

L.—*The Influence of Solvents on the Rotation of Optically Active Compounds. Part IX. A New General Method for Studying Intramolecular Change.*

By THOMAS STEWART PATTERSON and ANDREW McMILLAN, M.A.

It has been shown in previous parts of this investigation (Trans., 1905, 87, 313) that the rotation of ethyl tartrate may be considerably modified by admixture with inactive substances, and it is particularly noticeable that, in many cases, comparatively large effects are produced by small quantities of the inactive constituents. Thus, for instance, whilst the rotation of pure ethyl tartrate is $+9.354^{\circ}$, the addition of 25 per cent. of water raises it to $+10.242^{\circ}$, and the addition of 20 per cent. of chloroform lowers it to $+5.528^{\circ}$.

A consideration of the changes of rotation produced, either in concentrated or dilute solution by the addition of inactive solvents, suggested a further line of research, namely, an examination of the relative effects of isomeric solvents in modifying the rotation of active compounds, a problem which is at present being investigated. That symmetrical ethyl sulphite and asymmetrical ethyl sulphite, to take an example, will produce different effects on the rotation of an active compound dissolved in them is practically certain, but as to the magnitude of the difference, we can at present say nothing. This idea, however, in turn suggests the further possibility that if a substance capable of undergoing intramolecular change be dissolved in, say, ethyl tartrate, the rearrangement of the molecule of the former might be indicated and followed by the gradual alteration in the rotation of the latter, since the two different modifications of the inactive substance might have different solvent influences.

The present paper gives an account of some experiments which we have instituted in this direction. We chose as the first subjects for

examination the two oximes of benzaldehyde, passing then to anisaldoxime and to ethyl formylphenylacetate. In each case our expectations were realised, the results, especially in the case of the oximes, being of a much more striking character than could have been anticipated.

The polarimeter has, of course, often been used to follow the course of a chemical reaction as, for instance, the inversion of sucrose, which was studied by Wilhemy, or the mutual conversion of the nitro- and ψ -nitro-derivatives of camphor and π -bromo-camphor which Lowry (Trans., 1899, '75, 211) has described, but in all such cases the substance which undergoes change is the active compound itself, a condition which greatly limits the applicability of the method.

A polarimetric method which would make it possible to follow molecular change in inactive substances would obviously be of great service in various directions, and the possibility of establishing such a method, and one too of a general character, is certainly indicated by the above considerations.

EXPERIMENTAL.

It was of interest, to begin with, to ascertain the influence of benzantialdoxime on the rotation of ethyl tartrate, so we first directed our attention to this point.

The benzantialdoxime was prepared in the usual manner. It boiled at 122—123° at 19 mm. (oil-bath, 160°).

Determination of its density gave the following results :

Temperatures ...	18°	22°	26°	38°
Densities	1·11232	1·10854	1·10573	1·0957

Rotation of Ethyl Tartrate in Benzantialdoxime.

**p* : 79·90.

t° .	α_D^t (40 mm.).	Density.	$[\alpha]_D^t$.
16·4	+ 4·90°	1·1932	+ 12·85°
41·2	5·15	1·1680	13·79
61·3	5·32	1·1474	14·52
79·5	5·60	1·1285	15·52
94·4	5·80	1·1130	16·26
15·9	4·85	1·1938	12·71

Densities determined :

Temperatures	44·6°	47·5°	54·8°	64·75°	74·0°
Densities	1·1647	1·1616	1·1539	1·1443	1·1348

* *p* = grams of ethyl tartrate per 100 grams of solution.

$p: 49.6228.$

t° .	$\alpha_D^{t^{\circ}}$ (70 mm.).	Density.	$[\alpha]_D^{t^{\circ}}$.
13.8°	+4.25°	1.1644	+10.51°
20.5	4.40	1.1582	10.94
30.0	4.62	1.1493	11.57
37.8	4.80	1.1420	12.10
47.8	5.04	1.1326	12.81
67.1	5.45	1.1144	14.12
84.6	5.81	1.0980	15.23
91.1	5.94	1.0915	15.63
114.1	6.15	1.0720	16.53
131.5	6.30	1.0548	17.19
143	4.40	1.1640	10.88

Densities determined :

