

XIV.—*Optically Active Ethoxysuccinic acid.*

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IT has been shown in the preceding communication that inactive methoxysuccinic acid can be readily resolved into its active components by means of the difference in solubility of the cinchonine salts of the active acids. To procure the active ethoxysuccinic acids from the inactive compound, we naturally tried the same method, but preliminary experiments with cinchonine and other alkaloids did not give the expected result: we had recourse, therefore, to another of the methods discovered by Pasteur, namely, the selective action of moulds. We found that ethoxysuccinic acid succumbs readily to the action of *Penicillium glaucum*, the lævogyrate component being consumed during the growth of the mould, while the dextrogyrate component is left unaltered.

The acid used in our experiments was prepared by methods already described (Trans., 1881, **39**, 344; 1885, **47**, 865), but with modifications which we found to give a better yield of material. The ethyl fumarate, mixed with an equal bulk of alcohol, was treated at the ordinary temperature with sodium ethylate in the proportion of less

than $\frac{1}{10}$ th atom of sodium to 1 mol. ethereal salt. The product, after standing some days, was saponified with potassium hydroxide, and from the lead salt, procured by adding lead nitrate to the neutralised aqueous solution, the acid was prepared in the usual way. About 85 per cent. of the calculated yield of dry acid was obtained. The acid was found to be quite inactive.

Action of Penicillium glaucum.

For our experiments with this mould, we used hydrogen ammonium ethoxysuccinate. Solutions of this salt of various concentration, to which the necessary nutritive mineral salts were usually added, were sown with the spores of the mould, and left until the growth seemed to have ceased. Ten experiments in all were carried out with quantities of ethoxysuccinate varying from 3 to about 20 grams. The rapidity and mode of growth of the mould varied considerably, but in each case, whether spores were developed or only mycelium, a dextrogyrate solution was produced. The following experiments may be quoted as examples :—

1.—3·3 grams of the hydrogen ammonium salt were dissolved in 1 litre of water, and 1·5 grams of potassium phosphate added. The growth of the mould was observable in a week, and after three months a thick felt of mycelium without spores had been produced. The solution having been filtered, neutralised with ammonia, clarified with animal charcoal, and evaporated to a bulk of 15 c.c., gave a rotation of $+2^{\circ} 25'$ in a 220 mm. tube. The solution having been made up as before to 1 litre and resown, was left for a month ; there was no increase in the rotatory power.

2.—7 grams of the same salt were dissolved in a litre of ordinary tap-water, to which no salts were added. After three months the solution, having been treated as described, and evaporated to 15 c.c., showed a rotation of $+3^{\circ} 20'$. On concentrating still further, crystals of the active hydrogen ammonium salt separated, mixed, however, with a considerable quantity of the inactive salt. The whole was made up again to 1 litre, and resown with spores, some phosphate being added. Growth started again, though not vigorously. After two months, the activity had increased ; the solution, being concentrated to only 25 c.c., gave a rotation of $+3^{\circ}$.

3.—22 grams of the hydrogen ammonium salt were dissolved in 1 litre of water, to which 80 c.c. of a solution, containing 1 gram of potassium phosphate, 0·2 gram of magnesium sulphate, and 0·1 gram of calcium chloride per litre, was added. A thick mass of mycelium of a yellowish colour was quickly produced, and in two months the growth was at an end. On treating the liquid as before, the active

hydrogen ammonium salt crystallised in isolated prisms of considerable size. We found that the conditions observed in this experiment were the most favourable for the action of the mould, and for the subsequent extraction of the active substance.

