

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF COLUMBIA UNIVERSITY]

Oxygen Exchange Reactions of Organic Compounds and Water

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Introduction

Isotopic exchange reactions have been investigated not only because of their intrinsic interest, but with the hope of securing a clearer insight into the mechanisms of reactions. The work with deuterium² has aided greatly in the elucidation of the kinetics of prototropic and hydrolytic reactions. With the increased availability of the isotope O¹⁸,³ it became possible to investigate the exchange between heavy oxygen water (H₂O¹⁸) and a number of organic compounds. In this way we have a new approach to an old problem.

When the work was begun, we knew little in regard to possible exchange reactions between water and other compounds with respect to oxygen atoms. Generally it would be supposed that oxygen atoms doubly linked to carbon atoms might exchange through the mechanism of addition of water to form two OH groups attached to a single carbon atom. But the many experiments with deuterium show that quite unexpected results may be obtained. Exploratory experiments using a variety of substances were first made to determine what exchange reactions were possible and what the approximate velocities of exchange might be. It was then possible to investigate the rate of one of these reactions, namely, the exchange between acetone and water, quantitatively. The course of reaction was always followed by measuring the change in isotopic composition of the water.

Methods of Analysis

At the beginning of this work, the isotopic composition of the water was determined by means of a pressure float apparatus of the Gilfillan type.⁴ Since the density of the water differed from that of ordinary water not only because of the change in

isotopic composition of oxygen, but also hydrogen, it was necessary to electrolyze the water and recombine the oxygen with ordinary hydrogen in order to measure the effect of oxygen alone. The maximum density which could be measured on our float apparatus was about 20 parts per million heavier than normal water, with a precision of 1 part per million. In order to measure the water which was used (approximately 370 parts per million heavier than ordinary water), it was necessary to dilute about 20 times, thus introducing an error of 20 parts per million.

With the use of the mass spectrometer of the type described by Bleakney,⁵ the error in the analysis and the time required for analysis were reduced considerably. It is not convenient to measure the isotopic ratio of oxygen in water because it would necessitate baking out the instrument after each analysis. Nor is it desirable to use oxygen gas, since it reacts with the filament. Therefore, it was found most suitable to measure the isotopic ratio of oxygen in the form of carbon dioxide. This was accomplished by distilling a known amount of the recovered water under vacuum into a sample tube with a break seal on it, and adding 16 cc. of carbon dioxide at atmospheric pressure. The mixture was frozen with liquid air and sealed off in vacuum. The sample tube was then shaken vigorously at room temperature until equilibrium was reached. The time necessary to reach the complete equilibrium, CO₂¹⁶ + H₂O¹⁸ ⇌ CO¹⁶O¹⁸ + H₂O¹⁶, under these conditions, was determined experimentally. Table I shows that there was no change after three hours, but all samples were actually shaken for five hours to ensure equilibrium.

TABLE I

Time of shaking, hours	CO ₂ ¹⁸ /CO ¹⁸ O ¹⁸
1	359
2	505
3	548
4	550
Ordinary CO ₂	237

The readings on the mass spectrometer for typical analyses (no. 3 and ordinary carbon dioxide of Table I) are given below in Table II.

(5) Bleakney, *Phys. Rev.*, **40**, 496 (1932).

(1) Dissertation submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy in the Faculty of Pure Science of Columbia University in the City of New York.

(2) Bonhoeffer, *Z. Elektrochem.*, **40**, 469 (1934); Klar, *Z. physik. Chem.*, **B26**, 335 (1934); Bonhoeffer and Klar, *Naturwissenschaften*, **22**, 45 (1934); Halford, Anderson and Bates, *THIS JOURNAL*, **56**, 991 (1934); Hall, *ibid.*, **56**, 750 (1934); Schwartz and Stenier, *Z. physik. Chem.*, **B25**, 153 (1934); Ogawa, *Bull. Soc. Japan*, **11**, 310 (1936); O. Reitz, *Z. physik. Chem.*, **A176**, 363 (1936); **A179**, 119 (1937); Hammill and La Mer, *J. Chem. Phys.*, **4**, 294, 395 (1936); Wynne-Jones, *Chem. Rev.*, **17**, 135 (1935); Gross, Steiner and Suess, *Trans. Faraday Soc.*, **32**, 877 (1936); Orr and Butler, *J. Chem. Soc.*, 330 (1937).

(3) Huffman and Urey, *Ind. Eng. Chem.*, **29**, 531 (1937).

(4) Gilfillan, *THIS JOURNAL*, **56**, 406 (1934).