Temperatures	18°	22°	28.75°	40°
Densities	1.1605	1.1565	1.1504	1.1399

 $p: 22.819.$

t° .	$\alpha_D^{t^{\circ}}$ (70 mm.).	Density.	$[\alpha]_D^{t^{\circ}}$.
17.5	-0.04°	1.1352	-0.22°
26.1	+0.24	1.1274	+1.33
38.0	+0.60	1.1168	+3.36
41.2	+0.70	1.1140	+3.93
16.0	-0.08	1.1365	-0.37
56.4	+1.16	1.1101	+6.58
68.1	+1.52	1.0905	+8.73
82.3	+1.90	1.0780	+10.80
96.0	+2.12	1.0660	+12.45
117.5	+2.46	1.0484	+14.69

Densities determined :

Temperatures...	22°	28°	34.5°	45°	54.75°	77.7°
Densities.....	1.1313	1.1261	1.1204	1.1112	1.1027	1.0823

 $p: 10.372.$

t° .	$\alpha_D^{t^{\circ}}$ (100 mm.).	Density.	$[\alpha]_D^{t^{\circ}}$.
26.0°	-0.84°	1.1160	-7.26°
37.0	-0.39	1.1065	-3.38
56.1	+0.12	1.0905	+1.07
78.5	+0.70	1.0710	+6.30
96.0	+1.02	1.0565	+9.31
109.0	+1.24	1.0456	+11.43
122.5	+1.41	1.0392	+13.08
134.0	+1.52	1.0245	+14.30

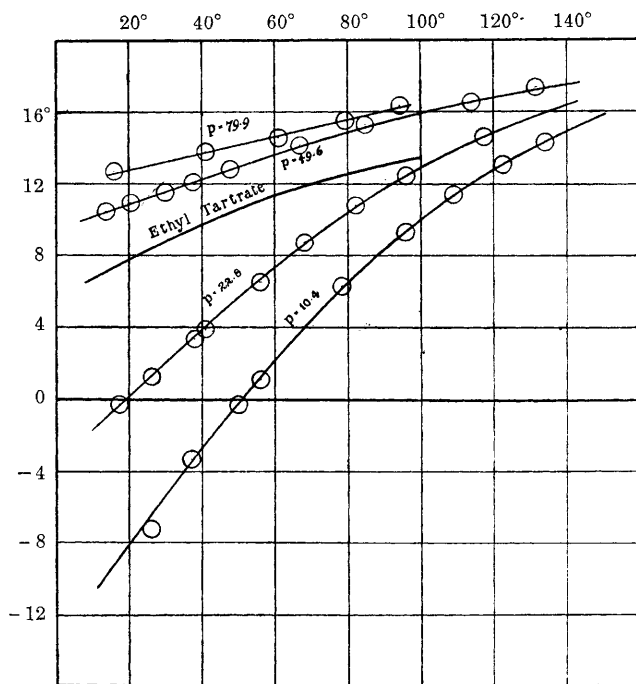
Densities determined :

Temperatures	21.5°	27.5°	33.6°	40.5°	44.5°
Densities	1.11976	1.11483	1.1096	1.1037	1.1003

The curves, which may be obtained from these data, showing the relationship between specific rotation and temperature, are reproduced

in Fig. 1, the graph for homogeneous ethyl tartrate being also shown for comparison. It will be observed at once that benzantialdoxime has a very remarkable effect on the rotation of ethyl tartrate. Whereas the rotation-temperature curves for the $p:80$ and $p:50$ solutions lie above that for the pure ester, those for solutions of $p:23$ and $p:10$ lie below it, at least at temperatures less than 100° . A behaviour similar to this has been observed in other cases, but the

FIG. 1.

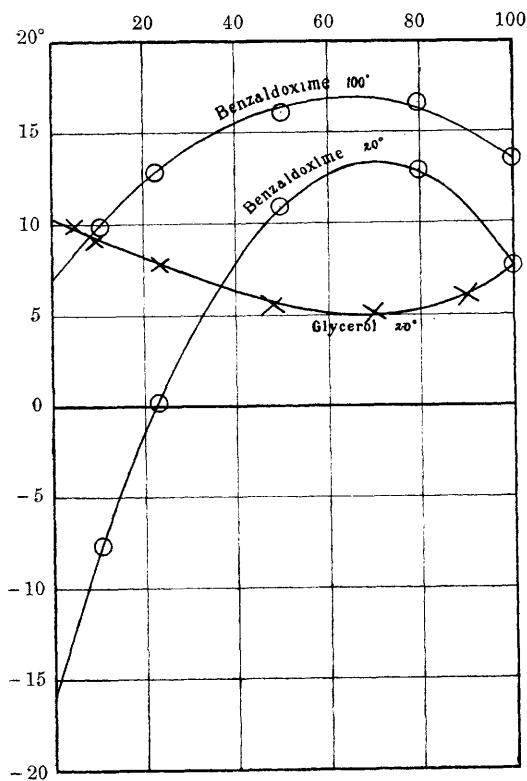
Temperature.*Temperature-rotation curves. Ethyl tartrate in benzantialdoxime.*

