LXIII.—*Enantiomorphism.*

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ENANTIOMORPHOUS substances are naturally divisible into two classes:
(*a*) consisting of those compounds in which the enantiomorphism is
determined by the structure of the chemical molecule, and (*b*) con-
sisting of those crystalline substances of which the enantiomorphism
is not inherent in the molecules, but is determined solely by their
arrangement.

The first class (*a*) consists of all compounds containing what is usually called an asymmetric carbon atom. Such substances not only condition circular polarisation in the amorphous or liquid state, this being one mode of expression of the enantiomorphism, but as we have previously shown (" Racemism and Pseudoracemism," Trans., 1897, 71, 989), they can only crystallise in one or other of the enantiomorphous crystalline systems ; the latter form is merely a more precise statement of Pasteur's law, the truth of which has been questioned by Walden (*Ber.*, 1896, 29, 1692), but which, as we pointed out, stands or falls with the present theory of crystal structure. Furthermore, it can be shown that, in the crystallisation of a substance consisting of enantiomorphous chemical molecules, the resulting crystalline structure can only be of the one hand ; that is to say, the crystals of a substance which is dextrorotatory in the amorphous state must be either right- or left-handedly enantiomorphous, but cannot be partly the one and partly the other.

To the second class (*b*) of enantiomorphous substances, namely, those in which the enantiomorphism is purely one of arrangement of the chemical molecules in the crystalline structure, belong compounds such as the cubic tetartohedral sodium chlorate and quartz ; such substances, of course, are not optically active in the amorphous or liquid state, but they crystallise in enantiomorphous systems, and their crystals sometimes rotate the plane of polarisation, this being again one mode of expression of the enantiomorphism.

Now the crystallisation of a substance such as sodium chlorate, which does not consist of enantiomorphous molecules, is obviously a different process from that of the crystallisation of an optically active substance ; whereas the latter must invariably give crystals which are either right- or left-handedly enantiomorphous, there is no *à priori* reason why the former should give crystals of the one hand in preference to those of the other. The average product of a large number of crystallisations of sodium chlorate from water should consist of 50 per cent. of crystals of each hand, because there is operative an equal tendency to deposit dextro- and lævo-sodium chlorates. The only quantitative data bearing on this point with which we are acquainted are those obtained by Landolt (*Ber.*, 1896, 29, 2404), who has determined the specific rotation of the crystalline powder of sodium chlorate, deposited from a pure aqueous solution, by examining it polarimetrically whilst suspended in a liquid of approximately the same refractive index ; Landolt showed that, taken collectively, the sodium chlorate crystals were inactive, although each individual was either right- or left-handed. Gernez (*Compt. rend.*, 1868, 66, 833) also states that on crystallising an aqueous solution of sodium chlorate, it yields " des

poids à peu près égaux de cristaux des deux espèces " ; no statistics of weight or number of crystals, however, are given.

The question of the proportion in which enantiomorphously related crystals are deposited in the case of such substances is one of prime importance for various reasons : firstly, because observations with which we deal below are on record to the effect that the proportion is not that of unity ; and, secondly, because it is necessary for our present purpose that the proportion should be accurately determined, since we show in this paper that the proportion can be varied by bringing to bear a suitable enantiomorphous or directive influence during crystallisation.   We have, therefore, examined the crystals of sodium chlorate deposited from pure aqueous solutions in order to determine whether the ratio of dextro- to lævo-sodium chlorate is that of unity ; since, however, Landolt's method was not applicable to the development of the work on the lines we proposed, we had to adopt a somewhat different mode of procedure.   Instead of showing, as Landolt did, that the weights of the two enantiomorphously related forms of sodium chlorate deposited are equal, we show that the crystals of each kind deposited are, on the average, the same in number.