Some difficulty was experienced in obtaining the active acid and its salts from the product of the fermentation. We found that the active acid, unlike the inactive, could not be precipitated as lead salt, and that precipitation as calcium salt, which is almost complete in the case of the inactive acid, was also unsuitable, owing to the greater solubility of the corresponding active compound. Extraction of the acid with ether likewise gave very unsatisfactory results. We therefore adopted the following methods: the solution resulting from the fermentation, having been filtered, neutralised with ammonia, and treated with animal charcoal, was evaporated to a small bulk, when some of the hydrogen ammonium salt usually crystallised. This was removed, and the uncrystallisable mother liquor, which contained the main quantity of the active substance, was largely diluted with water, and boiled with milk of lime as long as ammonia was evolved. The filtered liquid having been treated with carbon dioxide, and evaporated to dryness, the residue was shaken up for a long time with less than the quantity of cold water required for its complete solution; in this way the active calcium ethoxysuccinate was dissolved, and separated from any inactive salt which might be present. The calcium salt obtained by the evaporation of this solution was dried at 100°, weighed, dissolved as before in cold water, and then decomposed by adding to the solution rather less than the calculated quantity of sulphuric acid. The active ethoxysuccinic acid was procured by treating repeatedly with ether the residue left on evaporation.

Hydrogen Ammonium Dextro-ethoxysuccinate.

The hydrogen ammonium salts of the inactive and the active acids both crystallise well, but are easily distinguished from each other. When a solution of the former is sufficiently evaporated, the salt crystallises in bundles of long, radiating needles, which extend through the whole mother liquor; a solution of the latter, especially when left to evaporate spontaneously, deposits isolated, transparent, well-formed prisms of considerable size, sometimes a centimetre in length. A specimen of the inactive salt was prepared by neutralising one-half of a solution of inactive ethoxysuccinic acid with ammonia, and then adding to this the other half. The crystals obtained by evaporation, having been rapidly dried in folds of filter paper, were submitted to analysis with the following results:—

- I. 0.2527 gram of substance gave 0.3524 gram CO_2 and 0.1695 gram H_2O .
 II. 0.2801 gram of substance gave 0.3921 gram CO_2 and 0.1906 gram H_2O .
 III. 0.3101 gram of substance gave 20.2 c.c. N at 16.5° and 759 mm. bar.
 IV. 0.3514 gram of substance gave 23.2 c.c. N at 14.5° and 753.5 mm. bar.

	Calculated for $\text{C}_6\text{H}_{13}\text{O}_5\text{N}_3\frac{1}{2}\text{H}_2\text{O}$.	Found.			
		I.	II.	III.	IV.
C.....	38.30	38.03	38.18	—	—
H.....	7.45	7.45	7.56	—	—
N.....	7.45	—	—	7.69	7.79
O.....	46.80	—	—	—	—
	<hr/> 100.00				

The active salt was procured as described by evaporating the solution resulting from the growth of the mould. The crystals were picked out from a little inactive salt which had also crystallised, and were recrystallised from water. In this way, 3 grams of the substance were obtained from the fermentation experiment quoted as No. 3. Analysis yielded the following results:—

- I. 0.2681 gram of substance gave 0.3564 gram CO_2 and 0.1862 gram H_2O .
 II. 0.2627 gram of substance gave 0.3493 gram CO_2 and 0.1827 gram H_2O .
 III. 0.3494 gram of substance gave 21.3 c.c. N at 15.5° and 758 mm. bar.

	Calculated for $\text{C}_6\text{H}_{13}\text{O}_5\text{N}_3\frac{1}{2}\text{H}_2\text{O}$.	Found.		
		I.	II.	III.
C.....	36.55	36.26	36.26	—
H.....	7.61	7.72	7.73	—
N.....	7.11	—	—	7.21
O.....	48.73	—	—	—
	<hr/> 100.00			

The inactive and active salts, therefore, differ in respect of their water of crystallisation, the former crystallising with $\frac{1}{2}$ mol. H_2O , the latter 1 mol. H_2O .

