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ON THE INHIBITION OF CHEMICAL REACTIONS BY FOREIGN SUBSTANCES. I.

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IN a recent paper[1] attention was called to some very curious phenomena which showed themselves in the oxidation of solutions of stannous chloride by means of free oxygen. These phenomena consist in very marked reduction of the rate of the oxidation as a result of the presence of relatively small quantities of poisonous substances, especially alkaloids. It was, however, seen that potassium cyanide also possessed this power.

It was thought well to delay the further investigation of these curious actions until the course of the reaction between stannous chloride and free oxygen was somewhat more thoroughly understood. The attempt to follow the course of the reaction was successful,[2] but unfortunately, the result was to show that the reaction was complex, taking place in two stages, and on account of this complication, little suited to the investigations in question. It was, therefore, thought advisable to choose another reaction, provided one could be found which would be sensitive to these peculiar agencies.

A solution of arsenic trioxide in water was first tried, but

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[1] This Journal, **23**, 140.

[2] *Ibid.*, **23**, 450.

neither in acid, neutral nor alkaline solution was its oxidation rate sufficiently great to allow of its being used without enormous loss of time. Nor was sufficient acceleration produced by previously treating the solution with hydrogen sulphide or after boiling it for some time with arsenic sulphide.[1] The same difficulty was found with ferrous sulphate. Several other substances were tried, but their oxidation rates were found to be either too high (in which case the rate of oxidation is not independent of the action of the apparatus) or too low. Finally a solution of sodium bisulphite was tried and this gave more hopeful indications. The sodium bisulphite used was a commercial product and probably not very pure. Twenty-five cc. of a solution of this substance, of unknown strength, were placed in the shaking apparatus[2] at 25° C. This showed an oxidation rate of 0.2 cc. in three minutes. A trace of copper sulphate raised this to 0.3 cc. in two minutes, and finally the addition of a small quantity of ferrous sulphate raised the rate to 0.5 cc. in one minute. While the absorption was progressing at this last rate, a small quantity of a brucine hydrochloride solution was injected. From this point on the results are given in the following table. In this table $T =$ time in minutes ($T = 0 =$ time of injection of brucine).

$V =$ Volume reading on the gas burette.

$\frac{\Delta V}{\Delta T} =$ Average absorption per minute in each interval of observation.

$T =$	0	1	2	3	4	5	6
$V =$	45.5	42.50	40.80	40.00	39.70	39.55	39.45
$\frac{\Delta V}{\Delta T} =$	....	3.00	1.70	0.80	0.30	0.15	0.10
$T =$	7	9	10	15	20	30	38
$V =$	39.40	39.34	39.30	39.05	38.80	38.35	38.00
$\frac{\Delta V}{\Delta T} =$	0.05	0.03	0.04	0.05	0.5	0.045	0.044

At $T =$ thirty-eight minutes, the shaking was discontinued for twenty-two hours. During this time 10.2 cc. had been absorbed. On shaking, the following results were obtained :

$T =$	0	90.
$V =$	27.8	26.60
$\frac{\Delta V}{\Delta T} =$	...	0.013

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[1] See Mohr : "Titrir-methode," 1886, p. 364 ; also Young : This Journal, **23**, 143-144.

[2] This Journal, **23**, 119.

Further observations were made with this solution, which need not be recorded here. Gradual reduction of the rate of absorption was noted, due mainly, of course, to the gradual decrease in the concentration of bisulphite.

The results of this first experiment are given here in detail because they afford a good illustration of several of the phenomena to which this paper is devoted. They are: (1) acceleration by means of salts of copper and iron; (2) an initial acceleration upon adding a small quantity of brucine hydrochloride; (3) the rather rapid decrease of the reaction rate thereafter, to a very small value. As the bisulphite showed the phenomena sought in so satisfactory a manner, considerable time has been devoted to its study. It was, however, thought best to use the neutral sulphite as the basis of the solutions studied, as this could be studied equally well in acid, neutral or alkaline solution.

Before passing to a study of the results which are given in the following paper, I wish to suggest a terminology, which must, of course, be considered as subject to change. The phenomena involved are almost wholly new, and something of the sort seems necessary. Bredig,[1] working in a somewhat analogous field, has used the word "poisoning" (Vergiftung) to describe the effect of poisons upon the rate of catalysis by colloidal platinum and gold solutions.

In view of the apparently rather broad analogy existing between physiological poisoning and the phenomena in question one might be almost tempted to follow this usage in the present case. After some thought, it seems to me, however, that such usage is scarcely justifiable at present. In the first place, it is by no means true that the retarding actions under consideration are confined to physiological poisons; and in the second place it is by no means certain that the analogy, in general, is more than superficial. Under these conditions it would seem that the application of the concept of "poisoning" to an entirely new domain is likely to lead to confusion, useless speculation and to superficiality in the investigation of the field. I will, therefore, use the word "inhibition" to cover the phenomena in point, this word having, so far as I am aware, no present technical significance in chemistry. An "inhibitive agent" is then a substance producing an "inhibition," or having an "inhibitive effect." For the

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[1] Bredig and Müller von Berneck: *Ztschr. phys. Chem.*, **31**, 258, and later papers.

period beginning with the addition of the inhibitive agent and ending with the time when the inhibitive influence reaches its maximum the true period of development of the inhibition, or more simply, the "development period" will be used. The introduction of these terms, at least for present use, seems to me to be justifiable. The phenomena may naturally be included under the general head of negative catalysis.

It may be stated here that the results following lay no claim to being more than roughly quantitative. No special precautions were taken to purify the distilled water used, and as Bigelow[1] has shown, the character of the distilled water used has a considerable influence upon the rate of oxidation. The object has been solely to study the general character of the phenomena and their scope.

I. THE APPARATUS.

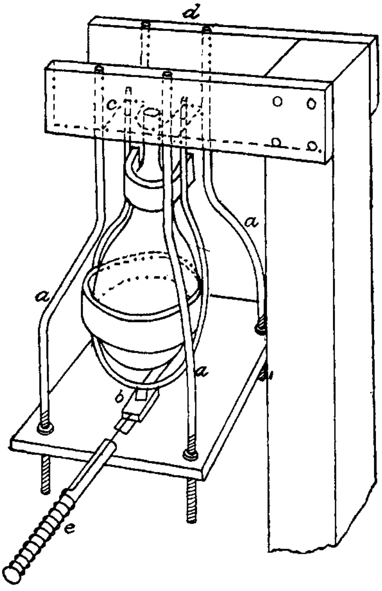

Fig. 1.

The apparatus used was a modification of the one used in the studies with stannous chloride. The chief modification is of sufficient importance to be sketched here. It lies wholly in the shaking part of the machine. Whereas this in the old machine[2] was fastened in the thermostat tank, in the new one it is wholly independent of this. The great advantage lies in the avoidance of the jarring and shaking of the thermostat, which sometimes, in the old machine, threatened to fall from its supports, and required constant vigilance. The new apparatus will run indefinitely without attention. The new arrangement is shown in Fig. 1. It consists of a stout wooden stand which can be raised and lowered at will. In the two horizontal arms of this stand are fixed four stout rods of $^1/_4$ inch brass, *a*, *a*, *a*, *a*, which are

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[1] *Ztschr. phys. Chem.*, **26**. 493.

[2] This Journal, **23**. 121.

doubly curved as in the drawing. The lower ends of these rods are threaded for a distance of about 4 inches. Upon these rods is supported a rectangular brass plate, $^1/_8$ inch thick, with $^1/_4$ inch holes at each corner. This platform is fastened to the rods by means of two nuts on each rod, one above and one below the plate. These, when screwed tight, hold the platform very firmly in place, and furthermore allow of adjusting the height of the platform, as may be desired.

Down the middle of the platform longitudinally is cut a slot in which runs a small carriage, *b*, also of brass. This slides freely back and forth in the slot, and is provided with a simple device for attaching the bottom of the carrier in which is held the flask. This carrier is the same as was used in the experiments with stannous chloride. The brass rods at the top of this carrier pass through holes in the brass plate *c* which is fastened to one of the horizontal arms of the wooden stand. The whole carrier and flask are thus easily removable from the apparatus. The shaking is brought about by an electric motor with variable resistance to regulate speed. A stout gut cord passes from the crank of the motor over a pulley fastened on the back of the far arm of the wooden stand (near *d*), thence downward under a second pulley (not shown) fastened at the far end of the brass platform. Thence it runs to the carriage *b*, to which it is fastened. The return of the flask to its original position after being pulled to the far end of the platform, is brought about by the spiral spring *e* of hardened brass wire. As a matter of fact. two such springs are used, one fastened to the carrier above, and the other below the platform. This insures more even working of the carriage in the slot. Simple devices allow of the regulation of the length of stroke, and of the tension of the springs. Having once gotten the apparatus in order, I have used it for nearly four months, almost daily, and some times for eight hours per day, without the necessity for the slightest repair or alteration, except that one gut string had to be replaced.