The method used was as follows.   About 200 c.c. of a saturated aqueous solution of sodium chlorate was put into a shallow glass crystallising dish of about 6 inches in diameter, and allowed to evaporate spontaneously ; great care was taken to avoid fluctuations of temperature which caused the deposition of small crystals unsuitable for subsequent examination, and to prevent dust from getting into the solution, as this seemed to cause the crystals to be deposited in aggregates.   In properly conducted experiments, each crystal developed apart from its fellows as a right-angled prism ; when the crop of crystals had grown until most were some 5 mm. or so in one direction, all were removed from the liquid, the faulty ones rejected without further examination, and the sign of the circular polarisation of each remaining crystal determined by examination in a polarising microscope under a 1-inch objective. This was done simply by rotating the analyser and noting in which direction extinction occurred ; if the analyser had to be rotated to the right to give extinction, the crystal under examination was dextrorotatory, and *vice versâ*.   All the crystals deposited from the solution, with the exception of at most 2 or 3 per cent., which were found unsuitable owing to opacity or aggregation, were thus examined ; and, in order to eliminate personal bias, we have included in our tables every observation of circular polarisation which was made, no crystal being rejected after its sign was known ; this is a very necessary precaution, because we are concerned with an average result.

The results of forty-six separate crystallisations, all we have made, are stated in Table I; it will be seen that in only two cases, namely,

TABLE I.—*Deposition of Sodium Chlorate from a Pure Aqueous Solution.*

1 Number.	2 Dextro-crystals. d.	3 Lævo-crystals. l.	4 Total. $d + l$	5 Percentage of dextro-crystals.	6 Percentage of lævo-crystals.
1	32	37	69	46·38	53·62
2	38	31	69	55·07	44·93
3	64	69	133	48·12	51·88
4	23	15	38	60·53	39·47
5	39	47	86	45·35	54·65
6	19	15	34	55·88	44·12
7	42	35	77	54·55	45·45
8	24	68	92	26·09	73·91
9	35	45	80	43·75	56·25
10	20	33	53	37·74	62·26
11	28	21	49	57·14	42·86
12	14	12	26	53·85	46·15
13	39	15	54	72·22	27·78
14	7	22	29	24·14	75·86
15	14	28	42	33·33	66·67
16	37	49	86	43·02	56·98
17	29	12	41	70·73	29·27
18	48	32	80	60·00	40·00
19	29	33	62	46·77	53·23
20	42	40	82	51·22	48·78
21	37	42	79	46·84	53·16
22	24	38	62	38·71	61·29
23	61	44	105	58·10	41·90
24	27	20	47	57·45	42·55
25	51	58	109	46·79	53·21
26	42	42	84	50·00	50·00
27	28	17	45	62·22	37·78
28	37	40	77	48·05	51·95
29	24	30	54	44·44	55·56
30	15	11	26	57·69	42·31
31	25	21	46	54·35	45·65
32	37	37	74	50·00	50·00
33	36	31	67	53·73	46·27
34	65	61	126	51·59	48·41
35	27	22	49	55·10	44·90
36	49	44	93	52·69	47·31
37	41	49	90	45·56	54·44
38	30	34	64	46·88	53·12
39	47	58	105	44·76	55·24
40	31	39	70	44·29	55·71
41	31	37	68	45·59	54·41
42	39	26	65	60·00	40·00
43	41	12	53	77·36	22·64
44	24	16	40	60·00	40·00
45	47	42	89	52·81	47·19
46	32	36	68	47·06	52·94

$$U_d = 50·83. \qquad W_d = 50·08. \qquad M_d = 50·08 \pm 0·11.$$

those of experiments numbered 26 and 32 respectively, were equal numbers of dextro- and lævo-rotatory crystals deposited, whilst in all other cases either more or less than 50 per cent. of the crystals obtained were dextro-rotatory. The experiments are numbered in the order in which they were performed, and in order further to eliminate personal bias, no calculations whatever were made until we considered that a sufficient number of experiments had been completed to ensure an accurate average; in fact, as little attention as possible was paid to the laboratory lists of data until the observations were concluded.

The method by which the means are calculated needs some comment. If d and l be the numbers of dextro- and lævo-rotatory crystals respectively deposited from any solution, the crop consists of $100d/(d+l)$ per cent. of dextro-, and $100l/(d+l)$ per cent. of lævorotatory individuals; these values are stated in columns 5 and 6 of Table I. An experiment, however, in which only 10 crystals are obtained is of less weight than one in which 100 crystals are obtained, the weight of an experiment being directly proportional to $(d+l)$. Consequently the mean value, $U_d = \dfrac{100}{n} \sum \left(\dfrac{d}{d+l}\right)$, where n is the number of experiments cencerned, is only the unweighted mean percentage of dextro-crystals deposited. The weighted mean percentage of dextro-crystals is obviously $W_d = \dfrac{100\Sigma d}{\Sigma(d+l)}$; the importance of the distinction thus introduced is evident from the fact that in this series of experiments $U_d = 50\cdot83$ whilst $W_d = 50\cdot08$. The weighted mean percentage of dextro-crystals is much more nearly 50 than is the unweighted mean.