remarkable effect which dilution produces on the rotation of the dissolved ethyl tartrate is much more striking than in any other case hitherto examined. A $p:10$ solution which has $[\alpha]_D -7.7^{\circ}$ at 20° , 15.4° less than the pure ester, is inactive at about 51° , and at 100° has $[\alpha]_D +10^{\circ}$ which is only 3.5° less than that of the pure ester. The cause, therefore, which brings about the diminution of rotation is very rapidly overcome by rise of temperature.

By interpolation from these curves we find for the specific rotations of the solutions at 20° and 100° the following numbers:

p .	$[\alpha]_D^{20^\circ}$.	$[\alpha]_D^{100^\circ}$.	p .	$[\alpha]_D^{20^\circ}$.	$[\alpha]_D^{100^\circ}$.
100.0	+7.76°	+13.5°	22.82	+0.2°	+12.8°
79.9	+12.9	+16.4	10.37	-7.7	+9.9
49.62	+10.8	+16.1	0.0	-16.0	+7.0

FIG. 2.
Concentration.



Concentration-rotation curves. Ethyl tartrate in benzaldehyde and in glycerol.

From these data, the complete curves (benzaldehyde) in Fig 2 have been drawn. The rotation of the pure ester is +7.76° at 20°. Addition of aldehyde increases this rotation gradually until $p:70$, when a maximum value for the specific rotation of +13.6° is reached. Further addition of aldehyde then diminishes the rotation, which has in a solution of $p:37$ the same value as the homogeneous ester; a solution of $p:22$ is inactive, whilst a $p:10$ solution has a rotation equal in

magnitude, but opposite in sign to that of the pure ester. At infinite dilution the specific rotation would be approximately -16° . The rotation therefore varies some 30° between the extreme limits and by about equal amounts on either side of zero.

The concentration-rotation curve at 100° is also shown in the diagram. It is obviously of the same kind as the curve for 20° , but somewhat modified in form. The maximum occurs in both at almost the same concentration, $p:70$, and it is worthy of note that the concentration corresponding to a mixture of 1 molecule ethyl tartrate and 1 molecule oxime is $p:63$.

In this, then, as in other cases, the influence of changing concentration on rotation is much less striking at 100° than at 20° , although in the present instance still very remarkable.

The solvent which causes a variation most like this is glycerol (Trans., 1901, 79, 178). The concentration curve for ethyl tartrate in glycerol at 20° is shown in Fig. 2 for comparison. It will be observed that it is similar in character to that for the oxime, but in an exactly opposite sense. Addition of glycerol to ethyl tartrate gradually depresses the rotation of the ester to reach a minimum value at $p:68$ at 20° . Further addition of glycerol increases the rotation to reach $+7.76^\circ$ at $p:26$, whilst the value at infinite dilution is $+10.6^\circ$.

The peculiar form of the concentration-rotation curve for the oxime might perhaps encourage the idea that at $p:70$ the oxime exists chiefly in one form, whilst in dilute solution the other form preponderates, but our subsequent experiments seem to show that this is not the case, and that the remarkable form of this curve must be otherwise explained.

Experiments with Benzsynaldoxime.—Having thus established the influence of benzantialdoxime on the rotation of ethyl tartrate, we proceeded to a study of the behaviour of mixtures of ethyl tartrate with benzsynaldoxime.

Benzsynaldoxime was prepared from its hydrochloride by the action of slightly more than the calculated quantity of sodium carbonate solution. The solid after washing and thorough drying was crystallised as rapidly as possible from dry chloroform heated to about 50° . The preparation used melted at 127° .

