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CLXVI.--*The Walden Inversion. Part II.*

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IN a former paper (J., 1928, 2447) the author set forth a new hypothesis of the reaction mechanism of the Walden inversion, the fundamental assumption being that the optically active molecule,

after splitting off one of the radicals linked to the asymmetric carbon atom, oscillates between two configurations, each of which, by the addition of a new radical, will produce only one of the two possible optical antipodes. A rigid mathematical treatment of this hypothesis would undoubtedly be very complicated, but by making certain simplifying assumptions, it was shown to lead to the equation

$$n = k.c_x.F \dots \dots \dots (1)$$

In this formula,  $n$  denotes that fraction of the reaction product which retains its original configuration,  $c_x$  the mean of the concentrations of the entering radical at the beginning and at the end of the reaction,  $F$  the kinetic activity factor of Brönsted (*Z. physikal. Chem.*, 1922, **102**, 169), and  $k$  a constant.

It is obvious that the above equation entails an unlimited increase of  $n$  by increasing  $c_x$ , whereas actually, of course,  $n$  can only vary from zero to unity; but this only means that, as a first approximation, a straight line has been substituted for the unknown theoretically correct curve. The application of equation (1) to some of the most accurate experiments upon the Walden inversion hitherto reported showed, in general, very good agreement between theory and experiment.

A number of Walden inversions now described were carried out under experimental conditions such as to conform as closely as possible to the requirements of the theory, and it will be seen that up to  $c_x = 0.4M$  the experimentally found values agree with great accuracy with the linear variation of  $n$  demanded by the simplified equation, whilst for greater variation in  $c_x$  the anticipated bending of the curve is realised. The immediate aim of this research is to accumulate sufficiently accurate data upon the Walden inversion; the deduction of a complete theory will be relegated to a later paper.

From the point of view of the new hypothesis we must postulate the existence of two distinct types of these inversions, depending upon the character of the non-asymmetric component in the reaction.

*Type 1.* Reactions where the splitting of the optically active molecule either occurs spontaneously or is caused by some molecule which is neither identical with nor contains the entering radical. In this type, both *d*- and *l*-forms are produced in amounts which depend upon the concentrations, and theoretical calculation of the stereochemical inhomogeneity of the reaction product based upon the views of the new hypothesis can therefore be applied. Besides the reaction between bromosuccinic acid and xanthogenates, to which the theory was applied in Part I (*loc. cit.*), we must include in this type all reactions where halogen linked to an asymmetric carbon atom is replaced by hydroxyl or by other radicals present

in the solution in the state of ions, as well as reactions where a hydroxyl group linked to an asymmetric carbon atom is replaced by the influence of halogen ions.

*Type 2.* This type comprises reactions where the splitting of the optically active molecule is brought about by a molecule containing the radical which displaces the ejected radical. This we must assume to be the case when the replacement of a hydroxyl group linked to an asymmetric carbon atom is caused by reagents such as phosphorus pentachloride, thionyl chloride, nitrosyl bromide, etc. In these cases it seems natural to follow the customary view which assumes that an addition or some very near position of the halogeno-compound molecule causes the splitting off of the hydroxyl group; and a similar mechanism must be assumed if a halogen atom linked to an asymmetric carbon atom reacts with a molecule of water or ammonia, producing an exchange of halogen for a hydroxyl or amino-group. Another example is afforded by the reaction between a nitrous acid molecule and an active amino-compound.

In such cases the entering radical must, at the moment of the splitting of the active molecule, always be very nearly at the same distance from the vacant place at the asymmetric carbon atom—a distance which depends upon the nature of the reacting molecules but is independent of the concentrations—and consequently the entering radical will always occupy very nearly the same time in taking that vacant place. The word “nearly” is used in the foregoing sentences because the addition may perhaps take place in slightly different ways even for the same reagent. Whether the replacement occurs in the first or in a later phase of the oscillation (*i.e.*, whether it does not or does produce inversion) will depend upon the structure of the molecules and the period of the oscillation, but as these quantities have constant values, we must expect that only one stereochemical form of the reaction product will result, and this type of Walden inversion is consequently not amenable to calculation of the composition of the reaction product. Of course, it is possible that accidental and uncontrollable influences, such as casual shocks from the surrounding molecules of the solvent, may cause divergencies, but in the main it seems natural to ascribe racemisation, if occurring in greater degree in reactions of this type, to secondary influences not directly connected with the double decomposition.