The method used in the following experiments was the same as was used in the studies with stannous chloride, and for further details the reader must be referred to that paper.

2. SCOPE OF THE PHENOMENON OF INHIBITION.

So far as I am aware almost all reactions which have heretofore shown the phenomenon of inhibition, *i. e.*, a marked reduction of the reaction rate under the influence of minute quantities of foreign substances, are reactions in which free oxygen is concerned in some way or other. Exceptions are apparently to be found in some cases, in the action of enzymes.

The reactions which are of the greatest importance for us here may be divided into two groups: (1) reactions in which hydrogen peroxide is decomposed with the evolution of free oxygen; (2) the voluntary (and catalytically accelerated) oxidation of certain substances by free oxygen. The literature bearing upon the first group has been brought together and materially extended by Bredig and his coworkers.[1]

In this group we have to do always with a deadening of the efficiency of a positive catalysor or accelerator. Among these catalysors we find certain organic ferments. platinum foil and black and colloidal platinum and gold solutions. The accelerating action of these substances is greatly diminished by the addition of minute quantities of a great variety of substances, including hydrogen sulphide, carbon bisulphide, hydrocyanic acid, mercuric chloride, etc. The catalytic action of the blood corpuscles is also reduced by minute traces of hydrocyanic acid. Bredig[2] states that strychnine is apparently without action in the catalysis of hydrogen peroxide by means of colloidal platinum.

In the second group we have to do with reactions in some cases, which are apparently not catalytically accelerated in the first place, *i. e.*, with a true negative catalytic effect.[3] All such cases, so far as I know, are reactions of oxidation by means of free oxygen. Among these are to be mentioned: (1) the influence of small quantities of foreign substances in oxygen upon the glowing of phosphorus;[4] (2) the phenomena observed by Bigelow[5] in connection with the oxidation of sodium sulphite by the oxygen of the air; (3) the phenomena involved in the oxidation of stannous chloride by means of oxygen.[6] A case of reduction of

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[1] Bredig and Müller von Berneck: *Loc. cit*; Bredig and Ikeda: *Ztschr. phys. Chem.*, **37**, 1; Bredig and Reinders: *Ibid.*, **37**, 323.

[2] *Loc. cit.*

[3] We may, for convenience, distinguish between "apparent" negative catalysis, or the reduction of the activity of a positive catalysor, and "true" negative catalysis, or the reduction of the rate of a reaction occurring without previous catalytic acceleration.

[4] The literature of this subject together with new results is to be found in a paper by Centnerzwer: *Ztschr. phys. Chem.*, **26**, 1.

[5] Bigelow: *Ibid.*, **26**, 493.

[6] *Loc. cit.*

reaction rate in an already catalytically accelerated oxidation was found by Ernst[1] in the oxidation of hydrogen by oxygen in presence of a colloidal platinum solution. The same phenomenon with platinum foil was observed by Faraday.

In order to gain some idea of the scope of these inhibitive actions in the oxidation of sodium sulphite, several experiments were carried out by me upon the oxidation by means of agents other than oxygen. The substances chosen were nitrous and nitric oxides ; both being gases. the phenomena allowed of being studied in the apparatus with which I was working.

a. Experiments with Nitrous Oxide.—The experiments with nitrous oxide were carried out exactly according to the method described in the previous paper[2] for studying the oxidation of stannous chloride. The nitrous oxide was prepared from ammonium nitrate and stored for use in a gas-holder. On beginning the experiment, a very marked decrease in the volume of the gas in the burette was noticed, due, of course, to the solubility of nitrous oxide in the solution. After this first rapid absorption had ceased, measurements were begun. After a time a quantity of brucine hydrochloride solution was added and measurements continued. The results of two series of measurements are given below. In the first series water was used in the gas burette. As it was thought that the slow decrease in volume might possibly be due to gradual absorption of the gas by the water in the burette, mercury was used in the second experiment, and this was. futhermore, allowed to stand for a couple of days after the measurements were discontinued in order to see to a certainty whether a reaction really occurred. T is given in minutes.

EXPERIMENT I.

					1 cc. $\frac{m}{10}$ brucine hydrochloride added.[3]		
$T =$	0	10	20	30	0	10	20
$V =$	36.2	35.85	35.5	35.2	35.45	35.10	34.75
$\frac{\Delta V}{\Delta T} =$	....	0.035	0.035	0.035	....	0.035	0.035

After making the solution slightly acid the rate of absorption remained unchanged.

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[1] Ernst: *Ztschr. phys. Chem.*, **37**. 448.

[2] *Loc. cit.*

[3] *m* is used here to represent the molecular or "molar" weight. *Cf.* Noyes: This Journal, **23**, 41.

Experiment 2.

	Mercury in gas burette.				1 cc. $\frac{m}{10}$ brucine hydrochloride added.		
$T =$	0	5	10	15	0	5	10
$V =$	39.7	39.55	39.40	39.20	39.35	39.15	38.95
$\frac{\Delta V}{\Delta T} =$	...	0.03	0.03	0.04	...	0.04	0.04

The volume after standing for twenty-four hours had decreased to 28.2 cc. After forty-eight hours to 19.3 cc. Thus during the whole time over 20 cc. of the gas had been absorbed, which shows conclusively that a reaction of some sort takes place. The evidence of both sets of observations goes to show, however, that the rate of this reaction is not measurably influenced by the addition of the indicated amount of brucine hydrochloride solution. The sulphite solution used in these experiments contained 2.5 grams of crystallized sulphite per 100 cc. of solution. As will be shown later the amount of brucine used here would have sufficed in case of oxidation with oxygen to have reduced the rate to $^1/_{15}$, or less, of its original value. The conclusion would seem to be justified that the reaction between nitrous oxide and sodium sulphite is uninfluenced by brucine.

b. Experiments with Nitric Oxide.—The first few attempts to follow the reaction between sodium sulphite and nitric oxide showed that the reaction goes too rapidly to be measured with certainty in the apparatus in use, and the same was found true of stannous chloride. A 0.2 normal solution of stannous chloride absorbed the gas at the rate of about 25 cc. per minute. No measurable influence was exerted by the addition of relatively large quantities of brucine hydrochloride. A solution of 5 grams of sodium sulphite in 200 cc. of solution gave approximately the same result. With such rapid absorption it is probable that it is more nearly the absorption rate than the oxidation rate that is measured. By using a solution only one-half as strong as the above, the rate was still too rapid for certainty. The results of such a series is given here. As will be seen the addition of the brucine hydrochloride has again no noticeable effect. Time in minutes:

			Added 1 cc. $\frac{m}{10}$ brucine hydrochloride.							
$T =$	0	½	1	1½	2½	3½	4½	6½	7½	10
$V =$	47.0	40.7	36.7	33.2	26.4	17.7	9.9	20.6	20.5	20.4
$\Delta V =$	...	6.3	4.0	3.5	6.8	8.7	7.8	—10.7	+0.1	+0.1

An inspection of these results shows no appreciable drop in the reaction rate upon addition of the brucine hydrochloride, or at least none in any way comparable with the drop noticed (see later) in results with oxygen. A most marked feature of the results is seen in the fact that the gas volume at first rapidly decreases, then increases very rapidly and finally very slowly decreases again. Several experiments showed this to be a constant phenomenon and use was made of it to determine, if possible, an influence of the alkaloid upon the rate or course of the reaction. Several series of observations were made upon solutions without addition of brucine hydrochloride and several with addition of this reagent. *T* in minutes:

a. Results without Brucine.