Determinations of the specific rotation of solutions of the salt, of varying concentration, gave the following results:—

$$\text{I. } \alpha[15^\circ] = +4.66^\circ; l = 200 \text{ mm.}; p = 7.9629; d 15^\circ/4^\circ = 1.0214; \text{ hence } [\alpha]_D = +\frac{100 \times 4.66}{2 \times 7.9629 \times 1.0214} = +28.65^\circ.$$

$$\text{II. } \alpha[16^\circ] = +2.67^\circ; l = 200 \text{ mm.}; p = 4.5368; d 16^\circ/4^\circ = 1.0119; \text{ hence } [\alpha]_D = +\frac{100 \times 2.67}{2 \times 4.5368 \times 1.0119} = +29.08^\circ.$$

$$\text{III. } \alpha[17^\circ] = +1.52^\circ; l = 200 \text{ mm.}; p = 2.5626; d 17^\circ/4^\circ = 1.0061; \text{ hence } [\alpha]_D = +\frac{100 \times 1.52}{2 \times 2.5626 \times 1.0061} = +29.48^\circ.$$

Determinations I and II were made with the pure salt of which analyses are given, III with a specimen similarly prepared from the product of another fermentation experiment. The results show that, within the limits of the conditions of our experiments, the specific rotation increases slightly with dilution. The results are calculated on the hydrated salt.

Calcium Dextro-ethoxysuccinate.—This was procured from the hydrogen ammonium salt, as already described. Like the inactive isomeride, it is more soluble in cold than in hot water, and is deposited anhydrous when a cold saturated solution is heated; it is, however, more distinctly crystalline than the inactive salt, being deposited from its solutions in minute needles, whilst the latter separates in a scaly or granular form.

An estimation of calcium in the active salt gave the following result:—

0.5035 gram of the substance, dried at 100° , gave 0.2515 gram CaCO_3 .

	Calculated for $\text{C}_6\text{H}_8\text{O}_5\text{Ca}$.	Found.
Ca.....	20.00 per cent.	19.98 per cent.

The following estimations of solubility show that the active salt is about seven times as soluble as the inactive. The solutions were made by keeping the salts in constant agitation with water for 12 hours at 15° .

25.5944 grams of the solution of the active calcium ethoxysuccinate gave, on evaporation, 1.0188 grams of dry salt, whilst 25.1110 grams of a solution of the inactive compound left 0.1576 gram of dry salt; the solubilities are, therefore—

Inactive salt.....	0.63 : 100
Active salt.....	4.15 : 100

The active salt showed the following specific rotation, the con-

centration, c , being found by evaporating 100 c.c. of the solution and weighing the dried residue:—

I. $\alpha[15^\circ] = +0.51^\circ$; $l = 200$ mm.; $c = 3.0390$; hence

$$[\alpha]_D = +\frac{100 \times 0.51^\circ}{2 \times 3.0390} = +8.39^\circ.$$

II. $\alpha[15^\circ] = +0.41^\circ$; $l = 200$ mm.; $c = 1.7916$; hence

$$[\alpha]_D = \frac{0.41 \times 100}{2 \times 1.7916} = +11.44^\circ.$$

The specific rotation, therefore, increases with diminishing concentration.

Dextro-ethoxysuccinic acid.—The acid was procured from the calcium salt, made for the most part from the uncrystallisable portion of the solutions resulting from the fermentations, as described above. The ethereal solution when evaporated yielded a syrup which, on standing in a vacuum, solidified to a mass of hard, transparent prisms, resembling the inactive acid in general appearance. A combustion of the substance gave the results which follow:—

0.2516 gram of the acid, dried in a vacuum, gave 0.4088 gram CO_2 and 0.1412 gram H_2O .

	Calculated for $\text{C}_6\text{H}_{10}\text{O}_5$.	Found.
C.....	44.44	44.31
H.....	6.17	6.24
O.....	49.39	—
	<hr/> 100.00	

Our preparations of the acid did not melt sharply, but it evidently melts at a lower temperature than the inactive compound. The melting points observed were, for the active acid, $76-80^\circ$; for the inactive, 86° .