Finally, we must also expect that reactions may occur which represent a transition stage between the two types, or which actually proceed simultaneously in the two different typical ways. Such an example is perhaps to be found in the processes which are usually attributed to the action of nitrosyl bromide upon active amino-compounds, although such reactions may be due both to (i) the

undissociated nitrosyl bromide molecules and to (ii) nitrous acid and bromine ions. From the views given above, we should expect the first of these processes to give only one stereochemical form and the other to give both the *d*- and the *l*-form of the resulting halogen compound. The results of this process reported in the literature seem to justify this explanation.

In the foregoing systematic classification, we have only taken account of the nature of the optically inactive component of the reaction, but that the nature of the optically active compound plays a considerable part in determining the stereochemical course of the process is well known, since, for example, an optically active ester and the corresponding free acid in some cases give different stereochemical forms of the reaction product with the same reagent. Apart from the influence of concentration and other experimental conditions, this phenomenon may be a direct consequence of the hypothesis now advanced, since the time of oscillation must necessarily be different for an ester and for its free acid—or, to take an example of another type, for bromopropionylglycine and for the free bromopropionic acid (Fischer, *Ber.*, 1907, 40, 489)—and if this difference is great enough, the two reactions can give rise to products of opposite sign.

Another important influence arises from the well-known fact that only in exceptional cases can the asymmetric carbon atom be assumed to occupy the centre of a perfectly regular tetrahedron, for generally the tetrahedron is more or less irregular. This point is of importance primarily for the mathematical treatment of our hypothesis; here it is only necessary to mention that, whilst in the diagrammatical case of a regular tetrahedron, the period of the first phase of the oscillation must be half that of each of the following phases, yet in all actual cases this ratio can be either greater or less than one-half.

The present paper describes the first of a series of researches, designed from the point of view of the author's hypothesis, upon the mechanism of the Walden inversion; and a process of Type I has been chosen in order to investigate the influence upon it of systematic variation of (*a*) the concentration, the ionic strength  $\mu$  (and consequently also the activity factor *F*) being kept constant, and (*b*) the ionic strength, the concentration being kept constant.

As the reaction between halogeno-succinic acids and xanthogenates has been shown by Holmberg (see Part I, *loc. cit.*) to proceed in a well-defined way, *l*-bromosuccinic acid and potassium xanthogenate were chosen for my purpose. It is assumed (see Part I, *loc. cit.*) that *l*-bromo- and *d*-xanthogeno-succinic acids have the same configuration, and this raises a point of fundamental importance.

When a radical linked to an asymmetric carbon atom is replaced by another radical, there is as yet no means of ascertaining *with certainty* which of the two possible forms of the reaction product has the same configuration as the original molecule; for, when an optically active molecule is transformed under different conditions (but without interference from other optically active molecules) into oppositely rotating forms of the same reaction product, all we can say is that a Walden inversion has taken place *in one of these reactions*. The literature contains numerous instances in which a Walden inversion is said to have taken place with or without a change in the sign of rotation, but these are necessarily only expressions of opinion in the light of various hypotheses, and the same applies to the present statement as to the bromo- and xanthogeno-succinic acids. The conception of the Walden inversion advocated here and in Part I leads to the conclusion that, in reactions of Type 1, that form of the reaction product which increases in amount with increasing concentration of the entering radical in the solution has the same configuration as the original substance. Moreover, if valid, this theory for reactions of Type 1 affords a means, hitherto lacking, of deciding which forms of related substances have corresponding configurations.

The results of the two types of experiment (a) and (b) are shown in Tables I and II and Figs. 1 and 2, respectively,  $n$  being recorded as a percentage of  $d$ -acid formed. When the values of  $n$  in Expts. 6—10 are multiplied by the factor  $48.9/43.6$ , *i.e.*, the ratio of the values in Expts. 11 and 10, we get those values of  $n$  which would

TABLE I.

(Bs = Bromosuccinic radical ; X = xanthogenate radical.)

