449. *The Walden Inversion. Part IV. Conversion of Bromosuccinic Acid into Malic Acid. Part V. Conversion of Aspartic Acid into Chloro- or Bromosuccinic Acid.*

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PART IV.

ACCORDING to the theory developed in Parts I—III of this work (J., 1928, 2447; 1929, 1282; 1930, 2017), during the changes leading to a Walden inversion, one of the four groups attached to the asymmetric carbon atom is removed, and the remainder of the molecule oscillates between the two possible extremes corresponding to the d- and the l-configuration; this continues until the replacing group secures its position in the molecule, so that the resulting configuration of any one molecule is determined by the phase at which this group enters. It follows that two types of Walden inversion are possible according to whether the optically active molecule (1) loses a group either spontaneously or by reaction with a different type of molecule which does not contain the entering atom or group, or (2) collides with a molecule containing the entering group. Reasons were advanced for the view that inversions of type 1 give rise to both d- and l-forms in proportion depending upon the concentration, ionic strength, etc., whereas those of type 2 lead to only one of the two stereoisomerides, since at the moment of scission the entering group is always at the same distance from the carbon atom and therefore always enters at the same phase in the oscillation.

In Part III, this hypothesis was developed mathematically by the introduction of Maxwell's distribution law and Einstein's law of the displacements of molecules and ions in solution; an equation was thereby deduced for calculating n, i.e., that fraction of the reaction product which is stereologous * with the original asymmetric molecule. When applied to the reaction between potassium xanthogenate and potassium l-bromosuccinate, a reaction of type 1, the equation deduced gave values for n which were in good agreement with those found experimentally over a large range of concentration $(0.0005\text{—}8.95M)$.

The only other attempt to correlate concentration with the stereochemical form of the product is that due to Holmberg (*Arkiv Kemi, Min., Geol.*, 1916, **6**, No. 8) and applied to the same reaction. He supposed that two processes occur simultaneously, *viz.*, a bimolecular reaction, wherein only the d-form of xanthogenosuccinic acid is produced, and a unimolecular reaction, which gives only the l-form. Since increase of concentration produces a relatively greater increase in the first than in the second reaction, it should lead to increasingly pure d-acid, and conversely, decreasing concentration should give purer l-acid. These deductions are, however, refuted by the experiments described in Part III, which show that, with decreasing concentration, n passes through a minimum at *ca.* $0.004M$ (corresponding to 94% l-form) and then rises again, in accordance with the author's theory, which requires that $n = 0.5$ when the concentration approaches zero (Part III, p. 2020). Holmberg's later work (*Svensk Kem. Tidsskr.*, 1929, **41**, 71) shows that he has misunderstood the author's conceptions.
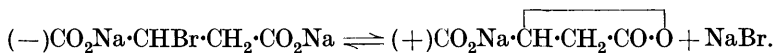
Walden (*Ber.*, 1899, **32**, 1833), by acting upon (—)halogenosuccinic acid with water or certain metallic bases, got (—)malic of varying rotatory power, whereas other oxides or hydroxides gave (+)malic acid, also of varying rotatory power. These results are often ascribed to structural differences, but since these appear to be inadequate to account for the phenomena, it was decided to reinvestigate the reaction, and the results afford an explanation of the differences, from which it appears that solubility played an important part in Walden's experiments.

The hydrolysis of halogenosuccinic acids involves several complications. The malic acid is accompanied by fumaric acid, and the separation of these acids without affecting the rotatory power of the former is by no means easy. Walden, and others, obtained the malic acid by repeated evaporation to dryness and extraction of the residue with acetone; by this method, fractionation of the acid into specimens

* By this term is meant "stereochemically analogous"; similarly, "astereologous" denotes stereochemical analogy with the optical antipode.

of different rotatory power cannot be avoided.   On the other hand, its extraction from aqueous solutions is difficult on account of its great solubility and the lack of solvents which will not also extract the other reaction products (see below) and the unchanged halogenosuccinic acid.

Moreover (Holmberg, *J. pr. Chem.*, 1913, **87**, 471; **88**, 553; Johansson, *Z. physikal. Chem.*, 1913, **81**, 573), the conversion of halogenosuccinic acid into malic acid takes place through the lactone of the latter :

$$(-)\text{CO}_2\text{Na·CHBr·CH}_2\text{·CO}_2\text{Na} \rightleftharpoons (+)\text{CO}_2\text{Na·}\overline{\text{CH·CH}_2\text{·CO·O}} + \text{NaBr}.$$

This process is unimolecular and reversible.   By continuously adding silver nitrate to a neutral solution of sodium *l*-bromosuccinate, Holmberg prevented the reverse reaction and obtained a solution containing chiefly the sodium salts of the lactonic acid and malic acid.   On standing, the former was hydrolysed, and a malic acid containing excess of (—)form was isolated.   If, on the contrary, bases were added in excess, either to the solution or to the lactone itself (isolated by extraction with ether), a malic acid containing excess of (+)form resulted.   Holmberg concluded that the reaction in alkaline solutions gives (+)malic acid, and in acid solutions (—)malic acid.