Estimations of the specific rotation gave the results which follow:—

I. $\alpha[17^\circ] = +7.4^\circ$; $l = 200$ mm.; $p = 10.8427$; $d\ 17^\circ/4^\circ =$

$$1.0283; \text{ hence } [\alpha]_D = +\frac{100 \times 7.4^\circ}{2 \times 10.8427 \times 1.0283} = +33.19^\circ.$$

II. $\alpha[17^\circ] = +7.35^\circ$; $l = 200$ mm.; $p = 10.8702$; $d\ 17^\circ/4^\circ =$

$$1.0287; \text{ hence } [\alpha]_D = +\frac{100 \times 7.35^\circ}{2 \times 10.8702 \times 1.0287} = +32.86^\circ.$$

III. $\alpha[19^\circ] = +3.62^\circ$; $l = 200$ mm.; $p = 5.4920$; $d\ 19^\circ/4^\circ =$

$$1.0131; \text{ hence } [\alpha]_D = +\frac{100 \times 3.62^\circ}{2 \times 5.4920 \times 1.0131} = +32.54^\circ.$$

II and III, for which the same preparation was used, show that the specific rotation varies but little with a change of concentration within the limits of our experiments.

The purity of the acid was proved by converting it into the hydrogen ammonium salt, and taking its specific rotation:—

$$\alpha[17.5^\circ] = +4.69^\circ; l = 200 \text{ mm.}; p = 8.0053; d \ 17.5^\circ/4^\circ = 1.0206; \text{ hence } [\alpha]_D = +\frac{100 \times 4.69^\circ}{2 \times 8.0053 \times 1.0206} = +28.72^\circ.$$

The specific rotation of the pure hydrogen ammonium salt already given was, for similar concentration, $+28.65^\circ$.

Barium Dextro-ethoxysuccinate.—This salt was made by heating a solution of the hydrogen ammonium salt with barium hydrate, and also directly from the acid. The active and inactive salts both dissolve readily in water, but the former is evidently the more soluble of the two. The inactive salt is deposited as a fine crystalline powder of silky lustre on evaporating its solution; the active salt under similar conditions yields a syrup which solidifies on further drying. It still retains water at 100° , and becomes anhydrous only at about 160° .

- I. 1.0132 gram of the salt, dried at 155° , gave 0.6660 gram BaCO_3 .
 II. 0.5014 gram of the salt, dried at 160° , gave 0.3307 gram BaCO_3 .

	Calculated for $\text{C}_6\text{H}_9\text{O}_5\text{Ba}$.	Found.	
		I.	II.
Ba.....	46.13	45.71	45.87 per cent.

The following observations show that the salt is dextrogyrate in dilute solution, and that the rotation decreases with increasing concentration, and finally becomes negative:—

- I. $\alpha = +0.58^\circ$; $l = 200 \text{ mm.}$; $c = 4.5608$; hence

$$[\alpha]_D = +\frac{100 \times 0.58}{2 \times 4.5608} = +6.37^\circ$$

- II. $\alpha = +0.53^\circ$; $l = 200 \text{ mm.}$; $c = 10.7696$; hence

$$[\alpha]_D = +\frac{100 \times 0.53}{2 \times 10.7696} = +2.46^\circ$$

- III. $\alpha[19^\circ] = -2.19^\circ$; $l = 200 \text{ mm.}$; $p = 21.4772$; $d \ 19^\circ/4^\circ =$

$$1.1678; \text{ hence } [\alpha]_D = -\frac{100 \times 2.19}{2 \times 21.4772 \times 1.1678} = -4.37^\circ.$$

The concentration was found by estimating the barium in aliquot portions of the solutions.

Hydrogen Potassium Dextro-ethoxysuccinate.—This salt was made directly from the acid. It is easily soluble in water, and crystallises from the syrupy mother liquor in transparent prisms containing 1 mol. H_2O , which is lost only partly at 100° , entirely at 120° . The salt undergoes no further change when heated to 140° , but melts and begins to decompose about 160° .

Estimations of water of crystallisation and of potassium gave the following result :—

0.5266 gram of the salt, dried in folds of filter paper, lost, at 120° ,
0.0441 gram, and gave 0.2121 gram K_2SO_4 .