Although the numbers given in Table I yield a weighted average result differing by only $0\cdot08$ per cent. from what was expected from theory, it is still necessary to calculate the probable mean squared error of the mean. Let the difference between the weighted mean and one individual percentage of dextro-rotatory crystals be $\Delta = \dfrac{100d}{d+l} - W_d$, then since each observation has the weight $(d+l)$ the probable error of the weighted mean is

$$r = 0\cdot6745 \sqrt{\frac{\Sigma\{(d+l)\Delta^2\}}{\{\Sigma(d+l) - 1\}\Sigma(d+l)}} = 0\cdot11,$$

and the final value M_d for the weighted mean percentage of dextrorotatory crystals is $M_d = 50\cdot08 \pm 0\cdot11$, and lies between $49\cdot97$ and $50\cdot19$.

We conclude, therefore, that on allowing sodium chlorate to crystallise spontaneously from pure aqueous solutions, on the average, equal numbers of the enantiomorphously related crystals are deposited.

This result is, as we have pointed out, indicated by theory and there-

fore supports the theory. But several substances which are not optically active in the amorphous state have been described by certain authors as separating from solution in unequal numbers of two enantiomorphously related crystalline forms. Thus Eakles (*Zeit. Kryst.*, 1896, **26**, 562) states that on crystallising sodium periodate from aqueous solutions containing sodium nitrate, more lævo- than dextro-rotatory crystals are deposited. Further, Wyrouboff (*Bull. soc. min. franç.*, 1896, **19**, 219) states that he has only obtained dextro-rotatory crystals of potassium silicotungstate, $K_4SiW_{12}O_{40},18H_2O$. Sodium periodate and potassium silicotungstate are, however, completely analogous to sodium chlorate in that their enantiomorphism is one of molecular, not of atomic, arrangement, and in face of the results now brought forward the above statements by Eakles and Wyrouboff can hardly be accepted as conclusive until quantitative evidence is forthcoming; further, on examining Table I it will be seen that solutions of sodium chlorate sometimes yield four or five consecutive crops of crystals in which one enantiomorphous form predominates, but yet, on the average, equal numbers of crystals of each hand are obtained. Some phenomenon such as this may have led to the results obtained by Eakles and by Wyrouboff.

A solution of an optically inactive substance, such as sodium chlorate, which crystallises in an enantiomorphous system deposits on the average equal numbers of crystals of the enantiomorphously related kinds, because no directive influence is brought to bear which tends to cause selective deposition of one or other enantiomorph. The conditions might, however, be quite different if in the crystallising sodium chlorate solution there were dissolved an enantiomorphous substance containing an asymmetric carbon atom such as dextroglucose; it could not be stated on *à priori* grounds that there would be the same tendency for dextro- as for lævo-sodium chlorate to crystallise from a solution containing dextroglucose, and dextro- and lævo-sodium chlorates might have different solubilities in a dextroglucose solution. Although as an abstract principle the above statement appears sound, yet no opinion can be formed as to how great the directive tendency of the dissolved optically active substance would be, and it might well be so slight as to be practically inappreciable. No experiments bearing on this question are on record, and we have therefore examined the way in which several carbohydrates containing asymmetric carbon atoms affect the crystallisation of sodium chlorate, the result being that positive evidence of an influence exerted by the optically active substance in solution has been obtained.

Deposition of Sodium Chlorate from a Dextrose Solution.

