acids given on a preceding page forms an excellent example of the combined effects of conjugation and of varying degrees of proximity of the unsaturated systems to the optically active group. Thus, when the acid group CO_2H remains attached to a carbonyl group, the anomaly is uniformly high, and is but slightly altered by successive removal of the phenyl group to more remote parts of the molecule, whilst the maximum exaltation occurs when there are two sets of conjugated systems in the molecule, although one of these is relatively distant from the asymmetric complex :

Brucine salt of :	$[M]_D$.	$[D]_D$.
Phenylglyoxylic acid, $\text{C}_6\text{H}_5\cdot\text{CO}\cdot\text{CO}_2\text{H}$	-32·6	+214·8
Phenylpyruvic „ $\text{C}_6\text{H}_5\cdot\text{CH}_2\cdot\text{CO}\cdot\text{CO}_2\text{H}$	+20·4	267·8
Benzylpyruvic „ $\text{C}_6\text{H}_5\cdot\text{CH}_2\cdot\text{CH}_2\cdot\text{CO}\cdot\text{CO}_2\text{H}$	-54·9	192·5
Benzoylpyruvic „ $\text{C}_6\text{H}_5\cdot\text{CO}\cdot\text{CH}_2\cdot\text{CO}\cdot\text{CO}_2\text{H}$	+60·1	307·5

On the other hand, Rupe's explanation is plainly supported by those salts wherein the conjugated system $C_6H_5 \cdot CO$ is itself progressively separated from the optically active part of the molecule.

For instance, brucine β -phenylpropionate has an anomaly of 39.7, whilst that of the β -benzoylpropionate is 63.3:

Brucine salt of:	[M] _D .	[D] _D .
Phenylglyoxylic acid, $C_6H_5 \cdot CO \cdot CO_2H$	-32.6	+214.8
Benzoylactic acid, $C_6H_5 \cdot CO \cdot CH_2 \cdot CO_2H$	180.0	67.4
β -Benzoylpropionic acid, $C_6H_5 \cdot CO \cdot CH_2 \cdot CH_2 \cdot CO_2H$	184.1	63.3

EXPERIMENTAL.

Menthyl pyruvate, *acetoacetate*, and *laevulate* have already been described by Cohen and Whiteley (Trans., 1901, **79**, 1309), Lapworth and Hann (Trans., 1902, **81**, 1479), and McKenzie (Trans., 1905, **87**, 1380), but in order that all three might be examined under identical polarimetric conditions their preparation was repeated. The author's specimens possessed physical properties agreeing with those described by the above authors, and furnished satisfactory analytical numbers.

The brucine salts, except in a few stated cases, were directly made up from the equivalent amounts, accurately weighed, of the pure alkaloid and acid, dissolved in the corresponding quantity of chloroform, and then measured in the polariscope, after which they were recovered, crystallised, and analysed.

Brucine glyoxylate, $C_{26}H_{30}O_4 \cdot C_{23}H_{26}O_4N_2 \cdot 4H_2O$, was prepared by mixing roughly equivalent quantities of the acid (prepared as described by Perkin and Duppa, Trans., 1868, **21**, 197) and base in alcohol, precipitating by ether, and finally crystallising from a mixture of ether and alcohol. It formed a cream, micro-crystalline powder, which frothed at 160°, and decomposed at about 200°:

0.1049 gave 0.2083 CO_2 and 0.0654 H_2O . C=54.14; H=6.93.

$C_{26}H_{30}O_8N_2 \cdot 4H_2O$ requires C=53.76; H=6.81 per cent.

Brucine Pyruvate, $C_3H_4O_3 \cdot C_{23}H_{26}O_4N_2 \cdot 3H_2O$. — Soft, cream-coloured crystals, readily soluble in water, melting at 85°, and evolving H_2O at 105—110°:

0.1417 gave 0.3028 CO_2 and 0.0895 H_2O . C=58.28; H=7.01.

$C_{26}H_{30}O_7N_2 \cdot 3H_2O$ requires C=58.21; H=7.09 per cent.

Brucine acetoacetate, $C_4H_6O_3 \cdot C_{23}H_{26}O_4N_2 \cdot 4H_2O$, was prepared from the sodium salt of the acid and brucine hydrochloride in absolute alcohol, subsequently crystallising from a mixture of ether and alcohol. It appeared as a white, soft, crystalline powder, partly melting at 147—150°:

0.1880 gave 0.3950 CO_2 and 0.1178 H_2O . C=57.30; H=6.96.