No.	Composition of mixture.			$c_x$ .	$n$ .
	$\text{Na}_2\text{Bs}$ .	KX.	$\text{KNO}_3$ .		
		$\mu = 0.8$ .			
1	0.101	0.1	0.4	0.05	16.5
2	"	0.2	0.3	0.15	25.0
3	"	0.3	0.2	0.25	31.4
4	"	0.4	0.1	0.35	34.8
5	"	0.5	0.0	0.45	40.6
6	0.100	0.1	0.4	0.05	13.8
7	"	0.2	0.3	0.15	21.6
8	"	0.3	0.2	0.25	30.6
9	"	0.4	0.1	0.35	37.8
10	"	0.5	0.0	0.45	43.6
		$\mu = 2.3$ .			
11	"	0.5	1.5	0.45	48.9
12	"	1.0	1.0	0.95	64.9
13	"	1.5	0.5	1.45	70.8
14	"	2.0	0.0	1.95	74.4

TABLE II.

 $\text{Na}_2\text{Bs} = 0.05$ ,  $\text{KX} = 0.05$ ,  $c_x = 0.025$ .

No.	$\text{KNO}_3$			$F$ .	No.	$\text{KNO}_3$			$F$ .
	added.	$\mu$ .	$n$ .			added.	$\mu$ .	$n$ .	
15	0.00	0.20	5.78	1.60	18	0.15	0.35	6.64	1.84
16	0.05	0.25	6.13	1.70	19	0.20	0.40	6.68	1.85
17	0.10	0.30	6.13	1.70	20	0.25	0.45	6.97	1.93

FIG. 1.

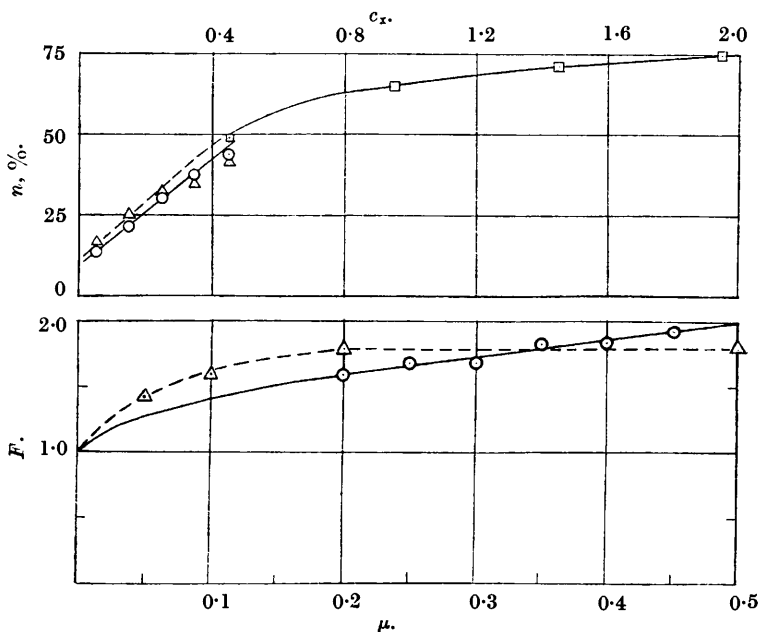
 $\Delta$ ,  $\odot$ , and  $\square$  = values of  $n$  in Expts. 1-5, 6-10, and 11-14, respectively. $\odot$  = values of  $F$  derived from experimental values of  $n$ . $\Delta$  " " " calculated from solubility data.

FIG. 2.

have been found in Expts. 6-10 had the ionic strength here been 2.3, and so the curve for Expts. 11-14 is continued down to  $c_x = 0.05$  as a broken line. Expts. 6-10 were a repetition of Expts. 1-5 but were carried out in a somewhat different manner, designed from the point of view of my conception of the reaction mechanism to ensure more definite results (see Experimental).

The values of  $F$  given in Table II and denoted by circles in Fig. 2 were obtained as follows: Since the results in Expts. 1-10 have shown that equation (1) is valid for the concentrations concerned, we are entitled to assume that the figures for  $n$  in Expts. 15-20 are proportional to the activity factor  $F$  in these experiments. If

these values of  $n$  are divided by 3.6 (found empirically) and the corresponding dividends are assigned to  $F$ , the curve obtained by plotting  $F$  against  $\mu$  intersects the ordinate axis at  $F = 1$ , which is the theoretically correct value for the activity factor for  $\mu = 0$ , and hence these values of  $F$  were adopted.