We first made up a solution of $p:90.11$ (that is, one containing 9.89 per cent. of *synoxime*). The oxime did not dissolve very readily and slight heating was necessary. This solution was examined in a 100 mm. tube in the polarimeter. At 17.3° the observed rotation was $+11.38^\circ$, and after standing for half an hour this had fallen to 11.18° . The rotation was thus changing gradually, and to accelerate the alteration the tube containing the solution was heated to 50° for more than an hour and allowed to cool.

On the following morning the rotation had become $+8.15^\circ$ at 17.3° . No further alteration was observed.

Now it is well known that *benzsynaldoxime* readily changes into *benzantialdoxime*, and it was necessary to ascertain whether the above solution, after a constant rotation had been reached, corresponded with the solutions of *antioxime* which had been examined previously. Its rotation was therefore redetermined, after constant rotation had been reached, at several temperatures, with the following results:

$p:90.11$.

t° .	α_D^{20} (100 mm.).	Density.	$[\alpha]_D^{20}$.
17.3°	$+8.15^\circ$	1.2012	$+10.76^\circ$
27.8	8.52	1.1903	11.35
44.0	9.15	1.1740	12.36
20.0^*	8.25^*	1.1982	10.85^*

Densities determined:

Temperatures	21.1°	26°	34.25°	43.50°
Densities	1.1975	1.1922	1.1835	1.1746

* Interpolated.

The value $[\alpha]_D^{20} + 10.85$, for this solution thus falls exactly on the concentration curve deduced from solutions of the *antioxime*, and therefore the *synoxime* had been converted completely into the *anti*-form. The solution behaved exactly as if it had been made up originally with the *anti*-form although its behaviour at first was totally different. The magnitude of the change in the rotation of the ethyl tartrate due to this intramolecular rearrangement is most striking. Mixture with *antioxime*, as has been shown, raises the rotation of the ethyl tartrate, but mixture with the *synoxime* has a much more pronounced effect in the same direction. The observed rotation in this instance fell from $+11.38^\circ$ to $+8.15^\circ$, or by 3.23° for only 100 mm., and it must be remembered that $+11.38^\circ$ is not the true initial value for the solution of the *synoxime*, since the rotation had been falling during the preparation of the mixture, and whilst it was lying in the jacket of the polarimeter to attain uniform temperature.

That this very considerable change could be brought about by rearrangement of only 9.89 per cent. of inactive substance indicated a very simple means whereby the velocity of transformation of *synaldoximes* into *antialdoximes* under varying external conditions could be measured directly and easily in ethyl tartrate solution, an optical method being of course by far the best for the purpose since the substance undergoing change may be left entirely undisturbed during the course of the reaction.

Certain reactions of the oximes have already been submitted to

measurement. Thus Hantzsch (*Zeitsch. physikal. Chem.*, 1894, 13, 509) has determined the velocity with which the acetates of the *syn*oximes are converted into nitriles in aqueous ethyl-alcoholic solution, whilst Ley (*Zeitsch. physikal. Chem.*, 1895, 18, 376) has studied the influence of temperature on the velocity of this reaction and has also, by an ingenious but somewhat difficult method, measured the velocity of transformation of the acetates of the *syn*oximes into the corresponding salts of the *antioximes* under the influence of hydrochloric acid, but no method has hitherto been available for measuring the rate of transformation of a *syn*- into an *anti*-oxime.

We therefore proceeded to test our method, using a solution containing less oxime, the results being given in the following table. The values for initial rotation are obtained by extrapolation, and the time in minutes after preparation of the solution is given in the column headed T :

$p: 92.82. \quad a = 4.37^\circ. \quad \text{Temperature } 20^\circ.$

T (minutes).	$\alpha_D^{20^\circ}$ (100 mm.).	$a - x.$	1000 $k.$
0	+15.60°	—	—
45	15.1	3.87°	2.69
80	14.8	3.57	2.53
130	14.53	3.30	2.16
155	14.45	3.22	1.96
1115	12.625	1.395	1.09
3975	11.23	—	—

Now the transformation of a *syn*- into an *anti*-oxime ought to be a unimolecular reaction, and if we assume that the change of rotation of the ethyl tartrate is directly proportional to the change of concentration of the *syn*oxime we obtain the second and third columns in the above table, where α^0 = total change of rotation, x^0 is proportional to quantity of *syn*oxime transformed after time T , and k is calculated from equation:

$$k = \frac{1}{T} \log_e \frac{a}{a - x}.$$

The values thus obtained for k are not constant. The velocity of the transformation seems to be nearly 3 initially, diminishing, however, to about one-third of this value after 1000 minutes. The time required for one quarter of the transformation to take place is roughly 140 minutes, for half-change 490 minutes, and for three-quarter change 1190 minutes.