It will be seen from the following experiments that this view must be modified, but it is of great importance, in that the problem of the inversion in this case is reduced to that of the opposite effects of acids and of bases.

These two final problems can only be solved by studying the effect of concentration upon the reaction, so as to examine it from the author's point of view, and none of the published experiments are suitable for this purpose.

After fruitless attempts to isolate the malic acid from the reaction product by mild treatment (see p. 2932), a process was devised which avoided the necessity for such isolation.   A solution of the lactone of malic acid was prepared from (—)bromosuccinic acid, the lactone extracted with ether, and the extract divided into equal portions. For alkaline hydrolysis each portion was then extracted with an accurately measured volume of standard sodium hydroxide solution. The lactone is thereby rapidly hydrolysed even in 0·1N-alkali. Nitric acid exactly equivalent to the alkali used was added, and the free malic acid titrated.   After addition of 0·5 mol. of ammonium molybdate per mol. of malic acid, the rotatory power was measured. (In the presence of this salt, signs of rotation are reversed.)

In the experiments upon acid hydrolysis, portions of the ethereal extract of the lactone were added to accurately measured volumes

of standard nitric acid, and the ether evaporated at room temperature. (The acid hydrolysis takes considerably longer than the alkaline, but racemisation is much slower in acid solution, so the longer standing did not introduce error from this cause.)   Thereupon the nitric acid was exactly neutralised, and the rotatory power of the malic acid measured as before.   By addition of sodium nitrate the ionic strength of the solution was brought to a fixed value during the hydrolysis in both acid and alkaline solutions.   For calculation of n, the rotatory power of pure $(-)$malic acid was measured in the same concentration and the same ionic strength as in the various experiments.   The results are in Tables I and II.

TABLE I.

Hydrolysis in acid solutions.

([H˙] = Hydrogen-ion concentration initially.*)

[H˙]	0·002	0·05	0·10	0·15
$[\alpha]_{578}^{25\cdot7°}$	+327·8°	+302·5°	+288·0°	+264·0°
n	0·28	0·30	0·31	0·32
[H˙]	0·20	0·89	1·5	2·0
$[\alpha]_{578}^{25\cdot7°}$	+144·2°	−101·5°	−126·0°	−288·0°
n	0·40	0·57	0·59	0·69

* In the first experiment, where no nitric acid was present, [H˙] was calculated on the assumption that the lactonic acid had the same dissociation constant as succinic acid, *viz.*, $6\cdot6 \times 10^{-5}$; in the other experiments [H˙] is equal to the concentration of nitric acid used.

TABLE II.

Hydrolysis in alkaline solutions.

([OH′] = mean of initial and final concentration of hydroxyl ion.)

| [OH′]	0·26	0·52	1·14
$[\alpha]_{578}^{25\cdot7°}$	−535°	−528°	−546°
n	0·86	0·86	0·87

The present investigation consequently shows (see p. 2931) that the reaction in acid solution is of Type 1, and therefore, contrary to earlier views, can give either $(-)$ or $(+)$malic acid according to the hydrogen-ion concentration, while the reaction in alkaline solution is of Type 2.

In acid solutions the opening of the lactone ring must therefore take place spontaneously between the asymmetric carbon atom and the oxygen atom as shown by the dotted line :
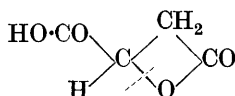
The molecule will then oscillate as usual, until it is transformed into malic acid by collision with a $H_3O^{\cdot}$ ion. In this ion, by the binding of a proton to a molecule of water, the valencies are so loosened that on collision with an oscillating molecule it readily yields a hydroxyl ion, and the more so because a hydroxyl ion is much more firmly bound to an alcohol radical (*viz.*, the asymmetric carbon atom) than to a hydrogen ion.

According to the views in this and the preceding papers the oscillating molecule, when reacting with the new entering substituent in large concentration, must produce that form of the reaction product which is stereologous with the original asymmetric molecule, and consequently the (+)malic acid, which is produced in the strongly acid solutions, must be stereologous with the (+)lactone, which is formed from the (−)bromosuccinic acid. This agrees with the fact (Holmberg, *loc. cit.*) that the (+)lactone acid with ammonia gives an amido-acid, which is hydrolysed to (+)malic acid :
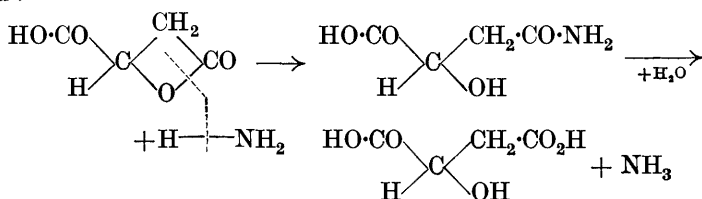
Since no valency linkage of the asymmetric carbon atom is affected by these two reactions, no change in configuration can occur, and so the consequences of the theory of the oscillating molecule are verified by one of the few instances in which the relation between the configurations of different asymmetric molecules is known with certainty.