1.			2.			3.			4.		
T.	*V.*	Δ*V.*	*T.*	*V.*	Δ*V.*	*T.*	*V.*	Δ*V.*	*T.*	*V.*	Δ*V.*
0	49.0	....	0	50.0	....	0	46.5	....	0	50.0	....
½	39.0	+10.0	½	45.0	+5.0	½	37.5	+ 9.0	½	39.0	+11.0
1	32.5	+ 6.5	1	42.0	+3.0	1	32.5	+ 5.0	1	30.5	+ 8.5
1½	26.0	+ 6.5	1½	38.5	+3.5	1½	27.0	+ 5.5	1½	22.5	+ 8.0
2	20.5	+ 6.5	2	35.5	+3.0	2	22.0	+ 5.0	2	16.5	+ 6.0
2½	15.5	+ 5.0	2½	30.0	+5.5	2½	18.0	+ 4.0	2⅓	14.2	+ 2.3
3	11.2	+ 4.3	3	25.4	+4.6	3	14.0	+ 4.0	3	21.5	— 7.3
3½	8.0	+ 3.2	3½	22.4	+3.0	3½	10.8	+ 3.2	3½	22.4	— 0.9
3⅚	6.5	+ 1.5	4	20.5	+1.9	4	8.5	+ 2.3	4	22.3	+ 0.1
4¼	11.0	— 4.5	4½	17.3	+3.2	4½	10.0	— 1.5	5	22.2	+ 0.1
4½	19.0	— 8.0	5	15.2	+2.1	5	20.0	—10.0			
5	21.4	— 2.4	5½	17.5	—1.8	5½	21.0	— 1.0			
6	21.1	+ 0.3	6	25.5	—8.5	8	20.6	+ 0.4			
8	20.9	+ 0.2	6½	25.8	—0.3	10	20.5	+ 0.1			
			7	25.65	+0.15	35	19.8	+ 0.7			
			8	25.4	+0.25	42 hrs.	5.1	+14.7			

b. Results with Brucine Hydrochloride.—In these experiments, the brucine hydrochloride was added before beginning the experiment. One cc. of $\frac{m}{10}$ brucine hydrochloride was used.

1.			2.			3.		
T.	*V.*	Δ*V.*	*T.*	*V.*	Δ*V.*	*T.*	*V.*	Δ*V.*
0	50.0	....	0	50.0	...	0	50.1	....
½	43.0	+ 7.0	½	38.0	+ 12.0	½	38.0	+ 12.0
1	37.0	+ 6.0	1	31.0	+ 7.0	1	26.0	+ 12.0
1½	31.0	+ 6.0	1½	26.0	+ 5.0	1½	19.0	+ 7.0
2	25.7	+ 5.3	2	24.5	+ 1.5	2	24.0	— 5.0
2½	21.5	+ 4.2	2½	23.5	+ 1.0	2½	29.5	— 5.5
3	19.0	+ 2.5	3	23.1	+ 0.4	3	29.6	— 0.1
3½	28.0	— 9.0	3½	26.0	— 2.9	5	29.4	+ 0.2
4	28.3	— 0.3	4	30.9	— 4.9			
5	28.2	+ 0.1	5	30.6	+ 0.3			

In the experiments without brucine hydrochloride, the turning-point in the volume reading occurred after respectively $3^5/_6$, 5, 4, and $2^1/_3$ minutes. With brucine, after respectively 3, 3, and $1^1/_2$ minutes. Without brucine hydrochloride, the turning-point occurred after the following volumes had been absorbed: 42.5 cc., 34.8 cc., 38 cc., and 35.8 cc.; with brucine hydrochloride, after respectively 31 cc., 27 cc., and 31 cc. had been absorbed.

The variations in all these results are undoubtedly due mainly to variations in the rate of shaking and in variations in local conditions, such as slight differences in the form of the flasks used, which might make much difference in the surface of the liquid exposed and consequently, at these high rates, in the oxidation rate. On the whole there are no more marked variations between the two series than between different experiments of either series, and the conclusion seems to be justifiable that the brucine hydrochloride exerts no influence upon the rate of the reaction, or if it does that its influence is of a wholly different order of magnitude from the influence exerted upon the oxidation by means of free oxygen.

Thus the evidence at hand seems to point rather distinctly toward the probability that the inhibitory actions in question are quite closely confined to reactions in which free oxygen is involved. Of course this point cannot be considered as definitely settled until a vastly greater amount of evidence is accumulated.[1]

3. PRELIMINARY EXPERIMENTS TO DETERMINE WHAT CLASSES OF SUBSTANCES SHOW INHIBITIVE ACTION.

A large number of experiments were carried out to determine how wide-spread the phenomenon of inhibition of the reaction between oxygen and sodium sulphite solution might be. The method of experimentation was to place 25 cc. of the sulphite

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[1] The anomalous conduct of the reaction with nitric oxide and sodium sulphite is readily explained upon the assumption that the nitric oxide at first reacts with the sulphite, forming an unstable compound which then rather rapidly breaks down with the evolution of some other gas. The final slow decrease in volume may be due merely to a residue of the original reaction between the much diluted reagents, or it may be due to the fact that the gas evolved is some substance capable of further reaction. In looking up the literature on this matter we find that nitric oxide, when conducted into an alkaline solution of sodium sulphite, yields nitrosohydroxylamine sulphonic acid in form of the sodium salt $Na_2SN_2O_5$. (Raschig: *Ann. Chem.* (Liebig), **241**, 230.) These salts show a tendency to decompose into sulphates and nitrous oxide. Several experiments made in my laboratory by Mr. Bruno Olshausen show that the ratio between the volume of nitric oxide absorbed and the volume of the gas given off is very nearly 2 : 1. The phenomena referred to above are thus readily explained, since, as has been previously shown, nitrous oxide itself seems to be slowly absorbed by sodium sulphite solutions.

solution in the flask of the shaking apparatus, to determine the rate of oxidation before any foreign substance was added, then to add an amount of the substance to be tested sufficient to make the solution approximately $^1/_{260}$ molar. Usually 1 cc. of a $^1/_{10}$ molar solution was used for this purpose. The solutions of sodium sulphite used from his point on were always prepared by dissolving 2.5 grams of the crystallized salt in 200 cc. of distilled water. These solutions were approximately $^8/_{100}$ normal. For this particular investigation, a knowledge of the exact strength of the solutions was wholly unnecessary. It was considered wise to prepare a fresh solution about every two hours, mainly because of the rather marked change in the oxidation rate of the solution on standing. The flasks used were cleaned after each experiment by soaking in chromosulphuric acid mixture. This was found necessary, as after simple washing with water, no matter how carefully done, there seemed to remain always enough of the foreign substance to throw out the results of the following set of observations. In working in neutral and alkaline solutions air was used instead of pure oxygen on account of the too rapid rate of oxidation with the latter.

a. Experiments with Brucine Hydrochloride.

The first substance investigated was brucine hydrochloride. This was found to possess a most marked inhibitive action in neutral solution, as the following measurements show (time in minutes):

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	Before adding brucine hydrochloride.			After adding brucine hydrochloride.			
$T =$	0	1	2	0	1	2	3
$V =$	49.25	47.90	46.60	46.20	46.05	45.95	45.85
$\frac{\Delta V}{\Delta T} =$	...	1.35	1.30	...	0.15	0.10	0.10

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$T =$	0	1	0	1	2	3
$V =$	50.00	48.50	48.50	48.40	48.3	48.22
$\frac{\Delta V}{\Delta T} =$	...	1.50	...	0.10	0.10	0.08

In slightly alkaline solution, the inhibitive action of brucine hydrochloride is vastly greater than in neutral solution. This is shown by the following experiment in which such a weakly alkaline solution was used, the concentration of brucine hydrochloride being the same as above; *viz.*, $^1/_{260}$ molar.

	Before adding brucine hydrochloride.			After adding brucine hydrochloride.			
$T =$	0	1	2	0	1	2	17 hours.
V	50.00	48.60	47.45	46.90	46.90	46.90	46.90
$\frac{\Delta V}{\Delta T}$	....	1.40	1.15	....	0.00	0.00	0.00

That is, aften seventeen hours, no measurable oxidation had taken place.

This enormous increase of inhibitive action in alkaline over neutral solution is, perhaps, even more strikingly shown in the following set of observations. In this case, the original solution was neutral and, after determining the normal rate, 1 cc. of a 0.0001 molar solution of brucine hydrochloride was added. This made the solution finally $^1/_{260.000}$ molar in brucine. The result, as will be seen, was an extremely small, if any, reduction of the oxidation rate. Next, a few drops of dilute potassium hydroxide solution were added. The enormous drop in the rate upon this may be seen from the figures:

Before adding brucine hydrochloride.			After adding brucine hydrochloride.			After adding potassium hydroxide.		
$T.$	$V.$	$\frac{\Delta V}{\Delta T}.$	$T.$	$V.$	$\frac{\Delta V}{\Delta T}.$	$T.$	$V.$	$\frac{\Delta V}{\Delta T}.$
0	50.00	...	0	44.90	...	0	41.40	....
1	47.50	2.50	1	43.00	1.90	1	41.20	0.20
2	45.30	2.20	2	41.60	1.40	50	40.94	0.005
						40 hours	39.75	0.016

As will be seen the rate is reduced to something less than 0.01 of the normal rate by the presence in alkaline solution of a quantity of brucine hydrochloride of the concentration of $^1/_{200.000}$ molar.