It was found in preparing the above mixture that the proportion of *syn*oxime used was still rather large to be brought into solution quite easily and, therefore, the next solution examined contained less oxime. The data for this solution were found as follows:

$p : 95.2$. Temperature 20° . $\alpha = 3.25^{\circ}$.

T (minutes).	α^2 (100 mm.).	$\alpha - x$.	1000 k .
0	13.95°	—	—
25	13.76	3.06°	2.41
40	13.60	2.90	2.85
85	13.33	2.63	2.49
130	13.13	2.43	2.23
220	13.00	2.30	1.57
295	12.83	2.13	1.43
360	12.73	2.02	1.31
415	12.60	1.90	1.29
1355	11.43	0.73	1.20
1590	11.25	0.55	1.12
1830	11.13	0.43	1.10
2840	10.73	—	—
3150	10.70	—	—
4170	10.70	—	—

It will be observed that the behaviour here is much the same as in the previous instance. The velocity of transformation falls off gradually as time elapses. It is possible that the value of k after 25 minutes is incorrect. From about 80 minutes on the values are almost the same as in the $p : 92.82$ solution, and the initial value is also probably nearly 3.

Influence of Temperature on the Velocity of Transformation.

We next proceeded to determine the influence of temperature on the velocity of transformation of the oxime, using two solutions of as nearly as possible $p : 95$. The results are recorded below. The temperature (t°) was kept as near 32.4° and 42.9° as we could, but it varied slightly :

$p : 95.10$. $\alpha = 2.56^{\circ}$.

T (minutes).	t° .	α_p° (100 mm.).	$\alpha - x$.	1000 k .
0	—	+ 14.3°	—	—
15	32.4°	14.14	2.4°	4.27
45	32.4	13.84	2.10	4.40
80	32.8	13.60	1.86	3.99
120	32.4	13.33	1.59	3.97
175	32.4	13.07	1.33	3.74
245	32.5	12.76	1.02	3.75
360	32.5	12.42	0.68	3.68
390	32.5	12.30	0.56	3.89
450	33.1	12.20	0.46	3.81
1190	32.8	11.74	—	—
1260	33.0	11.74	—	—

$$p : 95.2. \quad \alpha = 2.5^\circ.$$

<i>T</i> (minutes).	<i>t</i> °.	<i>α</i> °.	<i>a</i> - <i>x</i> .	1000 <i>k</i> .
0	—	+15.00	—	—
15	42.9°	14.62	2.12°	11.0
30	42.9	14.28	1.78	11.3
75	42.8	13.61	1.11	10.8
160	42.8	12.97	0.47	10.4
225	42.5	12.74	0.24	10.4
310	42.8	12.58	0.08	11.1
360	42.8	12.53	0.03	12.3
510	42.6	12.50	—	—
590	42.5	12.50	—	—

The initial velocities for these solutions found by plotting curves are about 4.6 and 11 respectively.

In regard to the data for these two solutions, two facts may be noticed. In the first place, the velocity of transformation increases rapidly with rise of temperature, having at 20° an initial value of about 3, at 32.4° one of about 4.6, and at 42.9° one of 11. In the second place it is very noticeable that whilst at 20° the values found for *k* diminish as time elapses, the diminution in the value of *k* at 32.4° is distinctly less, and at 42.9° *k* is practically a constant.

The variation in the value of *k* at the lower temperatures is perplexing. It may possibly be due to some tendency of the *synoxime* and tartrate to combine with each other, the combination taking place only slowly. This might hinder the change of the *syn*- into the *anti*-form, and diminish the rate of transformation, but it does not seem to prevent the change, since the solutions made up with *synoxime* assume, ultimately, exactly the same rotation values as solutions made up with the *antioxime*.