For comparison, some values of the factor  $F = f_1^2/f_2$  have been calculated from solubility experiments of Brönsted and Petersen (*J. Amer. Chem. Soc.*, 1921, **43**, 2274, 2282). The solubilities of *croceo*-tetranitrodiamminocobaltiate in salt solutions were used for the calculation of  $f_1$ , and those of *xantho*-oxalate for  $f_2$ . The values for  $F$  thus obtained are denoted by triangles in Fig. 2. It is seen that a common curve could be drawn to agree fairly well with all the points of the diagram, but the individual character of the two systems justifies different but similar curves.

#### EXPERIMENTAL.

Experiments 1—5 were carried out by dissolving a weighed quantity of *l*-bromosuccinic acid in the equivalent amount of sodium hydroxide solution, diluting it to a fixed volume, and adding solid potassium xanthogenate and solid potassium nitrate. Under these conditions, however, it is probable that some reaction takes place between the acid and the alkali before the addition of the xanthogenate, and in order to avoid this, the method was modified as follows: Weighed quantities of solid xanthogenate and nitrate were dissolved in an amount of sodium hydroxide solution equivalent to the quantity of *l*-bromosuccinic acid to be employed, and the solution was diluted to a fixed volume, and rapidly poured over the acid, which was brought into solution by vigorous shaking. The reaction mixture was then kept in the thermostat at 25.0° for about 72 hours, and the xanthogenosuccinic acid formed was isolated by acidification with sulphuric acid and extraction with ether. The ethereal solution was dried over calcium chloride and left to evaporate at room temperature. In most of the experiments xanthogenate was present in excess, and on acidification xanthogenic acid separated partly as a suspension and partly as a heavy oil; two or three filtrations through a wet filter-paper, however, sufficed to give a perfectly clear solution.

In the modified method of preparing the reaction mixture, the displacement of the bromine atom takes place in a solution in which the xanthogenate ion has the right concentration and the ionic strength is as required (except for the few moments necessary for dissolution of the acid); the corresponding experiments (Nos. 6—10) give a better curve than Nos. 1—5.

The xanthogenosuccinic acid thus obtained was yellowish-white

and crystalline, having a faint odour reminiscent of organic sulphides. It was not further purified for fear of fractionating it, and by titration with 0.1*N*-sodium hydroxide it gave an equivalent that agreed well with the theoretical value 119.1; hence, since Holmberg (*loc. cit.*) found the reaction to pursue a regular course, no further identification was thought necessary.

After being dried upon filter-paper, the acid was dissolved in ethyl acetate, and its rotation determined in 1-dm. tubes surrounded by a jacket, through which water from a thermostat was circulated, the temperature being ascertained by a thermometer inserted in the solution itself. These measurements were made by the monochromatic light of the yellow mercury line ( $\lambda = 578 \mu\mu$ ), and in some special cases by the green mercury line ( $\lambda = 546$ ) also, the light of a powerful mercury-quartz lamp being filtered through one of the two sets of aqueous solutions (1 cm. layer of each constituent solution):

A. Yellow line: (1) 5.76 g. of anhydrous copper sulphate in 100 c.c. of water; (2) 0.02 g. of tartrazine + 0.02 g. of erythrosin in 100 c.c. of water.

B. Green line: (1) the same as A1; (2) 18 g. of didymium chloride in 50 c.c. of water; (3) 0.02 g. of tartrazine in 100 c.c.

The *l*-bromosuccinic acid used was prepared from *l*-aspartic acid as described by Holmberg (*Ber.*, 1927, **60**, 2205). The sample used for Expts. 1—5 had  $[\alpha]_{578}^{25} = -74.67^\circ$  ( $c = 6.00$  in ethyl acetate), but that used in all the other experiments had  $[\alpha]_{578}^{25} = -73.84^\circ$  under the same conditions. Since Walden (*Ber.*, 1895, **28**, 2770) found  $[\alpha]_D = -72.6^\circ$  and Holmberg (*Arkiv Kemi, Min., Geol.*, 1916, **2**, No. 8) found  $[\alpha]_D^{17} = -76.3^\circ$ , it is clear that the samples used here contained a few units % of the *r*-form, but as this would only cause a very slight uniform displacement of the curves, and in view of the small quantity available, it was decided not to recrystallise the acid.