	Calculated for $\text{C}_6\text{H}_9\text{O}_5\text{K}_2\text{H}_2\text{O}$.	Found.
H_2O	8.25	8.37
K	17.93	18.08

The salt gave the following specific rotation in dilute solution :—

$\alpha[19^\circ] = +2.08^\circ$; $l = 200$ mm.; $p = 3.8717$; $d\ 19^\circ/4^\circ = 1.0142$;

$$\text{hence } [\alpha]_D = \frac{100 \times 2.08}{2 \times 3.8717 \times 1.0142} = +26.49^\circ$$

Normal Ammonium Dextro-ethoxysuccinate.—To find the specific rotation of this salt, a solution of known strength was procured by adding the calculated quantity of ammonia solution to a weighed portion of the hydrogen ammonium salt.

I. $\alpha[14.5^\circ] = +1.91^\circ$; $l = 200$ mm.; $c = 5.2210$; hence

$$[\alpha]_D = \frac{1.91 \times 100}{2 \times 5.2210} = +18.29^\circ$$

II. $\alpha[12^\circ] = +0.56^\circ$; $l = 200$ mm.; $c = 1.479$; hence

$$[\alpha]_D = \frac{0.56 \times 100}{2 \times 1.479} = +18.93^\circ$$

The solution II was too dilute to give an accurate result, but the experiment suffices to show that the specific rotation does not change very much within the range of concentration indicated.

Action of Alkaloids.

Methoxysuccinic acid having been resolved into its active components by means of the crystalline cinchonine salt, we thought that the same method would probably yield similar results with the ethoxy-acid. This proved, however, not to be the case. An aqueous solution of the acid cinchonine salt would not crystallise, but became milky on slow evaporation, and finally deposited an amorphous solid.

A solution of the normal salt yielded a small quantity of acicular crystals, but when decomposed with ammonia, the solution gave only a slight dextro-rotation, due, probably, to the presence of traces of the alkaloid.

Experiments made with the salts of cinchonidine and quinine were equally unsuccessful. The cinchonidine salt refused to crystallise, and, although a crystalline quinine salt, melting at about 135° , was obtained from a dilute aqueous solution, the ammonium ethoxysuccinate from it was inactive.

We found, however, that the desired result could be attained by means of the hydrogen cinchonidine salt of dextro-ethoxysuccinic acid, as it is less soluble in water than that of the corresponding lævo-acid. Having only a small quantity of ethoxysuccinic acid at our disposal, we were unable to make the experiments on a scale large enough to obtain the active components in the pure state, but we succeeded in procuring the dextro- and lævo-gyrate hydrogen ammonium salts, which crystallised exactly like the dextrogyrate salt already described, and showed a specific rotation approximating in amount to that of the latter.

24.5 grams of ethoxysuccinic acid were dissolved in 250 c.c. of water and a molecular proportion of cinchonidine was dissolved in the hot solution. The thick mass of feathery crystals, which was deposited on cooling, was collected and recrystallised from water. The recrystallised salt, weighing 21.5 grams, after being dried at 100° , was dissolved in water and freed from cinchonidine, as far as possible, by repeated treatment with ammonia. As the solution of the ammonium salt could not be made to crystallise, it was boiled with milk of lime until ammonia ceased to be evolved, and evaporated to dryness. The more soluble part of the residue was taken up with a large quantity of cold water, and treated with carbon dioxide; the solution was again evaporated to dryness, and the residue, after being treated with alcoholic chloroform to remove traces of the alkaloid, was shaken with cold water, so as to dissolve the active and leave the less soluble inactive calcium salt. The solution, which contained 2.2564 grams salt in 100 c.c., gave a rotation of $+0.25^{\circ}$ in a 200 mm. tube. On decomposing the calcium salt with rather less than the calculated quantity of sulphuric acid, some fumaric acid was found to be present, the origin of which is unexplained. This was separated as completely as possible by evaporating the liquid to a small bulk, and filtering it after it had stood some days. The solution of ethoxysuccinic acid, obtained in this manner, gave a rotation of $+4^{\circ}$, when examined in a 200 mm. tube, and yielded a hydrogen ammonium salt which crystallised exactly like the corresponding salt obtained by means of *Penicillium*. The crystals were dried in folds of filter-paper,