$C_{27}H_{32}O_7N_2 \cdot 4H_2O$ requires C=57.04; H=7.04 per cent.

Brucine Laevulate, $C_5H_8O_3, C_{23}H_{26}O_4N_2, 4H_2O$.—Very small, hard, white crystals, which melt sharply at 58° , froth up violently at 112 — 114° , and again leave a clear liquid:

0.1344 gave 0.2854 CO_2 and 0.0737 H_2O . $C = 57.91$; $H = 7.32$.

$C_{28}H_{34}O_7N_2, 4H_2O$ requires $C = 57.73$; $H = 7.22$ per cent.

Dibrucine Mesoxalate, $C_3H_4O_6, (C_{23}H_{26}O_4N_2)_2$.—A white, crystalline powder, showing no change in appearance below 250° :

0.1020 gave 0.2386 CO_2 and 0.0583 H_2O . $C = 63.80$; $H = 6.36$.

$C_{49}H_{56}O_{14}N_4$ requires $C = 63.63$; $H = 6.06$ per cent.

Dibrucine Oxalacetate, $C_4H_4O_5, (C_{23}H_{26}O_4N_2)_2, 2H_2O$.—Soft, white nodules from ethyl acetate, melting with much frothing at 163 — 166° :

0.1596 gave 0.3687 CO_2 and 0.0988 H_2O . $C = 62.98$; $H = 6.88$.

$C_{50}H_{56}O_{13}N_4, 2H_2O$ requires $C = 62.76$; $H = 6.28$ per cent.

Dibrucine acetonedicarboxylate, $C_5H_6O_5, (C_{23}H_{26}O_4N_2)_2, H_2O$, separates from benzene in large, transparent, cubical crystals, melting at 179 — 180° :

0.1551 gave 0.3655 CO_2 and 0.0905 H_2O . $C = 64.27$; $H = 6.48$.

$C_{51}H_{58}O_{13}N_4, H_2O$ requires $C = 64.29$; $N = 6.30$ per cent.

The necessary aromatic ketonic acids were obtained by methods devised by Claisen (*Ber.*, 1887, **20**, 655, 2196; 1888, **21**, 1131), Erlenmeyer (*Annalen*, 1892, **271**, 163), Perkin (*Trans.*, 1884, **45**, 178), and Fittig (*Ber.*, 1896, **29**, 2582), and the purity of each was controlled by determination of the melting point.

Brucine Phenylglyoxylate, $C_8H_6O_3, C_{23}H_{26}O_4N_2, H_2O$.—Colourless, stable crystals, by ethereal precipitation of the alcoholic solution; the salt decomposes, but does not melt at 230° :

0.1112 gave 0.2697 CO_2 and 0.0636 H_2O . $C = 66.15$; $H = 6.36$.

$C_{31}H_{32}O_7N_2, H_2O$ requires $C = 66.19$; $H = 6.05$ per cent.

Brucine Phenylpyruvate, $C_9H_8O_3, C_{23}H_{26}O_4N_2, 2\frac{1}{2}H_2O$.—A cream-coloured salt, melting and decomposing at 182 — 183° :

0.1190 gave 0.2774 CO_2 and 0.0685 H_2O . $C = 63.57$; $H = 6.40$.

$C_{32}H_{34}O_7N_2, 2\frac{1}{2}H_2O$ requires $C = 63.68$; $H = 6.46$ per cent.

Brucine Benzylacetate, $C_9H_8O_3, C_{23}H_{26}O_4N_2, 5\frac{1}{2}H_2O$.—Colourless, slender needles, readily soluble in water, melting and decomposing at 196° :

0.1216 gave 0.2600 CO_2 and 0.0776 H_2O . $C = 58.30$; $H = 7.09$.

$C_{32}H_{34}O_7N_2, 5\frac{1}{2}H_2O$ requires $C = 58.43$; $H = 6.85$ per cent.

Brucine Benzylpyruvate, $C_{10}H_{10}O_3, C_{23}H_{26}O_4N_2, 5H_2O$.—A colourless, crystalline powder, melting at 100 — 103° :

0.1093 gave 0.2405 CO_2 and 0.0670 H_2O . $C = 60.01$; $H = 6.81$.

$C_{33}H_{36}O_7N_2, 5H_2O$ requires $C = 59.81$; $H = 6.95$ per cent.