A quantity of a nearly saturated aqueous solution of sodium chlorate was gently warmed with dextroglucose until the latter was wholly dissolved; the colourless solution which then contained 200 grams of dextrose per litre was filtered and placed in crystallising dishes of about 6 in. diameter. The liquid thus obtained showed no evidence of chemical change

TABLE II.—*Crystals of Sodium Chlorate deposited from a Solution containing* 200 *grams of Dextrose per Litre.*

Number.	Dextro-crystals. *d.*	Lævo-crystals. *l.*	Total. *d + l.*	Percentage of dextro-crystals.	Percentage of lævo-crystals.
1	32	71	103	31·07	68·93
2	47	89	136	34·56	65·44
3	44	107	151	29·14	70·86
4	24	51	75	32·00	68·00
5	37	70	107	34·58	65·42
6	19	27	46	41·30	58·70
7	39	91	130	30·00	70·00
8	42	46	88	47·73	52·27
9	28	64	92	30·43	69·57
10	31	66	97	31·96	68·04
11	29	79	108	26 85	73·15
12	36	104	140	25·71	74·29
13	17	38	55	30·91	69·09
14	42	96	138	30·43	69·57
15	9	21	30	30·00	70·00
16	25	63	88	28·41	71·59
17	39	84	123	31·71	68·29
18	21	43	64	32·81	67·19
19	26	61	87	29·89	70·11
20	30	79	109	27·52	72·48
21	37	65	102	36·27	63·73
22	23	51	74	31·08	68·92
23	40	76	116	34·48	65·52
24	49	113	162	30·25	69·75
25	15	24	39	38·46	61·54

$$U_d = 32 \cdot 30. \qquad W_d = 31 \cdot 75.$$

having occurred, and on cooling deposited no crystals; on allowing the rather syrupy solution to evaporate spontaneously in the air at constant temperature and in as complete absence of dust as possible, large, well-developed crystals of sodium chlorate began to separate after a week or so. These crystals were separated as before, being sorted into dextro- and lævo-crystals; the results are given in Table II. After examination, the crystals were dissolved in the minimum quantity of hot water, the solution mixed with the mother liquor, and, after filtra.

tion, the liquid was again put to crystallise. The same precautions to avoid personal bias were taken as in the preceding case.

The results quoted in this table show distinctly that an optically active enantiomorphous substance dissolved in a solution of a purely crystallographically enantiomorphous compound materially affects the proportion in which the enantiomorphously related crystals are deposited. More than twice as many lævo- as dextro-rotatory crystals of sodium chlorate are deposited from a sodium chlorate solution containing 20 per cent. of dextrose. It is further not easy to realise that this directive influence could be attributed to chemical action ; the crystals deposited consist of sodium chlorate and the preponderance of the lævo-rotatory crystals apparently has a purely physical cause.

Deposition of Sodium Chlorate from Mannitol Solution.

It has been noted above that circular polarisation is only one mode of expression of enantiomorphism. It would not be expected, therefore, that the magnitude of the specific rotation of a dissolved substance should be directly connected with the influence which the latter substance exerts on the proportion in which enantiomorphously related crystals are deposited. The related factor is the enantiomorphism, which, in the case of dextrose, is an enantiomorphism of atomic arrangement, and in that of the sodium chlorate an enantiomorphism of molecular arrangement. In order to test the truth of this view, experiments were made with mannitol, which, although an enantiomorphous substance, is practically inactive in aqueous solution ; Müntz and Aubin (*Ann. chim. phys.*, [v], 10, 533) found it to be inactive in

TABLE III.—*Crystals of Sodium Chlorate deposited from a Solution containing 50 grams of Mannitol per Litre.*

Number.	Dextro-crystals. d.	Lævo-crystals. l.	Total. $d+l$	Percentage of dextro-crystals.	Percentage of lævo-crystals.
1	7	9	16	43·75	56·25
2	5	6	11	45·45	54·55
3	6	7	13	46·15	53·85
4	7	5	12	58·33	41·67
5	37	64	101	36·63	63·37
6	1	1	2	50·00	50·00
7	1	2	3	33·33	66·67
8	34	11	45	75·56	24·44
9	4	15	19	21·05	78·95
10	8	13	21	38·10	61·90
11	8	10	18	44·44	55·56

$U_d = 44·80.$ $W_d = 44·83.$

aqueous solution, and Bouchardat (*Compt. rend.*, 80, 120) assigns to it the specific rotation $[a]_D = -0.25°$, whilst dextroglucose has a high specific rotatory power greater than $[a]_D = 50°$.