In acid solution the influence of brucine hydrochloride is much less than in neutral solution and the period of development of the inhibition is much longer. The oxidation in weakly acid solution takes place very slowly and in most of the experiments under these conditions, the reaction was accelerated by means of a few drops of a solution of mixed copper and iron sulphates. The whole phenomenon in acid solution is quite complex and could be given here only with the aid of many words. The discussion of this point will be left therefore until later.

b. Experiments with Quinine Bisulphate.

Quinine was the next alkaloid studied and it was used in the form of the bisulphate. Some objection attaches to the use of an acid salt for this purpose, since the presence of free hydrogen ions markedly influences the reaction rate, and since further the influence of quinine in acid solution is also much less than in neutral or alkaline solution. Still the influence even with the acid salt is so clear and sharply defined as to leave the matter in no sort of doubt. I give here only a limited number of measurements to illustrate the action of quinine bisulphate. Many more were made, but there is no particular need of giving them here, as the same phenomenon was always observed under the same conditions.

The following figures show the influence of quinine bisulphate in neutral solution. The quantity of the alkaloid added was 1 cc. of a 0.1 molar solution, thus making the whole solution $^1/_{260}$ molar.

Before.			After.					
T.	V.	$\frac{\Delta V}{\Delta T}$.	T.	V.	$\frac{\Delta V}{\Delta T}$.	T.	V.	$\frac{\Delta V}{\Delta T}$.
0	45.00	...	0	44.10	...	6	41.10	0.52
1	44.18	0.82	1	43.70	0.40	7	40.64	0.46
			2	43.22	0.48	8	40.18	0.46
			3	42.70	0.52	9	39.75	0.43
			4	42.16	0.54	10	39.30	0.45
			5	41.62	0.54			

As will be seen there is at first a very marked reduction, to a little less than one-half. The rate, however, increases noticeably for about five minutes. The cause of this was easily found. After the experiment was discontinued, the solution in the flask was found to contain a considerable quantity of a glittering white crystalline substance. This is probably a very slightly soluble compound of quinine with sodium sulphite. Brucine shows the same phenomenon but to a very much smaller degree. The explanation of the increasing absorption rate is, however, readily explained since there is formed first a solution supersaturated as to the quinine compound. This then gradually crystallizes out, thereby reducing the concentration of the quinine and to some extent nullifying the inhibitive action. On account of this peculiar conduct an experiment with a solution of quinine bisulphate only one-tenth as strong as above is reported here. This is nearly but not quite free from the increasing reaction rate, but still shows a marked inhibitive influence on the part of the quinine, even though its concentration in the solution was only $^1/_{2600}$ molar.

Before.			After.					
T.	V.	$\frac{\Delta V}{\Delta T}$.	T.	V.	$\frac{\Delta V}{\Delta T}$.	T.	V.	$\frac{\Delta V}{\Delta T}$.
0	45.00	...	0	44.00	...	8	40.58	0.42
1	44.19	0.81	1	43.62	0.38	9	40.20	0.38
			2	43.20	0.42	10	39.84	0.36
			3	42.75	0.45	11	39.53	0.31
			4	42.30	0.45	12	39.28	0.25
			5	41.84	0.46	13	39.05	0.23
			6	41.42	0.42	14	38.87	0.18
			7	41.00	0.42			

As is to be seen the inhibitive action of quinine in neutral solution appears to be considerably less than that of brucine. This is possibly due to the influence of the free acid of the acid sulphate since in alkaline solution the quinine seems nearly as powerful as brucine. Following are the results of an experiment in weakly alkaline solution. The solution was made $^1/_{2600}$ molar in quinine.

Before.			After.		
T.	V.	$\frac{\Delta V}{\Delta T}$.	T.	V.	$\frac{\Delta V}{\Delta T}$.
0	45.00	...	0	43.50	...
1	43.65	1.35	1	43.40	0.10
			2	43.40	0.00
			5	43.40	0.00

That is, in alkaline solution, $^1/_{2600}$ molar quinine is sufficient to practically stop the oxidation of the sodium sulphite. This solution was $^1/_{10}$ normal in potassium hydroxide.

In acid solution quinine conducts itself very much as does brucine.

c. Experiments with Morphine Hydrochloride.

In this and all following experiments of this group of preliminary investigations, the method of procedure was the same as was used with brucine hydrochloride and with quinine bisulphate. In some cases, where the result in neutral solution was very decisive, the test in alkaline solution was omitted:

$^1/_{260}$ *Molar Morphine Hydrochloride.*

A.

T.	V.	$\frac{\Delta V}{\Delta T}$.
	Before.	
0	45.00	....
1	43.30	1.70
	After.	
0	43.30	....
1	42.96	0.34
2	42.80	0.16
3	42.65	0.15
4	42.50	0.15
5	42.35	0.15
10	41.68	0.134
15	41.23	0.092
45	38.90	0.077

B.

	Before.	
0	45.00	....
1	43.98	1.02
	After.	
0	44.00	....
1	43.94	0.06
2	43.88	0.06
3	43.82	0.06
4	43.76	0.06
5	43.70	0.06
10	43.42	0.056
15	43.10	0.060

d. $^1/_{260}$ *Molar Atropine Sulphate.*

T.	*V.*	$\frac{\Delta V}{\Delta T}$.
	Before.	
0	45.00	....
1	42.90	2.10
	After.	
0	42.70	....
1	42.25	0.45
2	41.83	0.42
3	41.45	0.38
4	41.10	0.35
5	40.75	0.35
10	39.33	0.284
15	38.30	0.206
20 hrs.	34.40	....
60 hrs.	31.00	....

e. $^1/_{260}$ *Molar Cane-Sugar.*

T.	*V.*	$\frac{\Delta V}{\Delta T}$.
	Before.	
0	45.00	....
1	43.35	1.65
	After.	
0	43.20	....
1	42.76	0.44
2	42.46	0.30
3	42.20	0.26
4	41.90	0.30
5	41.63	0.27
6	41.38	0.25
7	41.12	0.26
8	40.88	0.24
9	40.66	0.22
10	40.43	0.23

Added here 1 cc. normal potassium hydroxide.

0	40.20	....
5	40.20	0.00
10	40.20	0.00
15	40.20	0.00

f. $^1/_{260}$ *Molar Glycerine.*

T.	*V.*	$\frac{\Delta V}{\Delta T}$.
	Before.	
0	45.00	....
1	43.10	1.90
	After.	
0	42.70	....
1	42.30	0.40
2	42.08	0.22
3	41.86	0.22
4	41.08	0.18
5	41.50	0.18
10	40.60	0.18

Added here 1 cc. normal potassium hydroxide.

0	40.48	....
1	40.30	0.18
6	40.30	0.00
11	40.30	0.00
16	40.30	0.00

g. $^1/_{260}$ *Molar Potassium Cyanide.*

T.	*V.*	$\frac{\Delta V}{\Delta T}$.
	Before.	
0	45.00	....
1	43.10	1.90
	After.	
0	43.00	....
1	42.00	1.00
2	41.53	0.47
3	41.30	0.23
4	41.10	0.20
5	40.90	0.20
6	40.75	0.15
7	40.63	0.12
8	40.50	0.13
9	40.38	0.12
10	40.26	0.12

Added here 1 cc. normal potassium hydroxide.

0	40.20	....
1	39.95	0.250
6	39.92	0.006
11	39.82	0.020
16	39.80	0.004
21	39.80	0.000
26	39.80	0.000
31	39.80	0.000

h. $^1/_{260}$ Molar Ammonium Chloride.

T.	*V.*	$\frac{\Delta V}{\Delta T}$.
	Before.	
0	45.00	....
1	42.55	2.45
	After.	
0	42.50	....
1	41.25	1.25
2	39.95	1.30

Added here 1 cc. normal potassium hydroxide.