The fact that the stereochemical result of the hydrolysis in alkaline solutions is independent of the concentration can be interpreted in two ways, because the opening of the lactone ring can occur in two different places, *viz.*, between the oxygen atom and either (1) the asymmetric carbon atom or (2) the carboxyl carbon atom.

(1) The very great velocity of the hydrolysis in alkaline solutions makes it probable that the opening of the ring is caused by collision with a hydroxyl ion, whereby the molecule is set into oscillation. If the opening occurs at the asymmetric carbon atom, the hydroxyl ion, which has caused the opening, must at the moment of scission be at a definite distance from the vacant place ; the immediately ensuing addition must consequently (see Part II) normally take a definite time and therefore take place in a definite phase of oscillation

(the result shows that in this case it takes place in the first phase). The reaction is consequently representative of Type 2.
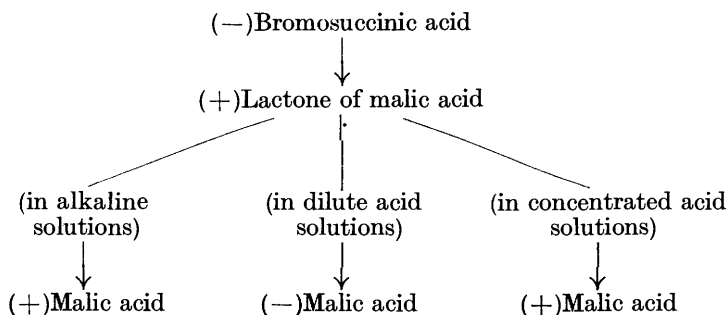
The partial racemisation occurring in alkaline solutions in this reaction has two causes. Besides the usual partial racemisation, which normally accompanies reactions of Type 2, it must be assumed that the slow spontaneous opening of the ring, which in acid solutions produces the reaction of Type 1, also occurs in basic solutions independently of the main reaction and here contributes to the partial racemisation; for the spontaneously opened molecules will oscillate as usual until they meet a new substituent (in alkaline solutions, a hydroxyl ion), which is then added in one or another phase.

(2) The second possibility can equally well explain the formation of mainly one form of the reaction product, but in this scission the addition of a hydroxyl ion will not suffice for the formation of malic acid, the addition of a molecule of water being required. This is not impossible, but such a mechanism would not explain the great effect of hydroxyl ions upon the reaction velocity. The partial racemisation must here, as before, be explained by the slow spontaneous opening of the ring.

Finally, the transformation of (−)bromosuccinic acid into the intermediate (+)lactone must necessarily be a reaction of Type 2, because the radical (viz., the carboxyl group) which is to be linked to the asymmetric carbon atom is part of the asymmetric molecule itself, and consequently the condition for Type 2, viz., constant distance between the vacant place and the new substituent, is fulfilled in this case. The partial racemisation, which normally is observed in Type 2, must in this special case be very slight.

Since reactions of Type 2 do not afford any means of deciding the relation between the configurations of the reacting molecules, it is still uncertain whether the (+)lactone is stereologous or not with (−)bromosuccinic acid from which it is produced.

The experimental results are qualitatively summarised in the scheme :

(−)Bromosuccinic acid

↓

(+)Lactone of malic acid

(in alkaline solutions)	(in dilute acid solutions)	(in concentrated acid solutions)
↓	↓	↓
(+)Malic acid	(−)Malic acid	(+)Malic acid

Detailed examination of Walden's papers shows that his experimental conditions, in spite of the presence of bases, ultimately produced acid solutions in all those cases in which (—)malic acid resulted. This is, of course, the case where water alone was used. Of the bases used in the first group mentioned on p. 2932 only thallous hydroxide is easily soluble, but even in this case, at least the last half of the hydrolysis was carried out in acid solution. In the group where (+)malic acid was produced, the bases used were all (with one exception, see below) present in excess and most of them were relatively soluble and would produce basic solutions; the formation of (+)malic acid was therefore to be expected. In one of the experiments with copper oxide, this was used only in equivalent amount, and alkaline reaction could not have persisted here. Moreover, the possibility of the formation of complex copper acids cannot be excluded (Holmberg, *Ber.*, 1928, **60**, 2198), and this would introduce complications, for other possibilities for the opening of the lactone ring must be considered and these require special experimental investigation.