Brucine β -Benzoylpropionate, $C_{10}H_{10}O_3, C_{23}H_{26}O_4N_2, 3H_2O$. — A cream-coloured, deliquescent, micro-crystalline powder, evolving water, and fusing at $101-103^\circ$:

0.1071 gave 0.2472 CO_2 and 0.0660 H_2O . $C = 62.94$; $H = 6.85$.

$C_{33}H_{36}O_7N_2, 3H_2O$ requires $C = 63.35$; $H = 6.71$ per cent.

Brucine Benzoylpyruvate, $C_{10}H_8O_4, C_{23}H_{26}O_4N_2, 2\frac{1}{2}H_2O$. — Hard, colourless tablets, losing water at 100° , melting and decomposing at 174° :

0.1126 gave 0.2587 CO_2 and 0.0678 H_2O . $C = 62.66$; $H = 6.69$.

$C_{33}H_{34}O_8N_2, 2\frac{1}{2}H_2O$ requires $C = 62.76$; $H = 6.18$ per cent.

Some of the amine salts employed in this work could not be obtained crystalline, or, at all events, sufficiently non-deliquescent for characterisation. Others, however, were definitely crystalline, and can be reported upon:

Di-n-butylamine Camphorate, $C_{10}H_{16}O_4(C_4H_9NH_2)_2$. — Delicate, white needles, melting at $150-152^\circ$:

0.1130 gave 0.2608 CO_2 and 0.1111 H_2O . $C = 63.17$; $H = 10.91$.

$C_{18}H_{38}O_4N_2$ requires $C = 62.94$; $H = 10.98$ per cent.

n-Butylamine Camphor- π -sulphonate,

$C_{10}H_{15}O \cdot SO_3H, C_4H_9NH_2, 1H_2O$.

—Wax-like, shining crystals, melting at 125° :

0.1204 gave 0.2342 CO_2 and 0.1000 H_2O . $C = 53.06$; $H = 9.25$.

$C_{14}H_{27}O_4NS, 1H_2O$ requires $C = 53.31$; $H = 9.22$ per cent.

Di-n-butylamine Tartrate, $C_4H_8O_6(C_4H_9NH_2)_2$. — Cream, deliquescent prisms, melting at $70-75^\circ$:

Dianiline Camphorate, $(C_6H_7N)_2, C_{10}H_{16}O_4, 1\frac{1}{2}H_2O$. — White, amorphous powder, softening at $255-260^\circ$:

0.1436 gave 0.3534 CO_2 and 0.0906 H_2O . $C = 67.11$; $H = 7.11$.

$C_{22}H_{30}O_4N_2, \frac{1}{2}H_2O$ requires $C = 66.83$; $H = 7.85$ per cent.

Diquinoline Camphorate, $(C_9H_7N)_2, C_{10}H_{16}O_4, 2H_2O$. — Deliquescent, crystalline mass, melting at $75-80^\circ$:

0.1226 gave 0.3046 CO_2 and 0.0766 H_2O . $C = 67.76$; $H = 6.94$.

$C_{28}H_{25}O_4N_2, 2H_2O$ requires $C = 68.01$; $H = 6.88$ per cent.

Di- α -naphthylamine Camphorate, $(C_{10}H_9N)_2, C_{10}H_{16}O_4, 2\frac{1}{2}H_2O$. — Small needles, turning reddish-purple in the air, and melting at 183° :

0.1180 gave 0.2938 CO_2 and 0.0827 H_2O . $C = 67.90$; $H = 7.79$.

$C_{30}H_{34}O_4N_2, 2\frac{1}{2}H_2O$ requires $C = 67.79$; $H = 7.35$ per cent.

α -Naphthylamine Camphor- π -sulphonate, $C_{10}H_9N, C_{10}H_{15}O_4S$. — Small, colourless flakes, turning blue-violet in the air, and melting at $194-196^\circ$:

0.1154 gave 0.2727 CO_2 and 0.0658 H_2O . $\text{C}=64.45$; $\text{H}=6.34$.

$\text{C}_{20}\text{H}_{25}\text{O}_4\text{NS}$ requires $\text{C}=64.00$; $\text{H}=6.37$ per cent.

ar-Tetrahydro- α -naphthylamine Camphor- π -sulphonate,

$\text{C}_{10}\text{H}_{13}\text{N}, \text{C}_{10}\text{H}_{16}\text{O}_4\text{S}, 4\frac{1}{2}\text{H}_2\text{O}$.