0	39.70	....
1	39.30	0.40
10	39.20	0.022
20	39.10	0.010
30	39.10	0.000
50	39.10	0.000
24 hrs.	39.10	0.000

i. $^1/_{260}$ Molar Sodium Acetate.

T.	*V.*	$\frac{\Delta V}{\Delta T}$.
	Before.	
0	45.00	....
1	42.90	2.10
	After.	
0	42.70	....
1	41.10	1.60

Added here 1 cc. normal potassium hydroxide.

0	40.80	....
1	39.25	1.55
2	38.60	0.65
3	38.25	0.35
4	38.00	0.25
5	37.80	0.20
10	37.16	0.13
15	36.78	0.08
20	36.56	0.044

j. $^1/_{260}$ Molar Pyrogallol.

T.	*V.*	$\frac{\Delta V}{\Delta T}$.
	Before.	
0	45.00	....
1	42.20	2.80
	After.	
0	42.00	....
1	41.85	0.15
2	41.83	0.02
3	41.81	0.02
4	41.80	0.01
5	41.78	0.02
10	41.73	0.01
15	41.63	0.02
20	41.56	0.014
25	41.50	0.012

Added here 1 cc. normal potassium hydroxide.

T.	*V.*	$\frac{\Delta V}{\Delta T}$.
0	41.50	....
1	39.00	2.50
2	37.20	1.80
3	36.30	0.90
4	36.10	0.20
5	35.93	0.17
10	35.84	0.018
20	35.78	0.006
30	35.76	0.002
40	35.71	0.005
54	35.67	0.004
18 hrs.	33.50	....

In these results for pyrogallol attention is to be called to the very great, but rapidly decreasing, acceleration upon addition of the potassium hydroxide solution. It is, of course, due to the absorption of oxygen by the pyrogallol itself, which takes place slowly in neutral, but rapidly in alkaline, solution. This phenomenon, however, gives a possible clue to the explanation of all initial accelerations of this sort, and will be treated more in detail in a later paper.

k. Experiment with $^1/_{260}$ Molar Resorcinol.

T.	*V.*	$\frac{\Delta V}{\Delta T}$
	Before.	
0	45.00	...
1	42.70	2.30
	After.	
0	42.40	...
1	42.10	0.30
2	41.87	0.23
3	41.68	0.19
4	41.48	0.20
5	41.28	0.20
Added here 1 cc. normal potassium hydroxide.		
0	41.10	...
1	40.80	0.30
6	40.80	0.00
11	40.80	0.00
42 hrs.	40.50	...

l. $^1/_{260}$ Molar p-Oxybenzoic Acid.

T.	*V.*	$\frac{\Delta V}{\Delta T}$.
	Before.	
0	45.00	...
1	43.05	1.95
	After.	
0	43.00	...
1	41.70	1.30
Added here 1 cc. normal potassium hydroxide.		
0	41.60	...
1	40.40	1.20
2	40.33	0.07
3	40.28	0.05
4	40.28	0.00
5	40.28	0.00
2½ hrs.	40.28	0.00

m. $^1/_{260}$ Molar Hydroxylamine Hydrochloride.

T.	*V.*	$\frac{\Delta V}{\Delta T}$.
	Before.	
0	45.00	...
1	43.70	1.30
	After.	
0	43.68	...
5	43.68	0.00
25	43.68	0.00
35	43.68	0.00

n. $^1/_{260}$ Molar Ethyl Alcohol.

T.	*V.*	$\frac{\Delta V}{\Delta T}$.
	Before.	
0	45.00	...
1	42.80	2.20
	After.	
0	42.80	...
1	42.58	0.22
2	42.44	0.14
3	42.30	0.14
4	42.17	0.13
5	42.05	0.12
Added here 1 cc. normal potassium hydroxide.		
0	42.00	...
1	41.60	0.40
6	41.60	0.00
11	41.60	0.00
24 hrs.	41.55	...

As the preceding studies show, the power to inhibit the oxidation rate of sodium sulphite to a very marked degree belongs to the most diverse organic compounds, as well as to ammonium compounds, hydroxylamine, and potassium cyanide, and in all cases, this power is vastly greater in alkaline than in neutral solution. Further, this inhibitive action is of noticeably different intensity in different cases, although in most cases in alkaline solution, the effect is so great in $^1/_{260}$ molar solution as to practically totally stop the reaction. In addition to the substances here studied, Bigelow[1] has shown that the power belongs, also, to mannite, succinic and tartaric acids, benzaldehyde, phenol, the three cresols, acetone, several alcohols and aniline. It would thus seem safe to say that this inhibitive action is characteristic to greater or less degree of all organic matter, and in addition, of many nitrogen compounds not organic. That the power belongs distinctly to ordinary distilled water, which contains traces of organic matter and of ammoniacal, or at least proteid, substances is shown very clearly by all attempts that I have made to obtain concordant results with simple water solutions. In such cases, the reaction rate always falls off very markedly toward the end of the reaction. Bigelow also noticed the same phenomenon.

4. EXPERIMENTS TO DETERMINE THE MINIMUM CONCENTRATION OF SEVERAL SUBSTANCES WHICH IS NECESSARY TO PRODUCE MEASURABLE INHIBITION.

In order to determine the minimum concentration of different substances which are capable of producing measurable inhibition a few substances were chosen and each subjected to the following treatment:

(1) A 0.1 molar solution of each substance was prepared and, from this, by successive dilution, were prepared solutions which were respectively 0.01, 0.001, 0.0001, etc., etc., molar.

(2) In each experiment, the normal rate of oxidation of 25 cc. of a solution of 2.5 grams of crystallized sodium sulphite in 200 cc. of distilled water was determined. One cc. of the reagent to be investigated was then added and the rate again measured, the observations being, in general, continued for a considerable time. The concentration of the reagent in the solution is, under these

[1] *Loc. cit.*

conditions, $^1/_{26}$ of that of the reagent added; *i.e.*, by using a 0.001 molar reagent, the solution becomes $^1/_{26,000}$ molar.

(3) Observations were begun in $^1/_{260}$ molar solution and continued with increasing dilution until the reagent failed to produce a noticeable effect.

(4) Each reagent was tested in alkaline and neutral, and sometimes in acid solution. In acid solution, oxygen was used, and in alkaline and neutral solutions, air was used.

The substances investigated in this manner were: Brucine hydrochloride, quinine bisulphate, morphine hydrochloride, cane-sugar and ammonium chloride.

A. Experiments with Brucine Hydrochloride.

1. In Neutral Solution.—The following tables show the results of several series of measurements with brucine hydrochloride:

TABLE I.—$^1/_{260}$ MOLAR BRUCINE HYDROCHLORIDE.

Before.			After.		
T.	V.	$\frac{\Delta V}{\Delta T}$.	T.	V.	$\frac{\Delta V}{\Delta T}$.
0	50.00	...	0	48.50	...
1	48.50	1.50	1	48.40	0.10
			2	48.30	0.10
			3	48.22	0.08

TABLE II.—$^1/_{2600}$ MOLAR BRUCINE HYDROCHLORIDE.

Before.			After.		
T.	V.	$\frac{\Delta V}{\Delta T}$.	T.	V.	$\frac{\Delta V}{\Delta T}$.
0	50.00	...	0	48.45	...
1	48.50	1.50	1	47.90	0.55
			2	47.35	0.55
			3	46.90	0.45
			4	46.50	0.40
			5	46.10	0.40
			6	45.70	0.40

TABLE III.—$^1/_{26\cdot000}$ BRUCINE HYDROCHLORIDE.

Before.			After.		
T.	V.	$\frac{\Delta V}{\Delta T}$.	T.	V.	$\frac{\Delta V}{\Delta T}$.
0	50.00	...	0	48.20	...
1	48.50	1.50	1	46.90	1.30
			2	45.70	1.20
			3	44.70	1.00
			4	43.80	0.90

TABLE IV.—$^1/_{260,000}$ BRUCINE HYDROCHLORIDE.

Before.				After.	
T.	V.	$\frac{\Delta V}{\Delta T}$.	T.	V.	$\frac{\Delta V}{\Delta T}$.
A.					
0	50.00	...	0	48.30	...
1	48.35	1.65	1	46.65	1.65
			2	45.10	1.55
			3	43.50	1.60
			4	42.00	1.50
B.					
0	50.00	...	0	44.90	...
1	47.50	2.50	1	43.00	1.90
2	45.30	2.20	2	41.60	1.40

As is to be seen from the above tables, the inhibitive action of brucine hydrochloride becomes too small to be detected in neutral solution at a concentration of $^1/_{260,000}$ molar. Even at $^1/_{260,000}$ molar, the initial effect is extremely small if at all present, the values of $\frac{\Delta V}{\Delta T}$ being so little smaller after than before the addition of the brucine hydrochloride that they are not readily distinguishable from normal values which would naturally decrease, owing to decreasing concentration both of sulphite and oxygen.