Bancroft and Davis (*J. Physical Chem.*, 1931, **35**, 1253) have recently investigated the effect of silver oxide and of buffer solutions upon (—)chlorosuccinic acid. Solutions of the acid were stirred with the oxide ; when equivalent amounts of the reagents were used, (—)malic acid was produced ; but excess of silver oxide afforded (+)malic acid. In the first case the solution necessarily became acid during the hydrolysis ; but in the second case, the stirring must have kept the solution alkaline, and the results consequently agree with those of Holmberg and of the author.

In the other series of experiments, buffer solutions of glycine and sodium hydroxide were added to solutions of sodium (—)chlorosuccinate. The p_H values of these mixtures (*viz.*, 9, 10, 12, or 13) were measured electrochemically, and the consumption of base during the hydrolysis was compensated by successive addition of sodium hydroxide in such a way that the p_H was maintained nearly constant. In all these experiments (+)malic acid was produced, the rotatory power increasing with increasing p_H.

Since, as shown in the present investigation, slightly acid solutions produce (—)malic acid, and moderately basic solutions produce (+)malic acid, it follows that a region of very slightly basic reaction must exist in which the stereochemical result varies with the p_H, and this is precisely what Bancroft and Davis found. With decreasing p_H the process of Type 1 produced by the slow spontaneous opening of the lactone ring, which also occurs in alkaline solutions, must finally become the dominant reaction, and as n in reactions of Type 1 at very low concentrations tends towards $n = 0.5$, com-

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plete racemisation is here approached both from the basic and from the acid side.

This theoretical point of complete racemisation will not necessarily coincide with the neutral point, for both $H_3O^{\cdot}$ ions and HO' ions can produce $(+)$malic acid as well as $(-)$malic acid, depending upon whether they meet the oscillating molecule in one or the other phase, and complete racemisation will therefore occur under conditions such that the rotatory power of the malic acid, formed by collisions of both $H_3O^{\cdot}$ ions and HO' ions with the spontaneously opened oscillating molecules, is just compensated by the rotatory power of the $(+)$malic acid produced by collisions between HO' ions and the unopened lactone molecules.

The other point of complete racemisation, which normally is to be found in Type 1, lies in the present case at about $[H^{\cdot}] = 0.7$, as seen from Fig. 1, in which the experimental values of n are indicated

FIG. 1.
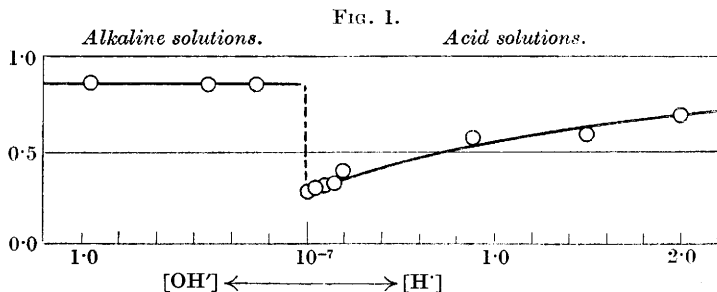
by circles. From Part III it is known that the approach of n to 0.5 at very low concentrations produces a curve, although the method of plotting used here shows an angle. Similarly, the transition part of the n curve, which could probably be substantiated by experiments upon the pure lactone in buffer solutions, is represented as a (broken) straight line, but a different system of plotting, e.g., n against p_H, would undoubtedly show a curve.

EXPERIMENTAL.

(A) Two identical solutions of the $(+)$lactone of malic acid were prepared. For each portion 7·98 g. of $(-)$bromosuccinic acid ($[\alpha]_{578}^{25°}$ $-74.64°$) were dissolved in 39·50 c.c. of 2·013N-NaOH, a few drops of K_2CrO_4 aq. were added, and the solutions placed in a thermostat at 25°. After the lapse of h hours, x c.c. of 1·1M-AgNO$_3$ were added to ppt. the Br' ion formed, the total vol. of AgNO$_3$ being denoted by y :

h	0·5	1·0	1·5	2	2·5	3	3·5
x	4·05	3·05	3·10	2·76	2·19	2·05	1·85
y	4·05	7·10	10·20	12·96	15·15	17·20	19·05
h	4·5	5·5	6·5	7·5	8·5	10·5	
x	3·15	2·88	2·05	1·83	1·88	2·30	
y	22·20	25·08	27·13	28·96	30·84	33·14	

The complete reaction requires 36·36 c.c. of $AgNO_3$; consequently 90% of the acid had been transformed; in order to complete all the measurements as rapidly as possible, lactonisation was not carried further. To each portion were then added 5·5 g. of $AgNO_3$ and 1·7 g. of $NaHCO_3$, both finely powdered.