It seemed of interest to ascertain if there exists in solution any equilibrium between *syn*- and *anti*-form. We therefore prepared solutions of ethyl tartrate and solid benzantialdoxime, m. p. 35° (which dissolves very readily), but we were unable with the means at our disposal to detect any increase in the rotation of these on standing; the change appears to be irreversible.

Another explanation of the inconstancy of *k* at 20° occurred to us. In making our calculation we have assumed that the change in rotation is directly proportional to the amount of *synoxime* transformed, but it is possible that this might not be so. To test the point, we made up several solutions, each containing the same total amount of oxime, but made up by mixing the *syn*- and *anti*-oximes in varying proportions.

These experiments were carried out with a fresh preparation of ethyl tartrate which, unfortunately, does not seem to have been quite pure.

514 PATTERSON AND McMILIAN: THE INFLUENCE OF SOLVENTS

It had been twice distilled, and gave $\alpha_D^{19.8} + 9.45^*$, but it possibly contained some moisture. The results are therefore not strictly comparable with the preceding, but they serve to elucidate the point under consideration:

I.—Ethyl tartrate.....95.09 }
 *syn*Oxime..... 4.91 } . Temperature 20°. $\alpha = 2.7^\circ$

<i>T</i> (minutes).	$\alpha_D^{20^\circ}$ (100 mm.).	$\alpha - x$.	1000 <i>k</i> .
0	+13.20°	—	—
25	12.72	2.22°	7.83
65	12.32	1.82	6.06
150	11.92	1.42	4.28
220	11.66	1.16	3.83
1235	10.66	0.16	2.28
1370	10.50	—	—
∞	10.50	—	—

II.—Ethyl tartrate.....95 per cent.

 Benzsynaldoxime 4 ,,

 Benzantialdoxime ... 1 ,,

$\alpha = 2.19^\circ$.

<i>T</i> (minutes).	$\alpha_D^{20^\circ}$ (100 mm.).	$\alpha - x$.	1000 <i>k</i> .
0	+12.70°	—	—
35	12.36	1.85°	5.11
105	11.96	1.45	3.89
165	11.81	1.30	3.16
225	11.70	1.19	2.71
540	10.70	0.19	1.93
2600	10.51	—	—

III.—Ethyl tartrate.....95.06 per cent.

 Benzsynaldoxime 2.47 ,, }

 Benzantialdoxime 2.47 ,, } 4.94.

$\alpha = 1.2^\circ$.

<i>T</i> (minutes).	$\alpha_D^{20^\circ}$ (100 mm.).	$\alpha - x$.	1000 <i>k</i> .
0	+11.70°	—	—
50	11.46	0.96°	4.46
115	11.30	0.80	3.52
220	11.16	0.66	2.71
320	11.03	0.53	2.55
1395	10.68	0.18	1.36
1525	10.65	0.15	1.36
1660	10.61	0.11	1.43
2800	10.50	—	—

* This is very near the rotation of pure ethyl tartrate, but since water raises the rotation of ethyl tartrate, the presence of a small quantity of moisture may easily escape detection.

IV.—Ethyl tartrate.....95·10 per cent.

Benzsynaldoxime 0·98	„	} 4·90
Benzantialdoxime 3·92	„	

$$a = 0·54^{\circ}.$$

T (minutes).	$\alpha_D^{20^{\circ}}$ (100 mm.).	$a - x$.	1000 k .
0	+11·04°	—	—
35	10·90	0·40°	8·57
65	10·80	0·30	9·04
140	10·73	0·23	6·09
1280	10·50	—	—

V.—Ethyl tartrate.....95·02 per cent.

Benzantialdoxime	... 4·98	„
------------------	----------	---

$$\alpha_D^{20^{\circ}} + 10·50.$$

The values for the initial rotations of these solutions were obtained by graphic extrapolation. When they in turn are plotted relative to concentration they are found to lie practically on a straight line, so that our assumption that the change in rotation is proportional to the concentration of the *synoxime* is justified.

The first of these solutions ought to have corresponded exactly with that for which data are given on p. 512, but this is not the case. Both the initial and end rotations are different, and k is considerably higher. This, as has been remarked, was due to insufficient purification of this sample of ethyl tartrate.

The values of k ought to be the same for all the solutions, and that this is not the case is, we think, due chiefly to the fact that these mixtures were made by heating the constituents together in a small open flask in a warm-water bath, and that possibly traces of moisture may have been introduced in this way in the first and last. The first three solutions agree fairly well, and it must be remembered that in the last the total change was small.