It is fairly safe to place the limit of the concentration at which the brucine hydrochloride shows measurable inhibitive effect at somewhere near $^1/_{26,000}$ molar, although, as later results will show, it is probably considerably less than this. In these earlier measurements, the significance of the "development period" was not fully realized.

2. In Alkaline Solution.—Preliminary experiments showed that brucine hydrochloride in alkaline solution exerts a vastly greater inhibitive action than in neutral solution. Therefore it is not necessary to give space here to tables of results obtained by using less than $^1/_{26,000}$ molar brucine hydrochloride. As will be seen, the inhibition even at this dilution is practically complete.

TABLE V.—$^1/_{26,000}$ BRUCINE HYDROCHLORIDE.

A.

$^1/_{40}$ Potassium Hydroxide.

T.	V.	$\frac{\Delta V}{\Delta T}$.	T.	V.	$\frac{\Delta V}{\Delta T}$.
	Before.			*After.*	
0	49.00	...	0	47.70	...
1	48.58	0.42	1	47.54	0.16
2	48.18	0.40	2	47.50	0.04
3	47.78	0.40	3	47.47	0.03
			4	47.45	0.02
			5	47.44	0.01
			10	47.40	0.008
			15	47.40	0.000

B.

$^1/_{10}$ Potassium Hydroxide.

T.	V.	$\frac{\Delta V}{\Delta T}$.
	Before.	
0	45.00	...
1	43.80	1.20
	After.	
0	43.70	...
1	43.60	0.10
2	43.58	0.02
3	43.58	0.00
4	43.58	0.00
5	43.58	0.00

TABLE VI.—$^1/_{260.000}$ BRUCINE HYDROCHLORIDE.

A.

$^1/_{40}$ Potassium Hydroxide.

T.	V.	$\frac{\Delta V}{\Delta T}$.
	Before.	
0	49.00	...
1	48.20	0.80
2	47.55	0.65
3	46.90	0.65
	After.	
0	46.80	...
1	46.34	0.46
2	46.05	0.29
3	45.78	0.27
4	45.54	0.24
5	45.32	0.22
6	45.10	0.22
7	44.90	0.20
8	44.70	0.20
9	44.50	0.20
10	44.30	0.20

B.

$^1/_{10}$ Potassium Hydroxide.

T.	V.	$\frac{\Delta V}{\Delta T}$.
	Before.	
0	45.00	...
1	44.47	0.53
2	43.93	0.54
3	43.48	0.45
	After.	
0	43.40	...
1	42.90	0.50
2	42.50	0.40
3	42.23	0.27
4	42.08	0.15
5	42.00	0.08
6	41.93	0.07
7	41.87	0.06
8	41.83	0.04
9	41.80	0.03
10	41.77	0.03
11	41.75	0.02
12	41.73	0.02
13	41.72	0.01
14	41.71	0.01

TABLE VII.—$^1/_{2,600,000}$ BRUCINE HYDROCHLORIDE.

A.

$^1/_{40}$ Potassium Hydroxide.

T.	V.	$\frac{\Delta V}{\Delta T}$.
	Before.	
0	44.00	...
1	43.49	0.51
2	43.00	0.49
3	42.50	0.50
	After.	
0	42.30	...
1	41.73	0.57
2	41.30	0.43
3	40.90	0.40
4	40.52	0.38
5	40.17	0.35

B.

$^1/_{10}$ Potassium Hydroxide.

T.	V.	$\frac{\Delta V}{\Delta T}$.
	Before.	
0	45.00	...
1	44.48	0.52
2	43.92	0.56
3	43.40	0.52
	After.	
0	43.30	...
1	42.66	0.64
2	42.05	0.61
3	41.50	0.55
4	41.00	0.50
5	40.53	0.47
10	38.92	0.322
15	38.13	0.158
20	37.58	0.110
21	37.50	0.08

An inspection of the above tables shows that in $^1/_{26,000}$ molar solution brucine acts so powerfully as to inhibit practically totally the oxidation of sodium sulphite in alkaline solution. The inhibition is complete in a somewhat shorter time in $^1/_{10}$ normal alkaline solution than in $^1/_{40}$ normal. In $^1/_{26,000}$ molar concentration the inhibition is still very marked, especially in $^1/_{10}$ normal alkaline solution. Here, after a little over 3 cc. of oxygen have been absorbed, the rate has fallen from about 0.5 cc. per minute to 0.01 cc. per minute. In $^1/_{40}$ normal alkaline solution the rate has fallen, after about the same amount of oxygen has been absorbed, to about one-third the original rate. The 25 cc. of the solution used would require for complete oxidation about 13–14 cc. of oxygen (calculated from titration numbers). Thus, neglecting change in concentration of oxygen, as this is relatively insignificant, the fall in the volume absorbed per unit of time under the above conditions should be less than one-fourth. We find with $^1/_{40}$ normal alkali a drop of about two-thirds which distinctly indicates inhibitive action. As to the presence of inhibitive action in 0.1 normal alkaline solution there can be no doubt, as it is very nearly complete.

In $^1/_{2,600,000}$ molar brucine hydrochloride and 0.1 normal potassium hydroxide the rate has fallen, after about one-half has been oxidized, to about one-seventh of the initial rate. Without inhibition it should have fallen to about one-half. In the case of the $^1/_{40}$ normal potassium hydroxide the evidence is not so clear as the experiment was interrupted too soon. One experiment was made with a solution which was $^1/_{26,000,000}$ molar as to brucine hydrochloride. This is here given as Table VIII.

TABLE VIII.

T.	V.	$\frac{\Delta V}{\Delta T}$.	T.	V.	$\frac{\Delta V}{\Delta T}$.
0	50.00	....	0	48.30	....
1	49.55	0.45	1	47.85	0.45
2	49.15	0.40	2	47.50	0.35
3	48.75	0.40	3	47.18	0.32
4	48.35	0.40	4	46.90	0.28
			5	46.68	0.22
			6	46.45	0.22
			7	46.23	0.21
			8	46.02	0.17
			9	45.85	0.15
			10	45.70	0.17

This, as will be seen, also gives positive evidence of inhibition. But the question arises as to what extent, with ordinary distilled water, inhibition might occur without the addition of brucine and owing solely to some impurity of the water itself or of the salt. To throw some light upon this point a number of observations were made in which no brucine or other substance was added and in which the experiment was continued until about one-half of the sulphite was oxidized. These gave roughly concordant results. One such set is given here:

TABLE IX.

T.	V.	$\frac{\Delta V}{\Delta T}$.
0	44.00	....
1	43.20	0.80
2	42.50	0.70
3	41.82	0.68
4	41.24	0.58
5	40.70	0.54
6	40.15	0.55
7	39.70	0.45
8	39.30	0.40
9	38.90	0.40
10	38.52	0.38
11	38.20	0.32
12	37.90	0.30
13	37.62	0.28
14	37.32	0.30
15	37.10	0.22
16	36.88	0,22
17	36.65	0.23
18	36.42	0.23
19	36.26	0.16
20	36.10	0.16

From this it will be seen that after one-half (about 7 cc.) of the requisite amount of oxygen for complete oxidation had been absorbed, the rate had fallen to about one-fourth of the original, thus giving some evidence of inhibition. And it may be added that this inhibition, although not quite so large as with $^{1}/_{26,000,000}$ brucine hydrochloride, is not with any great degree of certainty to be distinguished from it. Thus it is safe to say that the inhibition by brucine hydrochloride becomes practically indistinguishable from accidental inhibition somewhere between $^1/_{2,600,000}$ and $^1/_{26,000,000}$ molar concentration.

Attention is to be called, in passing, to the development period of the inhibition. With very dilute brucine hydrochloride the rate immediately after adding the reagent is almost as large and sometimes larger than before the addition. The rate then falls off more or less rapidly to a minimum. This, as will be seen later, is a very general phenomenon, and a separate investigation will be devoted to it. Also there is to be noted here the very common occurrence of an initial acceleration upon addition of the brucine hydrochloride. This will also be specially investigated.