The Ag salts of bromosuccinic, fumaric, and malic acid thus pptd. were filtered off together with the AgBr, whereas the Ag salt of the (+)lactone of malic acid, being easily sol. even in neutral solution, remained in the filtrate, which was acidified with H_2SO_4 and twice extracted with Et_2O. The extract was sucked from the funnel through a fine capillary tube, so as to avoid contamination with traces of the acid liquid adhering to the walls of the separator. The extracts from both portions were united and divided into portions of 60 c.c., which were added separately to the solutions $a_1—a_3$ and $b_1—b_3$ (see below), the alkaline solutions being contained in separating funnels, and the acid solutions in beakers. These solutions were : (a_1) 45·0 c.c. 2·013N-NaOH; (a_2) 22·0 c.c. 2·013N-NaOH + 23·0 c.c. 2M-$NaNO_3$; (a_3) 12·3 c.c. 2·013N-NaOH + 32·7 c.c. 2M-$NaNO_3$; (b_1) 45·0 c.c. 2N-HNO_3; (b_2) 20·0 c.c. 2N-HNO_3 + 25·0 c.c. 2M-$NaNO_3$; (b_3) 4·5 c.c. 2N-HNO_3 + 40·5 c.c. 2M-$NaNO_3$.

(1) The alkaline solutions were shaken, the aq. layer separated, and the ethereal layer washed thrice with 10·0 c.c. of H_2O; the aq. layer and washings were united, giving a total vol. of 75 c.c. 2N-HNO_3 was now added in amount calculated to neutralise the NaOH exactly, 45·29, 22·14, and 12·38 c.c. respectively being used, and H_2O was added to the second and third so as to bring them to the same vol. as the first (120·3 c.c.). 20·0 C.c. of each of these solutions were now titrated by 0·0903N-NaOH and required 12·10, 13·00, and 12·83 c.c., corresponding to 0·0273, 0·0294, and 0·0290M-malic acid respectively.

After addition of 0·5 mol. of $(NH_4)_2MoO_4$ per mol. of malic acid the rotatory power was measured ($l = 0·5$) :

	a_1.	a_2.	a_3.
a	— 1·00°	— 1·04°	— 1·04°
$[a]_{578}^{25·7°}$	−546	−528	−535

The whole process, from the neutralisation of the bromosuccinic acid, occupied 14·5 hr.

(2) The acid solutions were left at room temp. for 48 hr., the ether having then evaporated. The calc. vols. of 2·013N-NaOH, viz., 44·72, 19·87, and 4·49 c.c., were then added to b_1, b_2, and b_3 respectively, and the solutions diluted to 120·3 c.c. Titration of 20 c.c. of each by 0·0903N-NaOH required 4·70, 9·15, and 10·00 c.c., corresponding to 0·0212, 0·0413, and 0·0451N respectively with regard to total malic and lactonic acid.

To find the concentration of malic acid alone, 20·0 c.c. of each solution after addition of 20·0 c.c. of 2·013N-NaOH were heated on the water-bath for 0·25 hr. After cooling and addition of 20·0 c.c. of 2N-HNO_3 to each, titration was repeated with 2·013N-NaOH solution, 0·20, 0·40, and 0·49 c.c. being required, whence the concns. of the lactonic acid were calculated; after allowance for this, the malic acid formed in the acid hydrolysis was respectively 0·00466, 0·0147, and 0·0140M.

The rotations of these solutions were measured ($l = 1·0$) after addition of 0·5 mol. of $(NH_4)_2MoO_4$:

	b_1.	b_2.	b_3.
a	— 0·18°	— 0·20°	+ 0·27°
$[a]_{578}^{25·7°}$	−288°	−102°	+144°

(B) The ethereal solution of the (+)lactone was prepared as in (A) and divided in portions of 60 c.c. which were added to each of the solutions 1—6; these contained 0·0, 1·1, 2·2, 3·3, 33·7, and 45·0 c.c. of $2N$-HNO_3 together with $2N$-$NaNO_3$ sufficient to make the total vol. 45·0 c.c. in each case. After standing over-night, any remaining ether was removed in a current of air, and 3 days later, the calc. vols. of standard NaOH were added to neutralise the HNO_3, and all were diluted with H_2O to 120·8 c.c. 20·0 C.c. of each solution were titrated with $0·09005N$-NaOH and required 11·80, 11·90, 11·76, 12·07, 11·25, and 11·79 c.c. Allowance for lactonic acid was made as before, 10·0 c.c. of $0·09005N$-NaOH being added to each of the titrated portions. The molarities of malic acid were as stated in the following table, values of a being measured in a 1 dm. tube after addition of $(NH_4)_2MoO_4$.
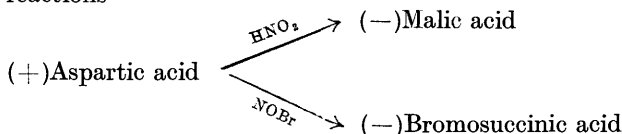
No.	Molarity of malic acid.	a.	$[a]_{578}^{25 \cdot 7^\circ}$.
1	0·0207	+0·91°	+328°
2	0·0212	+0·86	+303
3	0·0210	+0·81	+288
4	0·0218	+0·77	+264
5	0·0212	−0·36	−127
6	0·0230	−0·60	−195