—Glistening, colourless crystals, turning dark blue in the air, and melting somewhat indefinitely at $128-132^\circ$:

0.1053 gave 0.2016 CO_2 and 0.0854 H_2O . $\text{C}=52.22$; $\text{H}=8.49$.

$\text{C}_{20}\text{H}_{29}\text{O}_4\text{NS}, 4\frac{1}{2}\text{H}_2\text{O}$ requires $\text{C}=52.17$; $\text{H}=8.26$ per cent.

β -Naphthylamine Camphor- π -sulphonate, $\text{C}_{10}\text{H}_9\text{N}, \text{C}_{10}\text{H}_{16}\text{O}_4\text{S}$.—A cream-coloured, micro-crystalline powder, melting indefinitely at $118-121^\circ$:

0.1304 gave 0.2620 CO_2 and 0.0707 H_2O . $\text{C}=54.80$; $\text{H}=6.03$.

$\text{C}_{20}\text{H}_{25}\text{O}_4\text{NS}, 3\frac{1}{2}\text{H}_2\text{O}$ requires $\text{C}=54.80$; $\text{H}=5.84$ per cent.

Dianiline Tartrate, $(\text{C}_6\text{H}_7\text{N})_2, \text{C}_4\text{H}_6\text{O}_6$.—A soft, crystalline powder, turning pink in the air, but colourless again on heating; melts and decomposes at $184-185^\circ$:

0.1128 gave 0.2028 CO_2 and 0.0660 H_2O . $\text{C}=49.05$; $\text{H}=6.50$.

0.0631 lost 0.0086 at 100° . $\text{H}_2\text{O}=13.63$.

$\text{C}_{16}\text{H}_{20}\text{O}_6\text{N}_2, 3\text{H}_2\text{O}$ requires $\text{C}=49.22$; $\text{H}=6.67$;

$\text{H}_2\text{O}=13.85$ per cent.

Dipyridine Tartrate, $(\text{C}_5\text{H}_5\text{N})_2, \text{C}_4\text{H}_6\text{O}_6$.—Crisp, colourless flakes, melting at 158° :

0.1152 gave 0.2112 CO_2 and 0.0582 H_2O . $\text{C}=49.99$; $\text{H}=5.39$.

$\text{C}_{14}\text{H}_{16}\text{O}_6\text{N}_2, 1\frac{1}{2}\text{H}_2\text{O}$ requires $\text{C}=50.16$; $\text{H}=5.67$ per cent.

Diquinoline Tartrate, $(\text{C}_9\text{H}_7\text{N})_2, \text{C}_4\text{H}_6\text{O}_6$.—A brick-coloured, crystalline powder, melting at 131° :

0.1093 gave 0.2142 CO_2 and 0.0551 H_2O . $\text{C}=53.44$; $\text{H}=5.60$.

$\text{C}_{22}\text{H}_{20}\text{O}_6\text{N}_2, 5\text{H}_2\text{O}$ requires $\text{C}=52.99$; $\text{H}=6.03$ per cent.

Ditetrahydroquinoline Tartrate, $(\text{C}_9\text{H}_{11}\text{N})_2, \text{C}_4\text{H}_6\text{O}_6$.—Crisp, cream-coloured flakes, turning green in air, and melting and decomposing at $118-120^\circ$.

Dibenzylamine camphorate, $(\text{C}_7\text{H}_7\cdot\text{NH}_2)_2, \text{C}_{10}\text{H}_{16}\text{O}_4, \frac{1}{2}\text{H}_2\text{O}$, forms crisp, colourless crystals, melting at $188-189^\circ$:

0.1162 gave 0.2907 CO_2 and 0.0983 H_2O . $\text{C}=68.21$; $\text{H}=8.05$.

$\text{C}_{24}\text{H}_{34}\text{O}_4\text{N}_2, \frac{1}{2}\text{H}_2\text{O}$ requires $\text{C}=68.10$; $\text{H}=8.25$ per cent.

Benzylamine camphor- π -sulphonate crystallised in slightly pink scales, darkening, without melting, at 230° .

Dibenzylamine tartrate, $(\text{C}_7\text{H}_7\cdot\text{NH}_2)_2, \text{C}_4\text{H}_4\text{O}_6$, consists of small, colourless needles, melting at 112° :

0.1100 gave 0.2263 CO_2 and 0.0678 H_2O . $\text{C}=56.10$; $\text{H}=6.85$.