3. In Acid Solution.—In carrying out the investigation in acid solution a somewhat different method was used. On this account and because the results are of a somewhat different character from the above all studies in acid solution will be brought together under one head at some later time.

B. Experiments with Quinine Bisulphate.

1. In Neutral Solution.—These experiments, as well as those in alkaline solution, were carried out exactly as were those with brucine hydrochloride.

TABLE X.—$^1/_{260}$ MOLAR QUININE BISULPHATE.

T.	*V.*	$\frac{\Delta V}{\Delta T}$.
	Before.	
0	45.00	...
1	44.18	0.82
	After.	
0	44.10	...
1	43.70	0.40
2	43.22	0.48
3	42.70	0.52
4	42.16	0.54
5	41.62	0.54
6	41.10	0.52
7	40.64	0.46
8	40.18	0.46
9	39.75	0.43
10	39.30	0.45

TABLE XI.—$^1/_{2,600}$ MOLAR QUININE BISULPHATE.

T.	*V.*	$\frac{\Delta V}{\Delta T}$.
	Before.	
0	45.00	...
1	44.19	0.81
	After.	
0	44.00	...
1	43.62	0.38
2	43.20	0.42
3	42.75	0.45
4	42.30	0.45
5	41.84	0.46
10	39.84	0.40
15	38.70	0.23
20	38.15	0.11
30	37.65	0.05
40	37.33	0.023
50	37.15	0.018

TABLE XII.—$^1/_{26.000}$ MOLAR QUININE BISULPHATE.

T.	V.	$\frac{\Delta V}{\Delta T}$.
	Before.	
0	45.00	...
1	44.05	0.95
	After.	
0	44.20	...
1	43.05	1.15
2	41.75	1.30
3	40.70	1.05
4	39.55	1.15
5	38.25	1.30
10	34.50	0.75
15	34.03	0.094
20	33.94	0.018

TABLE XIII.—$^1/_{260.000}$ MOLAR QUININE BISULPHATE.

T.	V.	$\frac{\Delta V}{\Delta T}$.
	Before.	
0	45.00	...
1	44.20	0.80
	After.	
0	44.20	...
1	43.10	1.10
2	41.90	1.20
3	40.83	1.07
4	39.90	0.93
5	39.10	0.80
10	34.35	0.95
15	33.48	0.18

TABLE XIV.—$^1/_{2.600.000}$ MOLAR QUININE BISULPHATE.

T.	V.	$\frac{\Delta V}{\Delta T}$.
	Before.	
0	45.00	...
1	44.13	0.87
	After.	
0	44.10	...
1	43.30	0.80
2	42.48	0.82
3	41.72	0.76
4	41.00	0.72
5	40.28	0.72
10	36.95	0.666
15	35.15	0.36

An examination of these results shows that in dilutions as great as $^1/_{2,600}$ molar, quinine bisulphate shows very distinct inhibitive action. In $^1/_{26.000}$ molar concentration, a distinct initial acceleration is noticed which, however, goes over later into an inhibitive effect. This is more marked when the full set of values per minute is seen, although quite apparent from the abridged table (XII) given here. In Table XIII ($^1/_{260.000}$ molar quinine sulphate), the same acceleration is noticed, while (especially when the table is seen in full) the inhibition is not distinct. In $^1/_{2.600.000}$ molar concentration, the reaction conducts itself as about normal; neither initial acceleration nor inhibition beyond what might be due to the water are apparent. In comparison with brucine hydrochloride, quinine bisulphate acts inhibitively to about the same dilution but shows noticeable initial acceleration, which was not noticed with brucine hydrochloride in neutral solution. The fact that in high concentrations quinine bisulphate does not act so powerfully as brucine hydrochloride, may possibly be wholly explainable by the formation of the insoluble compound referred to above.

2. *In Alkaline Solution.*—The following tables (XV to XVIII) show the influence of quinine sulphate in alkaline solution. The solutions used were always 0.1 normal in potassium hydroxide.

TABLE XV.—$^1/_{2,600}$ MOLAR QUININE BISULPHATE.

T.	*V.*	$\frac{\Delta V}{\Delta T}$.
	Before.	
0	45.00	....
1	43.65	1.35
	After.	
0	43.50	....
1	43.40	0.10
2	43.40	0.00
3	43.40	0.00
4	43.40	0.00

TABLE XVI.—$^1/_{26,000}$ MOLAR QUININE BISULPHATE.

T.	*V.*	$\frac{\Delta V}{\Delta T}$.
	Before.	
0	45.00	....
1	43.55	1.45
	After.	
0	43.50	....
1	43.30	0.20
2	43.20	0.10
7	42.90	0.06
12	42.77	0.026

TABLE XVII.—$^1/_{260,000}$ MOLAR QUININE BISULPHATE.

T.	*V.*	$\frac{\Delta V}{\Delta T}$.
	Before.	
0	45.00	....
1	44.06	0.94
	After.	
0	43.90	....
1	42.90	1.00
2	42.33	0.57
7	41.17	0.23
12	40.45	0.14

TABLE XVIII.—$^1/_{2,600,000}$ MOLAR QUININE BISULPHATE.

T.	*V.*	$\frac{\Delta V}{\Delta T}$.
	Before.	
0	45.00	...
1	43.50	1.50
	After.	
0	44.00	....
1	42.40	1.60
2	41.50	0.90
5	40.08	0.49
10	38.75	0.27
15	38.00	0.15

The result here is wholly comparable to that found for brucine hydrochloride. Out to a dilution of $^1/_{260,000}$ molar the inhibitive action is undoubted. At $^1/_{2,600,000}$ molar, inhibition also seems undoubtedly present and that in much higher degree than that usually shown by solutions in ordinary distilled water without any addition of foreign substances (see Table IX).

C. Experiments with Morphine Hydrochloride.

Beginning with the morphine hydrochloride the remainder of the measurements given under this section of the work were carried out in a somewhat different manner; namely, the normal rate without addition was first determined, then the foreign substance injected in the desired quantity and the rate noted, this giving the inhibition in neutral solution, while finally, the further injection of 1 cc. of a normal potassium hydroxide solution and the further determination of the rate gave the result in alkaline solution. All such solutions were thus $^1/_{27}$ normal in potassium hydroxide. The slight change in the concentration of the inhibitive agent may be neglected for present purposes.

This method of procedure has a great advantage over the older one, in point of time saved, while it has the disadvantage of not allowing one to follow the development of the inhibition very far in neutral solution, especially at considerable dilutions, as were this done, the solution would become so far oxidized that the results in alkaline solution might be uncertain. However, as the whole matter of the development period is to be made the subject of special treatment, no particular harm will result.

The following tables (XIX to XXII) give the results with morphine hydrochloride.

TABLE XIX.—$^1/_{260}$ MOLAR MORPHINE HYDROCHLORIDE.

T.	*V.*	$\frac{\Delta V}{\Delta T}$.
	Before.	
0	45.00	...
1	43.98	1.02
	After.	
0	44.00	...
1	43.94	0.06
2	43.88	0.06
3	43.82	0.06
4	43.76	0.06
5	43.70	0.06
10	43.42	0.056
15	43.10	0.060

TABLE XX.—$^1/_{2.600}$ MOLAR MORPHINE HYDROCHLORIDE.

T.	*V.*	$\frac{\Delta V}{\Delta T}$.
	Before.	
0	45.00	...
1	42.60	2.40
	After.	
0	42.50	...
1	42.20	0.30
2	41.90	0.30
3	41.62	0.28
4	41.40	0.22
5	41.20	0.20
	Added here 1 cc. normal potassium hydroxide.	
0	41.10	...
1	40.88	0.22
6	40.84	0.008
11	40.80	0.008
16	40.80	0.000

TABLE XXI.—$^1/_{26.000}$ MOLAR MORPHINE HYDROCHLORIDE.

T.	*V.*	$\frac{\Delta V}{\Delta T}$.
	Before.	
0	45.00	...
1	43.70	1.30
	After.	
0	43.50	...
1	42.75	0.75
2	42.02	0.73
	Added here 1 cc. normal potassium hydroxide.	
0	42.00	...
1	41.50	0.50
2	41.08	0.42
3	40.80	0.28
4	40.60	0.20
5	40.42	0.18
10	39.96	0.092
15	39.75	0.04
20	39.70	0.01
30	39.70	0.00

TABLE XXII.—$^1/_{260.000}$ MOLAR MORPHINE HYDROCHLORIDE.