The rotatory power of pure $0·02112M$-(−)malic acid under corresponding conditions in a solution that was also $0·75M$ in respect of $NaNO_3$ was found to be $a + 2·18°$; $[a]_{578}^{25 \cdot 7^\circ} + 770°$. The purest (−)bromosuccinic acid, repeatedly recryst., had $[a]_{578}^{25^\circ} - 77·14°$. Since the acid used for the experiments only had $[a]_{578}^{25^\circ} - 74·64°$, the calculation of n in this paper was based upon a malic acid of a rotatory power $[a]_{578}^{26^\circ} = 770 \times 74·64/77·14 = 745°$.

The rotatory powers of the malic acid produced in Expts. A,b_1 and B,6 under the same conditions were different; the higher value must be the better, and is therefore used in Table I.
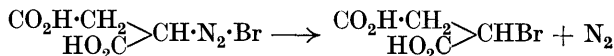
<div align="center">PART V.</div>

In the reactions

$$(+)\text{Aspartic acid} \underset{\overset{\nearrow}{\underset{NOBr}{\searrow}}}{\overset{HNO_2}{}} \quad \begin{array}{l} (-)\text{Malic acid} \\ \\ (-)\text{Bromosuccinic acid} \end{array}$$

Walden thought that transformation was effected by nitrosyl bromide, supposed to be formed when oxides of nitrogen were passed into the solution containing free bromine, but later, Holmberg (*Ber.*, 1927, **60**, 2194) showed that the free bromine could be replaced by bromides, and the reaction is now interpreted as a diazotisation.

Since aromatic diazonium salts do not give off nitrogen until they have been transformed into the un-ionised *syn*-diazo-compounds (see, *e.g.*, Hantzsch and Reddelien, " Die Diazoverbindungen," Berlin, 1921), it must be assumed that here also the formation of a corresponding un-ionised labile diazo-compound is an intermediate step in the reaction :

$$\begin{array}{l} CO_2H\cdot CH_2 \\ HO_2C \end{array}\!\!\!>\!CH\cdot N_2\cdot Br \longrightarrow \begin{array}{l} CO_2H\cdot CH_2 \\ HO_2C \end{array}\!\!\!>\!CHBr + N_2$$

The removal of nitrogen linked to the asymmetric carbon atom will set the molecule in oscillation, but since the bromine atom is at a fixed distance from the asymmetric carbon atom, the reaction must be of Type 2, *i.e.*, the bromosuccinic acid produced should be of constant rotatory power independently of the concentration (see Part II, J., 1929, 1282).

The author's experiments were made by passing a stream of N_2O_3 mixed with N_2 into ice-cooled aqueous solutions of (+)aspartic acid and hydrochloric or hydrobromic acid. The resulting halogeno-succinic acid was extracted with ether, thus avoiding the optical fractionation which would have resulted if the acid had been crystallised, a process which has obscured the type of inversion for this reaction in earlier investigations. The halogenosuccinic acid produced had constant rotatory power, although the concentrations in the various experiments were widely different, and consequently the reaction is of Type 2, as expected.

The values of n (see Part IV) calculated from the rotatory power are shown below, the ionic concentration, [Br'] or [Cl'], being the mean between the initial and the final concentration in each case.

Formation of bromosuccinic acid.

[Br']	....	3·31	0·761	0·546	0·367	0·358	0·196	0·088
n	....	0·96	0·96	0·94	0·95	0·97	0·96	0·98

Formation of chlorosuccinic acid.

[Cl']	....	5·12	2·72	2·57	2·49	2·42	0·097
n	....	0·96	0·95	0·95	0·95	0·94	0·96

Since ions disappear in the reaction, the ionic strength did not remain constant, but as the process is of Type 2, it is unaffected by ionic strength (see Part II).

As shown in preceding parts, only reactions of Type 1 afford the means of deciding the configurative relations of the reacting molecules, and consequently it cannot be settled whether (—)bromo-succinic acid is stereologous or astereologous with the (+)aspartic acid from which it is produced; *i.e.*, whether the above values represent n or $1 - n$.

The stereochemical type of the reaction aspartic acid $\longrightarrow$ malic acid is evident from Holmberg's work (*Ber.*, 1928, **61**, 1893) : by diazotisation of (+)aspartic acid in solution containing nitric acid, he got (—)malic acid of a rotatory power which increased with the content of nitric acid as seen from Table I, in which his results are shown together with values of n calculated therefrom. Although the malic acid was isolated by crystallisation, and the consequent optical fractionation must have somewhat altered the rotatory powers and

hence n, yet there can be little doubt that the results prove the reaction to be of Type 1.