Owing to the sparing solubility of mannitol, less of this carbohydrate was dissolved than in the case of dextrose. Each litre of saturated sodium chlorate solution had dissolved in it 50 grams of carefully purified mannitol; the solution was put to crystallise, and the crystals were examined as before, with the sole exception that we did not take

TABLE IV.—*Crystals of Sodium Chlorate deposited from a Solution containing* 60 *grams of Mannitol per Litre.*

Number.	Dextro-crystals. d.	Lævo-crystals. l.	Total. $d + l$	Percentage of dextro-crystals.	Percentage of lævo-crystals.
1	5	6	11	45·45	54·55
2	4	13	17	23·53	76·47
3	3	10	13	23·08	76·92
4	10	9	19	52·63	47·37
5	4	6	10	40·00	60·00
6	3	4	7	42·86	57·14
7	7	9	16	43·75	56·25
8	9	8	17	52·94	47·06
9	7	11	18	38·89	61·11
10	6	13	19	31·58	68·42
11	11	24	35	31·43	68·57
12	21	36	57	36·84	63·16
13	13	16	29	44·83	55·17
14	19	18	37	51·35	48·65
15	14	20	34	41·18	58·82
16	11	19	30	36·67	63·33
17	27	36	63	42·86	57·14
18	17	28	45	37·78	62·22
19	19	41	60	31·66	68·34
20	21	16	37	56·76	43·24
21	7	12	19	36·84	63·16
22	39	57	96	40·63	59·37
23	22	34	56	39·29	60·71
24	36	59	95	37·89	62·11
25	27	14	41	65·85	34·15
26	19	29	48	39·58	60·42
27	11	26	37	29·73	70·27
28	31	48	79	39·24	60·76
29	7	11	18	38·89	61·11
30	3	9	12	25·00	75·00
31	14	10	24	58·33	41·67
32	39	62	101	38·61	61·39
33	24	37	61	39·34	60·66
34	12	20	32	37·50	62·50
35	14	15	29	48·28	51·72
36	10	17	27	37·04	62·96
37	16	21	37	43·24	56·76

$U_d = 40.58.$ $W_d = 40.55.$

any special precautions to keep the liquid dust-free. The results are summarised in Table III.

The results show that, whilst the weight of the mannitol used was only one-fourth of the weight of dextroglucose used in the previous experiments, the deviation from equal proportions of dextro- and lævo-sodium chlorate deposited is about one-third as great with the mannitol as with the dextrose solutions. Weight for weight, then, in spite of its scarcely perceptible rotatory power in aqueous solution, mannitol would seem to exert at least as great a directive influence as dextrose in experiments of this kind.

Another series of experiments was made with a slightly stronger solution of mannitol, namely, one containing 60 grams of mannitol per litre of saturated sodium chlorate solution, and the results tabulated in Table IV will be seen to show a greater diminution in the number of dextro-sodium chlorate crystals deposited; care was taken in this case to keep the solutions dust-free and at uniform temperature. We do not lay much stress upon the percentage of carbohydrate present in the solution, as although we know the amount put into the solution, we do not know exactly what proportion was present during crystallisation after a certain amount of water had necessarily evaporated.

Although mannitol is nearly inactive in aqueous solution, yet it was just possible that the sodium chlorate might exert an influence similar to that of boric acid and increase the specific rotatory power very considerably. In order to gain information on this point, quantities of 2, 3, 4, and 6 grams of mannitol were dissolved and made up to 100 c.c. with saturated sodium chlorate solution, and examined polarimetrically; in no case could rotation be observed in 400 mm. tubes, showing that the rotation was less than 3 or 4 minutes. The specific rotatory power of mannitol in saturated sodium chlorate solution is thus of the same order as in aqueous solution; this may perhaps be considered as corroborative evidence of the absence of chemical action between the sodium chlorate and the carbohydrate.

Crystals of Sodium Chlorate deposited from Isodulcitol Solution.

A few experiments made with a saturated solution of sodium chlorate containing 50 grams of isodulcitol per litre indicated that such solutions deposit a greater number of crystals of dextro- than of lævo-sodium chlorate. The quantity of isodulcitol at our disposal was, however, small, and as we had already obtained ample experimental evidence that optically active substances in solution do exert a directive or enantiomorphous influence on the kind of crystal deposited, the experiments were not carried out in detail.