Experiments with Anisaldoxime.—It seemed next of interest to ascertain whether the behaviour we have observed with the benzaldoximes was a specific property of these substances or whether it applied to oximes generally. We used for the purpose some anis-synaldoxime prepared by Mr. Andrew Henderson, M.A., B.Sc., to whom we have pleasure in expressing our thanks. The *synoxime* used was recrystallised in small quantities from warm benzene. It melted at 125°.

Anis-synaldoxime in Ethyl Tartrate. $p:95.13$. Temperature 20° . $\alpha = 2.504^{\circ}$.

T (minutes).	$\alpha_D^{20^{\circ}}$ (100 mm.).	$\alpha - x$.	1000 k .
0	+13.77°	—	—
25	13.533	2.267°	3.95
50	13.343	2.077	3.72
165	12.563	1.297	3.98
210	12.383	1.117	3.84
285	12.088	0.822	3.91
370	11.863	0.597	3.87
430	11.749	0.483	3.83
605	11.499	0.233	3.92
∞	11.266	—	—

A solution of concentration similar to the preceding one, but made up with *anisantaldoxime*, gave a rotation at 20° which agrees with the end rotation of the *synoxime* solution.

If we compare the values of k found for this solution with those already given for a $p:95$ solution of *benzaldoxime*, we find that, while the velocity of change is somewhat higher and the total change of rotation less, the constancy of k is much better. Quarter change takes place in about seventy-five minutes, half change in 175 minutes, and three-quarter change in 360 minutes.

We next examined *anissynaldoxime* in a mixed solution of ethyl tartrate and *isobutyl* alcohol, and also in a solution of ethyl tartrate and benzene, with the object of ascertaining the relative influences of *isobutyl* alcohol and benzene on the velocity of the intramolecular change.

The results are given below :

Anis-synaldoxime, Ethyl Tartrate and isoButyl Alcohol.

Composition of solution $\left\{ \begin{array}{l} \text{isoButyl alcohol} = 73.17 \text{ per cent.} \\ \text{Ethyl tartrate} = 24.39 \text{ ,, ,,} \\ \text{Anis-synaldoxime} = 2.44 \text{ ,, ,,} \end{array} \right\} p:9.10 \text{ of oxime.}$

$$\text{Ratio} \dots \dots \dots \frac{E.T.}{\text{Oxime}} = \frac{10}{1}.$$

Temperature 20° . $\alpha = 0.368^{\circ}$.

T (minutes).	$\alpha_D^{20^{\circ}}$ (400 mm.).	$\alpha - x$.	1000 k .
0	+6.778°	—	—
45	6.726	0.316°	3.37
95	6.686	0.276	3.02
210	6.617	0.207	2.73
345	6.534	0.124	3.15
2805	6.410	—	—
∞	6.410	—	—

Anis-synaldoxime Ethyl Tartrate and Benzene.

Composition of solution	Benzene	= 73.29 per cent.	} <i>p</i> : 9.135 of oxime.
	Ethyl tartrate	= 24.27 „ „	
	Anis-synaldoxime	= 2.44 „ „	
Ratio.....		$\frac{E.T.}{\text{Oxime}} = \frac{10.05}{1}$	

Temperature 20°. $\alpha = 3.667^\circ$.

<i>T</i> (minutes).	α_D^{20} (400 mm.).	$\alpha - \alpha_0$	1000 <i>k</i> .
0	8.980°	—	—
50	7.713	2.400°	8.48
105	6.794	1.481	8.63
150	6.289	0.976	8.82
200	5.988	0.675	8.46
235	5.863	0.550	8.07
270	5.713	0.400	8.21
1310	5.313	—	—

From these data it appears that the change in rotation in the solution containing *isobutyl* alcohol is comparatively slight. The values for *k*, however, agree fairly closely and do not seem to diminish with lapse of time.

The numbers for the benzene solution are most striking. The total change in rotation is considerable, 3.667°, the velocity of change is much greater than in *isobutyl* alcohol or in undiluted ethyl tartrate and the values for *k* show a very fair constancy.

We also examined a solution similar to the last two, but containing chloroform as a third constituent. The result was as follows :

Anis-synaldoxime, Ethyl Tartrate and Chloroform.