$\text{C}_{18}\text{H}_{24}\text{O}_6\text{N}_2$ requires $\text{C}=56.54$; $\text{H}=6.81$ per cent.

Menthyl Esters of Corresponding Aromatic Carboxylic and Sulphonic Acids.

The carboxylic esters have already been described by Tschugaëff (*loc. cit.*); the samples of these compounds prepared by the author possessed melting points in agreement with Tschugaëff's data.

The sulphonic esters were prepared from the respective acid chlorides and menthol in the cold in the presence of pyridine, as recommended by Patterson and Frew (*Trans.*, 1906, **80**, 332), who have described the benzene- and β -naphthalene-sulphonates of menthol. These esters are excellently adapted for polarimetric work, since they crystallise especially well, and are thus very easily and certainly purified.

Menthyl p-Tolylsulphonate, $C_7H_7 \cdot SO_3 \cdot C_{10}H_{19}$.—Long, hard, stout, colourless needles, sparingly soluble in cold alcohol, and melting at 97° :

0.1418 gave 0.3424 CO_2 and 0.1105 H_2O . $C=65.80$; $H=8.66$.

0.1292 „ 0.0950 $BaSO_4$. $S=10.09$.

$C_{17}H_{26}O_3S$ requires $C=65.80$; $H=8.39$; $S=10.32$ per cent.

Acyl Derivatives of Cinchonine and Cinchonidine.

The *acetyl* compounds, $CH_3 \cdot CO \cdot C_{19}H_{21}ON_2$, were prepared by heating the alkaloids on the water-bath with excess of acetic anhydride for two hours. After cooling, the reaction mixture was poured into water and rendered alkaline with dilute sodium hydroxide. The products were then isolated by extraction with ether, and purified from unchanged base by solution in a large amount of boiling light petroleum, which was finally removed under diminished pressure at the ordinary temperature, leaving the compounds in the form of cream-coloured, amorphous powders:

Acetylcinchonine melted at $51-53^\circ$:

0.1138 gave 0.3118 CO_2 and 0.0716 H_2O . $C=74.73$; $H=6.99$.

$C_{21}H_{24}ON_2$ requires $C=75.01$; $H=7.14$ per cent.

Acetylcinchonidine melted at $47-49^\circ$:

0.1602 gave 0.4400 CO_2 and 0.0992 H_2O . $C=74.88$; $H=6.90$.

The *benzoyl* derivatives, $C_6H_5 \cdot CO \cdot C_{19}H_{21}ON_2$, resulted when 3 parts of the alkaloid and 5 parts of benzoyl chloride were boiled together in benzene solution for two hours. The product appeared as an oily hydrochloride, from which the benzene was removed by decantation and repeated washing with ether. The salt was then dissolved in cold water, and excess of ammonia added. The liberated base, after being filtered and dried, was usually rendered pure by one or two crystallisations from ether.

The *benzenesulphonyl* compounds, $C_6H_5 \cdot SO_2 \cdot C_{19}H_{21}ON_2$, were obtained in a precisely similar manner from equal weights of benzenesulphonyl chloride and cinchonine or cinchonidine.

Benzoylcinchonine crystallises in hard nodules from light petroleum or ether, but is too soluble in benzene or alcohol to crystallise well therefrom at the usual temperature. It melts somewhat indefinitely at 104—105°:

0.1574 gave 0.4510 CO_2 and 0.0982 H_2O . $C=78.14$; $H=6.93$.

$C_{26}H_{26}O_2N_2$ requires $C=78.39$; $H=6.54$ per cent.

Benzoylcinchonidine separates from ether in small, hard needles, soluble in alcohol, insoluble in light petroleum, melting to a clear liquid at 183°:

0.1040 gave 0.2992 CO_2 and 0.0621 H_2O . $C=78.47$; $H=6.64$.

Benzenesulphonylcinchonine crystallises from ether, but is almost insoluble in benzene:

0.1223 gave 0.3089 CO_2 and 0.0669 H_2O . $C=68.88$; $H=6.08$.

$C_{25}H_{26}O_3N_2S$ requires $C=69.11$; $H=5.99$ per cent.

Benzenesulphonylcinchonidine may be obtained from a boiling benzene solution as small needles, melting at 166°:

0.1924 gave 0.4896 CO_2 and 0.1080 H_2O . $C=69.37$; $H=6.24$.

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