Crystals of Sodium Chlorate deposited from Solutions containing Dulcitol.

Until recently there has been some doubt as to whether dulcitol is, or is not, an enantiomorphous substance, but the work of Crossley (*Ber.*, 1892, **25**, 2564) and others has definitely shown that this carbo-hydrate is not enantiomorphous. It seemed of interest, however, to determine the proportion in which dextro- and lævo-sodium chlorate

TABLE V.—*Crystals of Sodium Chlorate deposited from Solutions containing* 20 *grams of Dulcitol per Litre.*

Number.	Dextro-crystals. d.	Lævo-crystals. l.	Total. $d+l$.	Percentage of dextro-crystals.	Percentage of lævo-crystals.
1	36	44	80	45·00	55·00
2	54	58	112	48·21	51·79
3	27	19	46	58·70	41·30
4	26	31	57	45·61	54·39
5	46	25	71	64·79	35·21
6	26	25	51	50·98	49·02
7	17	23	40	42·50	57·50
8	32	41	73	43·84	56·16
9	36	41	77	46·75	53·25
10	19	24	43	44·19	55·81
11	42	33	75	56·00	44·00
12	21	21	42	50·00	50·00
13	34	27	61	55·74	44·26
14	26	18	44	59·09	40·91
15	34	26	60	56·67	43·33
16	29	24	53	54·72	45·28

$U_d = 51·42.$ $W_d = 51·27.$

separate from solutions containing dulcitol, but owing to the sparing solubility of dulcitol in water or sodium chlorate solution, little positive evidence could be obtained. The saturated sodium chlorate solution contained 20 grams of dulcitol per litre, and the results, which are given in Table V, show that nearly equal numbers of dextro- and lævo-sodium chlorate crystals are deposited. It ought to be observed that we should not be justified in drawing the conclusion that a substance is not enantiomorphous from experiments of the kind described in the present paper ; we could, however, conclude with certainty that a com-pound was enantiomorphous if the value of W_d differed considerably from 50.

The results described in the preceding pages are summarised in Table VI, and allow of the deduction of the following conclusions.

1. On crystallising a substance which is not enantiomorphous in the

TABLE VI.—*Comparison of Results.*

Solution.	Number of		U_d.	W_d.
	Experi-ments.	Crystals.		
Pure NaClO$_3$ solution	46	3137	50·83	50·08
NaClO$_3$ sol. $+20$ per cent. dextrose	25	2460	32·30	31·75
,, $+5$,, mannitol......	11	261	44·80	44·83
,, $+6$,, ,, ...	37	1386	40·58	40·55
,, $+2$,, dulcitol	16	985	51·42	51·27

amorphous state, but is enantiomorphous in the crystalline state, under conditions such that no enantiomorphous influence is brought to bear, equal numbers of the enantiomorphously related crystals are on the average deposited.

2. On crystallising a substance which is not enantiomorphous in the amorphous state, but is enantiomorphous in the crystalline state, the average ratio of the numbers in which the enantiomorphously related crystals are deposited may be made to differ from unity by introducing into the crystallising solution a substance which is enantiomorphous in the amorphous state.

3. The results obtained by crystallising sodium chlorate from solutions containing mannitol indicate that the deflection of the ratio of dextro- to lævo-crystals of sodium chlorate deposited is not directly dependent on the specific rotatory power of the dissolved substance; in doubtful cases, it might be possible to prove that a substance is enantiomorphous in the amorphous state by examining crystals of sodium chlorate deposited from its aqueous solution.

4. The enantiomorphism of a chemical nature of one substance may influence the enantiomorphism of a purely physical or crystallographic nature of another substance.

Attention should be drawn to the analogy between the results now recorded and those which we have recently obtained by crystallising sodium ammonium dextro- and lævo-tartrates from solutions containing dextroglucose (Proc., 1898, 113). On crystallising an externally compensated mixture of the two tartrates from an aqueous solution containing dextrose, the first crop contains a large excess of sodium ammonium dextrotartrate; the dextrotartrate thus appears to be less soluble than its lævo-isomeride in dextrose solution, just as lævo sodium chlorate seems to be less soluble than its dextro-isomeride in dextrose solution. Further experiments respecting these points are in progress.

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