and dissolved in water for a determination of the specific rotation, the result being as follows :—

$$\alpha[16.5^\circ] = +2.42^\circ; l = 200 \text{ mm.}; p = 4.4641; d 16.5^\circ/4^\circ = 1.0114; \text{ hence } [\alpha]_D = +\frac{100 \times 2.42}{2 \times 4.4641 \times 1.0114} = +26.80^\circ.$$

The specific rotation of the purest specimen of the salt obtained by means of *Penicillium*, for similar concentration, was $+29.08^\circ$.

The mother liquors containing the more soluble portion of the cinchonidine salt, having been treated in the same way as the crop of crystals, gave a lævogyrate calcium salt, from which a lævogyrate acid was obtained, showing a rotation of -1.83° in a 200 mm. tube. The quantity of lævo-calcium salt obtained was less than that of the dextro-, hence the lower rotation of the solution of the lævogyrate acid. The crystallised hydrogen ammonium salt, into which the acid was converted, gave the following results when examined with the polarimeter :—

$$\alpha[13^\circ] = -1.32^\circ; l = 200 \text{ mm.}; p = 2.5175; d 13^\circ/4^\circ = 1.0064; \text{ hence } [\alpha]_D = -\frac{100 \times 1.32^\circ}{2 \times 2.5175 \times 1.0064} = -26.05^\circ.$$

It is probable that a more complete separation of the active acids might be made with the aid of strychnine.

General Considerations.

For purposes of comparison we append a list of the specific rotations of dextromethoxysuccinic and dextro-ethoxysuccinic acids and their salts (p. 239). We omit, as unnecessary, the specific rotations found for lævomethoxysuccinic acid and its salts. Two determinations of the specific rotation of calcium lævomethoxysuccinate, however, are given in the table, in order to show the effect of dilution on the rotation, as a similar experiment was not made with the oppositely active isomeride. In cases where the specific gravity of the solutions and their percentage composition were found, the concentration c has been calculated from these data for the sake of uniformity. The specific rotations were calculated on the anhydrous salts.

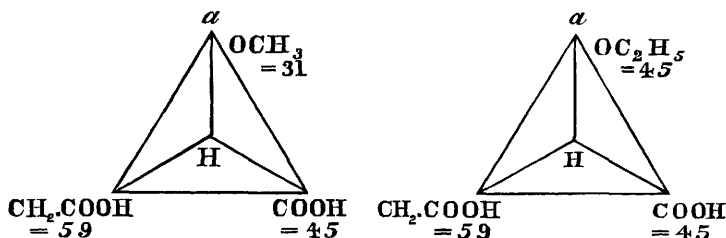
As might be expected, we find a close parallelism between the relations of active ethoxysuccinic acid and its salts and those of the corresponding methoxy-compounds. The remarks made at the conclusion of the preceding paper, with respect to the active methoxysuccinic acids, apply in general to dextro-ethoxysuccinic acid. The active acids in both cases have a lower melting point than the inactive; the rotatory power of the ammonium salts, and the potassium salts in dilute solution, is of the same sign as that of the free acids, but not so great, and the specific rotation does not alter much, with