Composition of solution	Chloroform	= 73.24 per cent.	} <i>p</i> : 9.16 of oxime.
	Ethyl tartrate	= 24.31 „ „	
	Anis-synaldoxime	= 2.45 „ „	
Ratio.....		$\frac{T.}{\text{Oxime}} = \frac{9.92}{1}$	

Temperature 20°. $\alpha = 0.15$.

<i>T</i> (minutes).	α_D^{20} (400 mm.).	$\alpha - \alpha_0$	1000 <i>k</i> .
0	-1.600°	—	—
115	1.544	0.094°	4.06
180	1.514	0.064	4.73
265	1.450	—	—
1300	1.450	—	—

The alteration in rotation is very small, and this is probably due to the great depressing influence of chloroform on the rotation. Chloro-

form has so great an influence in this direction that it might be expected that a small proportion of another substance, even if exceptionally powerful, would only have a very slight effect. It is particularly noticeable that whereas in all cases examined, the rotation is raised by addition of *synoxime* and gradually falls, in chloroform the depressed rotation is raised by addition of *synoxime* and that change into *anti-oxime* brings about a further rise in rotation. On account of the change of rotation being so small we lay no stress on the values of the constant which can be calculated from the rotation data, although we have included the numbers in the table.

Experiments with Ethyl formylphenylacetate.—In order to ascertain if this method was applicable also to other types of intramolecular change, we obtained some of each of the two forms of formylphenylacetic ethyl ester* and examined solutions of these in ethyl tartrate. In mixtures containing 5 per cent. of the acetic ester the change in rotation was very slight. We therefore prepared a *p*:60:44 solution of the solid (β or aldo) form in ethyl tartrate. Heating was necessary to bring about solution and on cooling to 20° the solid ester crystallised out. We, therefore, determined the rotation of this mixture at several higher temperatures in order to obtain the value for 20° by extrapolation.

The following are the data :

t° .	α_D^{20} .	t° .	α_D^{20} .	t° .	α_D^{20} .
58.6°	+4.77°	43.5°	+4.69°	29.0°	+4.58°

The value at 20° by extrapolation is +4.53°, but we found that after the heating necessary in these experiments the acetic ester no longer crystallised out on cooling and the rotation could be determined even at 11.5° when its value was +4.44° which is in agreement with the numbers given above. Since the acetic ester did not crystallise out, it is apparent that change had taken place and this may have been accompanied by some alteration in rotation, but this was probably slight since the value found at 11.5° after the mixture had stood overnight agreed with those obtained at higher temperatures.

We then prepared a similar solution of the liquid (α or enol) form, which is the less stable, and were able to observe in this case a distinct, although not very great, change at 20°. The results were as follows :

* Our thanks are due to Mr. R. Boyd who prepared these for us.

Ethyl Formylphenylacetate (α -form) in Ethyl Tartrate $p:59\cdot90$.

Temperature 20° . $\alpha = 0\cdot424^{\circ}$.

T (minutes).	α_D^{20} (50 mm.).	$\alpha - \alpha$.	1000 k .
0	$+3\cdot972^{\circ}$	—	—
65	4·066	$0\cdot330^{\circ}$	3·84
190	4·149	$0\cdot247$	2·78
310	4·199	$0\cdot197$	2·47
1390	4·316	$0\cdot080$	1·19
1540	4·349	$0\cdot047$	1·42
∞	4·396	—	—

In this case the rotation of the solution increases gradually and by nearly one degree for a length of 100 mm. The constant obtained from our data is not very satisfactory, diminishing to a considerable extent with lapse of time. Possibly the cause may be the same as that which operates in the case of benzsynaldoxime in ethyl tartrate. The results are promising, however, and indicate that we have in this method a means of following quantitatively changes that have hitherto only been susceptible of qualitative examination. The method, we think, may be fairly described as general, inasmuch as, although it may fail in certain cases, it is probable that some active compound may always be found the rotation of which will alter in response to intramolecular change in an inactive substance.

The experiments which we have recorded here are to some extent of a preliminary character. The apparatus which we have used was not specially designed for the purpose and we intend with more suitable and more delicate appliances to extend this investigation in some of the many directions that readily suggest themselves—to the influence of various media on velocity of transformation, to the use of other active substances as media, and to the investigation of various examples of tautomeric change.

THE UNIVERSITY,
GLASGOW.