The experimental details are given below.

*Experiment 1.* The quantities used were 3.006 g. of *l*-bromosuccinic acid, 2.404 g. of potassium xanthogenate (in the tables abbreviated to KX), 6.065 g. of potassium nitrate, and 30.75 c.c. of 1.0*N*-sodium hydroxide solution. Total volume, 150.0 c.c. The xanthogenosuccinic acid was extracted by four 50-c.c. portions of ether, whereby 3.09 g. were obtained:  $[\alpha]_{578}^{25} = -71.81^\circ$  ( $c = 6.03$  in ethyl acetate). The specific rotation of *l*-xanthogenosuccinic acid is estimated (see below) to be  $[\alpha]_{578}^{25} = -107^\circ$ ; hence the content of *d*-form in the acid obtained in this experiment is calculated as  $n = 16.45\%$ .

In Expts. 2—5 the quantities of *l*-bromosuccinic acid and sodium hydroxide solution, the total volume, and the time of reaction (72



hours) were the same as in Expt. 1. The other quantities were as shown, and in every case the specific rotation refers to approximately 0.6 g. of acid in 10 c.c. of ethyl acetate (*i.e.*,  $c = 6$ ).

Expt.	KX, g.	KNO <sub>3</sub> , g.	Acid obtained, g.	$[\alpha]_{578}^{25^{\circ}}$	$n, \%$
2	4.808	4.549	3.10	-53.06°	25.00
3	7.212	3.033	3.02	-38.75	31.39
4	9.616	1.516	3.10	-32.48	34.83
5	12.020	—	3.32	-20.04	40.64

Expts. 6—10. 2.955 G. of *l*-bromosuccinic acid and 29.91 c.c. of sodium hydroxide solution (not the same as above) were used, the other conditions being the same as for Expts. 1—5.

6	2.405	6.066	3.34	-77.47*	13.80
7	4.809	4.550	3.24	-60.70*	21.64
8	7.214	3.033	—	-41.44*	30.64
9	9.618	1.517	—	-26.14*	37.74
10	12.023	—	—	-13.80*	43.55

\* At 25.4°.

Expts. 11—14. The reaction product in these experiments was extracted successively with 100, 75, and 50 c.c. of ether; in all other respects the conditions were as in Expts. 6—10.

11	12.023	22.75	3.50	- 2.33	48.91
12	24.05	15.17	3.25	+31.79	64.86
13	36.07	7.583	—	+44.58†	70.84
14	48.09	—	—	+52.31‡	74.39

†  $\alpha_{578}^{25^{\circ}} = +2.67^{\circ}$ ;  $\alpha_{546}^{25^{\circ}} = +3.11^{\circ}$  ( $c = 5.99$ ).

‡ At 25.2°;  $[\alpha] = +53.31^{\circ}$  at 20.9°.

From the observed rotations of Expt. 13, extrapolation shows that  $[\alpha]_{589}^{25^{\circ}}$  (*i.e.*,  $[\alpha]_{D}^{25^{\circ}}$ ) is 93% of the value of  $[\alpha]_{578}^{25^{\circ}}$ ; also the measurements in Expt. 14 show that a rise of 4.3° causes a decrease of 2% in  $\alpha$ . From these and from Holmberg's value  $[\alpha]_{D}^{20^{\circ}} = \pm 101.5^{\circ}$  for the pure xanthogenosuccinic acid, we can calculate that for this compound  $[\alpha]_{578}^{25^{\circ}} = \pm 107^{\circ}$  (approx.), and this value has therefore been used in the present paper for the calculation of  $n$ .

Expts. 15—20. 1.478 G. of *l*-bromosuccinic acid, 1.202 g. of potassium xanthogenate, and 15.00 c.c. of sodium hydroxide solution were used in each case, the total volume being 150 c.c. The remaining data were:

Expt.	KNO <sub>3</sub> , g.	Acid obtained, g.	$[\alpha]_{578}^{25^{\circ}}$	$n, \%$
15	—	1.63	-94.64°	5.78
16	0.758	1.63	-93.89	6.13
17	1.516	1.64	-93.89	6.13
18	2.275	1.62	-92.79	6.64
19	3.032	1.61	-92.70	6.68
20	3.790	1.64	-92.08	6.97