Substance.	c.	$[\alpha]_D$.	Substance.	c.	$[\alpha]_D$.
d-Methoxysuccinic acid	11·2083	+ 33·30°	d-Ethoxysuccinic acid	11·1496	+ 33·19°
" "	5·5863	+ 33·04	" "	11·1822	+ 32·86
" "	—	—	" "	5·5640	+ 32·54
Hydrogen ammonium salt	6·0640	+ 25·86	Hydrogen ammonium salt	8·1333	+ 31·53
" "	—	—	" "	4·5908	+ 32·00
Normal "	5·7620	+ 12·32	" "	2·5782	+ 32·44
" "	2·8225	+ 12·22	Normal "	5·2210	+ 18·29
Hydrogen potassium "	8·1501	+ 23·26	" "	1·4790	+ 18·93
" "	4·0100	+ 23·46	Hydrogen potassium "	3·9267	+ 28·87
" "	4·0132	+ 23·45	" "	—	—
Normal "	12·1620	+ 9·54	" "	—	—
" "	5·0190	+ 9·36	" "	—	—
Calcium "	5·3080	+ 10·10	Calcium "	3·0390	+ 8·39
" salt (from laevo-acid)	5·4816	+ 10·03	" "	1·7916	+ 11·44
Barium "	2·2100	+ 4·30	" "	—	—
" "	26·1248	+ 14·27	Barium "	25·0811	+ 4·37
" "	12·4164	+ 7·36	" "	10·7696	+ 2·46
" "	5·7464	+ 2·21	" "	4·5608	+ 6·37
" "	1·1492	+ 3·16	" "	—	—

change of concentration, within the limits observed in our experiments. The potassium salts are less active than the ammonium salts, and the normal salts less active than the acid ones. The behaviour of the barium salt of both acids is in marked contrast to that of the other salts just alluded to; its specific rotation varies very much with change of concentration, the salts being lævogyrate or dextrogyrate, according to the strength of the solution, but the variation is in both cases of the same kind, that is to say, dilution has the effect of diminishing the lævo- and increasing the dextro-rotation. The calcium salts present a similar phenomenon. In saturated solution, calcium dextromethoxysuccinate is lævogyrate, calcium dextro-ethoxysuccinate is dextrogyrate, but from the analogy of the barium salts, it was to be expected that dilution would diminish the activity of the former and increase that of the latter, and this was found to be the case.

As Guye has distinctly pointed out, it is hazardous to draw conclusions regarding the relations of optical activity to the nature of the radicles which are united to the asymmetric carbon atom from observations made on dilute solutions of acids and their salts, when the disturbing influences of dissociation or formation of complex hydrates are unknown. The two acids which we have investigated are, however, so closely allied in constitution and composition, that the effect of such influences will probably be nearly the same on both of them, and we venture, therefore, to point out the bearing of our observations on the subject alluded to.

The dextrogyrate methoxy- and ethoxy-acids, which we have described, have a comparatively large and nearly equal specific rotation, amounting to about $+33^\circ$ in a 5 to 10 per cent. solution. As it is very improbable that the simple substitution of a methyl for an ethyl group could have the effect of converting a dextrogyrate activity of 33° into a lævogyrate activity of about the same amount; the two dextrogyrate acids have doubtless the same configuration, as indicated in the following tetrahedral diagrams:—



The numbers found for the specific rotations of the acids would show that methoxysuccinic acid has a slightly greater activity than its homologue. We do not attach any importance, however, to this

slight difference, as it is within the limits of error of our experiments, so it may be said that the substitution of OC_2H_5 for OCH_3 does not produce much effect on the activity of the free acid, although it is very considerable in the case of the corresponding salts, the ethoxysuccinates being in every instance more dextrorotatory or less lævorotatory than the corresponding methoxysuccinates. The difference is most strongly marked in the calcium salts, saturated solutions of which give rotations of opposite sign; and in the barium salts, to which the same remark applies for solutions having a concentration of between 5 and 10 per cent.

These differences are not such as Guye's theory (*Ann. Chim. Phys.* [6], 25, 145) would lead us to expect. According to this theory, the influence on optical activity of the radicles united to an asymmetric carbon atom depends chiefly on their mass, and only in a subordinate degree on the distances of their centres of gravity from the asymmetric carbon atom. By increasing the mass of the radicle at the angle α (see figure), as by the substitution of OC_2H_5 for OCH_3 , its mass approximates more to that of the radicle COOH ; the dissymmetry of the molecule, and consequently the optical activity of the compound should be diminished. The substitution in question, however, so far as the evidence of the alkyloxysuccinates goes, produces in most cases an opposite effect. It may be remarked that the two radicles COOH and OC_2H_5 , being equal in mass, free ethoxysuccinic acid is an example, like some others discussed by Guye, of a compound which, according to his theory, must owe its activity to the radicles being situated at different distances from the asymmetric carbon atom or at the angles of an irregular tetrahedron.