T.	V.	$\frac{\Delta V}{\Delta T}$.
	Before.	
0	45.00	...
1	43.15	1.85
	After.	
0	43.20	...
1	41.35	1.85

Added here 1 cc. normal potassium hydroxide.

0	41.20	...
1	39.95	1.20
2	39.40	0.55
3	39.15	0.25
4	38.95	0.20
5	38.80	0.15
10	38.36	0.088
15	38.16	0.040
20	38.10	3.010
30	37.88	0.020
40	37.84	0.004
50	37.84	0.000
24 hrs.	37.84	0.000

D. Experiments with Cane-Sugar.

TABLE XXIII.—$^1/_{260}$ MOLAR CANE-SUGAR.

T.	V.	$\frac{\Delta V}{\Delta T}$.
	Before.	
0	45.00	....
1	43.35	1.65
	After.	
0	43.20	....
1	42.76	0.44
2	42.46	0.30
3	42.20	0.26
4	41.90	0.30
5	41.63	0.27
10	40.43	0.24

Added here 1 cc. normal potassium hydroxide.

0	40.20	....
1	40.20	0.00
5	40.20	0.00
10	40.20	0.00
15	40.20	0.00

TABLE XXIV.—$^1/_{2600}$ MOLAR CANE-SUGAR.

T.	V.	$\frac{\Delta V}{\Delta T}$.
	Before.	
0	45.00	....
1	43.00	2.00
	After.	
0	43.00	....
1	41.60	1.40

Added here 1 cc. normal potassium hydroxide.

0	41.50	....
1	40.80	0.70
2	40.53	0.27
3	40.38	0.15
4	40.33	0.05
5	40.31	0.02
10	40.20	0.02
15	40.20	0.00

TABLE XXV.—$^1/_{26.000}$ MOLAR CANE-SUGAR.

T.	V.	$\frac{\Delta V}{\Delta T}$.
	Before.	
0	45.00	...
1	42.60	2.40
	After.	
0	42.50	...
1	40.70	1.80

Added here 1 cc. normal potassium hydroxide.

0	41.00	...
1	39.30	1.70
2	38.60	0.70
3	38.00	0.60
4	37.60	0.40
5	37.25	0.35
10	36.40	0.16
15	36.08	0.064
20	35.89	0.040
24 hrs.	35.40	...
4 days	35.40	...

TABLE XXVI.—$^1/_{260,000}$ MOLAR CANE-SUGAR.

T.	*V.*	$\frac{\Delta V}{\Delta T}$.
	Before.	
0	45.00	...
1	43.00	2.00
	After adding 1 cc. normal potassium hydroxide.[1]	
0	42.50	...
1	41.25	1.25
2	40.45	0.80
3	39.85	0.60
4	39.60	0.25
5	39.35	0.25
6	39.20	0.15
7	39.03	0.17
8	38.93	0.10
9	38.85	0.08
10	38.79	0.06

E. Experiments with Ammonium Chloride.

TABLE XXVII.—$^1/_{260}$ MOLAR AMMONIUM CHLORIDE.

T.	*V.*	$\frac{\Delta V}{\Delta T}$.
	Before.	
0	45.00	...
1	42.55	2.45
	After.	
0	42.50	...
1	41.25	1.25
2	39.95	1.30
	Added here 1 cc. normal potassium hydroxide.	
0	39.70	...
5	39.28	0.084
10	39.20	0.016
15	39.10	0.020
20	39.10	0.000
24 hrs.	39.10	0.000

TABLE XXVIII.—$^1/_{2600}$ MOLAR AMMONIUM CHLORIDE.

T.	*V.*	$\frac{\Delta V}{\Delta T}$.
	Before.	
0	45.00	...
1	42.80	2.20
	After.	
0	42.00	...
1	40.60	1.40
	Added here 1 cc. normal potassium hydroxide.	
0	40.30	...
1	39.50	0.80
2	39.35	0.15
3	39.16	0.19
4	39.00	0.16
5	38.85	0.15
10	38.33	0.104
15	38.03	0.060

TABLE XXIX.—$^1/_{26,000}$ MOLAR AMMONIUM CHLORIDE.

T.	*V.*	$\frac{\Delta V}{\Delta T}$.
	Before.	
0	45.00	...
1	43.00	2.00
	After adding 1 cc. normal potassium hydroxide.	
0	42.80	...
1	41.10	1.70
2	40.00	1.10
3	39.30	0.70
4	38.80	0.50
5	38.48	0.32
10	37.10	0.275

The results of the investigations with morphine chloride, cane-sugar and ammonium chloride are thus in a general way wholly comparable with those for quinine and brucine salts. Morphine

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[1] In this experiment the potassium hydroxide was added at the same time as the inhibitive reagent. The same is true in Table XXIX.

hydrochloride seems somewhat more active in neutral solution than the other substances. The influence of cane-sugar in alkaline solution seems of about the same value as of the alkaloids, being still very distinct at $^1/_{260.000}$ molar. Ammonium chloride exerts an influence in alkaline solution which rapidly weakens with dilution. Its influence seems to be, in $^1/_{2600}$ molar solution, only about as great as that of morphine hydrochloride in a one hundred times more dilute solution; namely, $^1/_{260.000}$ molar.

5. EXPERIMENTS IN ACID SOLUTIONS.

As has been already stated the study of the oxidation rate of sodium sulphite in acid solution, particularly under the influence of such catalytic accelerators as copper and iron salts is rather complicated. A number of interesting and curious phenomena have been noticed but they have not been sufficiently investigated at present to allow of any report being made. The inhibitive action of organic substances is very much smaller than in neutral solution, and from some observations seems to be zero. In the case of stannous chloride, however, as has been shown,[1] the action in acid solution is very marked. These investigations in acid solution will be carried further.

6. DISCUSSION AND SUMMARY.

In the present incomplete state of this investigation there is no object in entering into any extended discussion of the results. From the results already given, however, certain generalizations are possible.

1. Evidence is shown, tending to lead to the conclusion that only oxidations by means of free oxygen are subject to inhibition by small quantities of foreign substances.

2. A considerable number of organic substances not previously studied by Bigelow[2] show inhibitive action in high degree. In view of the great number of most diverse substances of organic nature which have been shown by Bigelow and by me, to possess this power, it seems safe to conclude that probably all organic substances possess it.

3. In addition to organic substances the power has been shown to belong also to potassium cyanide, hydroxylamine and ammonium salts.

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[1] This Journal, **23**, 137.

[2] *Loc. cit.*

4. The inhibitive effect has been shown in all cases to be not instantaneous, but to develop somewhat slowly with the oxidation of the solution. Ernst[1] noticed the same phenomenon in studying the influence of foreign substances on the catalytic acceleration of the oxidation of hydrogen by colloidal platinum solution. Bigelow[2] noticed the same depression of the oxidation rate toward the end of the reaction, but ascribed it to other causes.

5. As a very common accompaniment of these phenomena, initial accelerations have been found. It is possible that the method of procedure is alone the cause of these not being observed in all cases.

6. The limit of the dilution at which substances still show inhibitive effects differs for different substances, being in some cases still noticeable at a dilution of $^1/_{2,600,000}$ molar. Investigations are now being carried on whose purpose is to subject these phenomena of development periods and of initial accelerations to a careful study in the hope of finding some simple explanation of them. Until this can be done and the phenomena in question either eliminated or controlled, it is hopeless to attempt any exact quantitative investigation of the subject as a whole.

STANFORD UNIV., CAL.,
January 9, 1902.

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE PENNSYLVANIA STATE COLLEGE.]

THE ACTION OF METHYL AND ETHYL ALCOHOLS UPON THE BROMIDES OF CERTAIN PROPENYL COMPOUNDS.

BY F. J. POND, E. S. ERB, AND A. G. FORD.

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IT has been known for a number of years that certain bromine derivatives of anethol, isosafrol, isoapiol, and other analogous compounds, containing a propenyl group, C_3H_5, joined to a benzene nucleus, dissolve in ethyl alcohol with apparent decomposition, or on boiling with alcohol, they are converted into compounds which contain a less percentage of bromine. Thus Hell and Günthert[3] found that anethol dibromide, $C_{10}H_{12}O.Br_2$, is changed into a dark-colored oil on boiling with absolute alcohol; this oil was not prepared in a chemically pure condition, but on

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[1] Ernst: *Ztschr. phys. Chem.*, **37**, 478.

[2] *Loc. cit.*

[3] Hell and Günthert: *J. prakt. Chem.*, **52**, 199.