TABLE I.

HNO_3, M ...	0	0·125	0·25	0·312	0·375	0·5	0·75	1·0
$[a]$	−40·3°	−52·3°	−54·3°	−191°	−255°	−306°	−321°	−405°
n	0·55	0·56	0·56	0·72	0·79	0·85	0·87	0·97

By analogy with the formation of halogenosuccinic acid, it must be assumed that by the diazotisation in nitric acid an ester of malic acid with nitric acid is primarily formed, and such a compound was found by Holmberg to accompany the malic acid. This ester is, however, rapidly hydrolysed to malic acid by $H_3O^{\cdot}$ ions. The reaction mechanism of this hydrolysis must be analogous to the acid hydrolysis of the lactone of malic acid (Part IV), and must consequently consist in a *spontaneous* opening of the linking between the oxygen atom and the asymmetric carbon atom, whereby the remainder of the molecule oscillates between the d- and the l-form until it meets a $H_3O^{\cdot}$ ion :
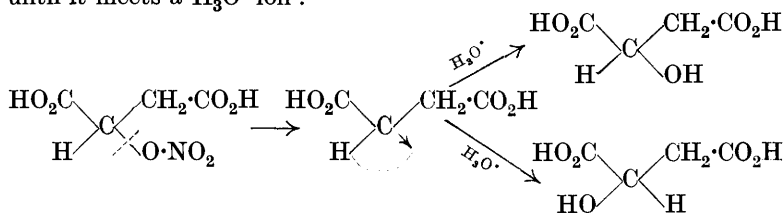
Hence the rotatory power of the malic acid depends upon the intermolecular distances in the solution, *i.e.*, the reaction is of Type 1.

Kenyon and Phillips have shown (J., 1930, 1676) that l-phenylmethylcarbinyl p-toluenesulphinate is spontaneously transformed into optically inactive p-tolyl-α-phenylethylsulphone :
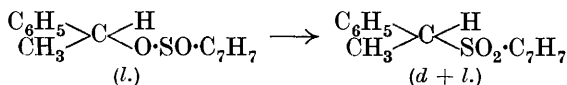
They regard this as a proof that " a tercovalent carbonium kation cannot maintain its configuration unchanged but oscillates between two forms of opposite configuration :

" In absence of the special mechanism which leads to a Walden inversion it would therefore appear that the replacement of a group attached to an asymmetric carbon atom must inevitably yield an optically inactive or racemised product." This idea of an oscillating kation containing tervalent carbon is identical with that put for-

ward by the author (Part I; J., 1928, 2447); but the conclusion drawn by those authors is incorrect.

It would seem that their reaction is a true parallel to the decomposition of the diazo-compound now investigated. In both cases a radical which has been split off from the asymmetric carbon atom is subsequently added. From the theory advanced here this should result in a reaction of Type 2, and actually does so in the formation of halogenosuccinic acid from the diazo-compound. The complete racemisation found by Kenyon and Phillips appears to be contrary to that theory, but closer inspection shows that it is not so. The radical is split off as a sulphinate group, but is added as a sulphone group. Although the time necessary for this transformation is presumably constant, yet the dissociated parts meantime will be brought at fortuitously varying distances by collision with the surrounding molecules, with the result that the probability of addition is the same in each of the oscillation phases. Complete racemisation will be the natural result.

This reaction is only an extreme case, in which the partial racemisation always occurring in reactions of Type 2 becomes complete owing to the relatively long time which must elapse before the dissociated parts can unite again.

Autoracemisation, like a Walden inversion, must be assumed to be caused by the spontaneous splitting off of a radical attached to the asymmetric carbon atom, and only differs from the inversion in that here the dissociation is followed by addition of the same radical as that split off, whereas in a Walden inversion a new molecule is produced. Since the regenerated molecule has the same tendency to split off the radical again (contrary to the case when a molecule of new sort is produced), this process will continue, and since such scission always gives a chance that by casual shocks from surrounding molecules the dissociated parts may be so widely separated before they meet again that the addition will occur in the opposite oscillation phase, the result will be a continuous increase of inversion until $n = 0.5$ is reached, which value cannot, of course, be exceeded.

This theory does not apply to racemisations where enolisation of some sort underlies the process. In such cases racemisation is caused by differences in molecular stability and consequently is outside the problems considered here.

EXPERIMENTAL.

The experiments were carried out by passing a stream of N_2O_3 mixed with N_2 into aq. solutions of (+)aspartic acid and HCl or HBr. The N_2O_3 was obtained by dropping conc. $NaNO_2$ aq. into fuming HNO_3 in a flask, which, like all other parts of the apparatus, including wash-bottles, was placed in

ice. The N_2 was taken from a cylinder and washed twice with alk. pyro-
gallol and then with NaOH aq. All joints in the apparatus were of ground
glass, and the flask in which the diazotisation took place was furnished with
a long reflux condenser.