Crum Brown, in the paper already alluded to (*Proc. Roy. Soc. Edin.*, 17, 181), does not make any assumption regarding the nature of the special function of the radicles, differences of which determine the amount of the optical activity of a compound, except that in general this unknown function, which for convenience he calls κ , is increased by addition to the radicle. From a consideration of the changes of sign of rotation produced by substitution in tartaric acid, lactic acid, and amylic alcohol, he concludes that the κ of C_2H_5 is greater than that of CH_3 , and that of CH_3 , in spite of the smaller mass of the radicle, greater than that of COOH . If these conclusions and the general assumption be correct, then the κ of OCH_3 and of OC_2H_5 should be greater than that of COOH , and this accords with our observations, for the methoxysuccinates and ethoxysuccinates are less active than the free acids. It would appear that the κ of OCH_3 is greater than that of COOM , except when M is barium or calcium, in which case, the specific rotation is reversed. Further, the κ of OC_2H_5 should be still greater than that of COOM , and this is perhaps confirmed by the

observation that the dextro-ethoxysuccinates are more dextrogyrate than the corresponding methoxysuccinates. The effect of increasing the radicle at *a* is particularly noticeable in the barium and calcium salts. The pure barium salts of the dextro-acids are evidently both really lævogyrate, but the ethoxysuccinate is much less so than the methoxysuccinate. The effect of replacing the hydrogen of the acid by metal is partly neutralised by the increase of the radicle at *a*, and the barium salts of higher alkyloxysuccinic acids will no doubt be dextrogyrate even in very concentrated solutions.

Comparing the alkyloxysuccinic acids with malic acid, we find that in dilute solution they show a general parallelism as regards the relative activity of the salts of different metallic radicles; the ammonium salt is more active than the potassium salt, whilst the barium salt in each case exhibits the same rapid change of activity with change of concentration. It is striking to observe what a great increase of activity attends the substitution of alkyl groups for the hydrogen of the alcoholic hydroxyl. The specific rotation of ordinary malic acid in a 10 per cent. solution is only -2.1° , whilst that of dextro-ethoxysuccinic acid under similar conditions is about $+33^\circ$. It is impossible to say whether the dextroalkyloxysuccinic acids are derivatives of ordinary, so-called lævo-, malic acid, or of its oppositely active isomeride. With the view of deciding this point, we have attempted, but hitherto without success, to prepare the alkyloxysuccinic acids direct from malic acid, by treating the ethereal salts of the latter with sodium, and heating the resulting sodium compound with alkyl iodide. We purpose repeating these experiments. Although meantime it is impossible to say with certainty whether the substitution of alkyl groups for the hydrogen of the alcoholic hydroxyl of malic acid has the effect of reversing the sign of rotation or not, it is difficult in any case to account, according to Guye's theory, for the high rotatory power of the alkyloxysuccinic acids.

If it be assumed that the change of activity produced by the substitution of OCH_3 for OH is of the same kind as that produced by the substitution of OC_2H_5 for OCH_3 , that is to say, an increase of dextro- or decrease of lævo-rotation, an inspection of the specific rotations of the three barium salts points to the conclusion that the dextroalkyloxysuccinic acids are derivatives not of ordinary but of dextromalic acid, for it is the barium salt of dextromalic acid which is more lævogyrate than the barium alkyloxysuccinates.

In order to bring the alkyloxysuccinic acids strictly within the scope of Guye's theory, we intend to prepare and determine the specific rotations of some of the ethereal salts of these acids.

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