(A) *Conversion of* (+)*Aspartic Acid into Bromosuccinic Acid.—Expt. No.* 1.
(*a*) The solution contained 13·31 g. of (+)aspartic acid, 50 c.c. of 2·015N-
HBr, 50 c.c. of 1·788N-H_2SO_4, and 20 c.c. of H_2O. After the gaseous mixture
had been passing for 15 min., it was stopped, the excess of N_2O_3 removed
from the solution by a rapid stream of N_2, and the solution extracted with
ether. The extract was dried (Na_2SO_4) over-night, and evaporation of the
ether left 3·71 g. of bromosuccinic acid.

(*b*) After the extraction with ether, the solution was again saturated with
the gaseous mixture during 15 min., and then worked up as before, giving
6·49 g. of bromosuccinic acid.

(*c*) The same procedure was again repeated for $\frac{1}{2}$ hr. : yield 1·96 g.

(*d*) As (*c*); yield 0·41 g.

Expt. No. 2. As in 1, but 5·324 g. of (+)aspartic acid and 200 c.c. of
0·252N-HBr were used; passage of N_2O_3 continued for 2 hr.; yield 2·54 g.

Expt. No. 3. As in 2, but with 6·655 g. of acid in 50 c.c. of 3·722N-HBr.
Addition of N_2O_3 lasted $1\frac{1}{4}$ hr., but before the extraction with ether, 3·11 g.
of bromosuccinic acid, which had crystallised, were filtered off. The filtrate
yielded 5·10 g. to ether. The purpose of this procedure was to examine
whether crystallisation had caused optical fractionation. The two fractions
are denoted by 3*a* and 3*b*.

Expt. No. 4. 2·662 G. of (+)aspartic acid in 225 c.c. of 0·1N-HBr; 2 hr. :
yield 0·62 g.

The rotatory power of the bromosuccinic acid produced in these experi-
ments was measured in EtOAc solution. The results are collected in Table
II. For the calculation of n the value $[a]_{578}^{25°} - 77·14°$ (see Part IV) was used
for pure (−)bromosuccinic acid.

TABLE II.

Expt. No.	Halogeno-succinic acid, g.	Ethyl acetate, c.c.	l, dm.	a.	n.
1*a*	0·6456	10·0	1	−4·56°	0·96
1*b*	0·6168	10·0	1	−4·18	0·94
1*c*	0·6058	10·0	1	−4·23	0·95
A 1*d*	0·2510	5·00	0·5	−1·82	0·97
2	0·3249	5·00	0·5	−2·28	0·96
3*a*	0·2878	5·00	0·5	−2·12	0·98*
3*b*	0·2949	5·00	0·5	−1·98	0·94*
4	0·3092	5·00	0·5	−2·77	0·98
5	0·3006	5·00	0·5	−1·59	0·96
6*a*	0·3307	5·00	0·5	−1·72	0·95
B 6*b*	0·3049	5·00	0·5	−1·59	0·95
6*c*	0·3231	5·00	0·5	−1·66	0·95
6*d*	0·3011	5·00	0·5	−1·53	0·94
7	0·2266	5·00	0·5	−1·20	0·96

* In the table on p. 2941 the mean value of 3*a* and 3*b* (0·96) is used.

(B) *Conversion of* (+)*Aspartic Acid into Chlorosuccinic Acid.*—The experi-
ments were quite analogous to those made under A.

Expt. No. 5.   6·655 G. of (+)aspartic acid in 50 c.c. of 5·50N-HCl; 1 hr. : yield 5·70 g. of chlorosuccinic acid.

Expt. No. 6.   13·31 G. of (+)aspartic acid in 100 c.c. of 2·75N-HCl. Extractions were conducted after 0·5, 1·0, 1·25, and 1·57 hr., and the successive yields were 1·0, 4·5, 2·6, and 2·2 g. of chlorosuccinic acid (referred to as *a, b, c, d* respectively).

Expt. No. 7.   1·331 G. of (+)aspartic acid in 100 c.c. of 0·104N-HCl; after passage of N_2O_3 for 1 hr., the solution was left for 3 hr. with the excess of N_2O_3; yield 0·2266 g.

Rotatory power was measured as before. For use in the calculation of *n*, the sp. rotatory power of pure (—)chlorosuccinic acid was found by recrystallising a sample until it attained a maximum; 0·2130 g. of the acid dissolved in 5·00 c.c. of EtOAc ($l = 0.5$) gave $a - 1.23°$, $[a]_{578}^{25°} - 57.75°$, and this is the value used.

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     COPENHAGEN, DENMARK.   [*Received, August 3rd,* 1932.]