TABLE II

Ordinary CO ₂		Ratio
Intensity in arbitrary units Mass 44	Mass 46	
1803	7.51	240.0
2039	8.58	237.6
2032	8.70	233.6
2079	8.80	236.3
Average		236.9

Sample 3		Ratio
Intensity in arbitrary units Mass 44	Mass 46	
1857	3.37	551.0
1877	3.45	544.1
1837	3.35	548.4
Average		547.8

Ratio of Sample 3:ordinary CO₂, 2.311.

The $\%O^{18}$ in the water may be calculated from the equilibrium equation, since the measured value in carbon dioxide, the number of moles of water and of carbon dioxide equilibrated are known. The value of the equilibrium constant of this reaction has been found by Weber⁶ to be 1.047 at 0°. The tank carbon dioxide, always used as standard in our analyses, was found experimentally to have the same isotopic concentration before and after equilibration with water, which indicated that the tank carbon dioxide previously had been brought to equilibrium with water. Since all measurements of the isotopic composition of the carbon dioxide were made relative to this standard, the equilibrium constant was implicitly taken into account by using the ratio 250 for CO₂¹⁶/CO¹⁶O¹⁸ in the standard carbon dioxide, corresponding to the value 500 reported for the relative abundance of O¹⁶:O¹⁸ by the Committee on Atoms of the International Union of Chemistry.⁷ Thus the relative abundance of the isotopes in Sample 3 above becomes 2.311 × 500, or 1156. There is very little loss of precision due to dilution of the concentration of O¹⁸ in this method, since the number of moles of carbon dioxide used is very small compared to the number of moles of water and there is only a small difference between the calculated isotopic composition of the water before equilibration with carbon dioxide and the isotopic composition of the carbon dioxide actually measured.

Exploratory Experiments

The organic compounds which were used in this investigation were those containing the most common type of oxygen groups, namely, the hydroxyl,

(6) Weber, Urey and Wahl, *J. Chem. Phys.*, **3**, 129 (1934).

(7) Aston, Bohr, Hahn, Harkins and Urbain, *Rev. Sci. Instrum.*, **7**, 334 (1936).

the carboxyl, and the carbonyl groups. Waters of several different isotopic concentrations were available, ranging from 0.080 to 0.750%O¹⁸.

The procedure in all cases was to mix about 1.5 g. of purified water of known isotopic composition with an equivalent amount of the organic compound. The water was purified by refluxing with alkaline permanganate and then distilling; it was again distilled from chromic acid. Because fumaric acid, succinic acid, amyl acetate, and urea did not dissolve completely, these compounds were shaken while in contact with the water. The water was separated from the organic compound and again analyzed for its isotopic composition. In the case of the solid substance, the water was recovered by distilling under vacuum and condensing the water with solid carbon dioxide. In the case of compounds more volatile than water, the water was separated from the solution by vacuum distillation at 0° for experiments run at 25° and by fractional distillation at atmospheric pressure for those run at 100°. In the case of butyric acid, it was necessary to add metallic sodium and redistil in order to obtain water free of butyric acid. In the early work, the recovered water was analyzed by means of the float method, in the later work, by means of the mass spectrometer. As already mentioned, in the former method dilution was necessary and it was also necessary to purify the water by oxidation of any residual organic material with alkaline permanganate and chromic acid; both processes introduced a considerable error in the density determination, in the worst case, 15%. With the use of the mass spectrometer, it was not necessary to purify the recovered water and the error was reduced to approximately 1.5% as shown in Table II. Because of the increased precision in the analysis, it was possible to use less concentrated water; the water used in conjunction with the mass spectrometer differed from ordinary water by 115 parts per million in density compared to 370 used previously. The results of these experiments are tabulated below; F refers to the float method of analysis and M refers to the mass spectrometer.

The only doubtful result was the exchange with monochloroacetic acid, and the uncertainty was due to the simultaneous occurrence of the hydrolysis reaction.⁸ The results with trichloroacetic acid are not subject to the same objections, since the rate of decomposition of trichloroacetic acid

(8) Dawson and Pycock, *J. Chem. Soc.*, 153 (1936).

TABLE III

Compound	Temp., °C.	Time	Result
Methyl alcohol	25	24 hours	No exch. (F)
	100	7 hours	No exch. (F)
Glycerol	25	2 weeks	No exch. (F)
	100	6 hours	No exch. (F)
Phenol	25	44 hours	No exch. (M)
Butyric acid	25	2 weeks	No exch. (F)
	100	24 hours	No exch. (F)
Monochloroacetic acid	25	24 hours	Partial (F)
Trichloroacetic acid	25	42 hours	Complete (F)
Fumaric acid	25	44 hours	No exch. (M)
Succinic acid	25	44 hours	No exch. (M)
Amyl acetate	25	44 hours	No exch. (M)
Acetaldehyde	25	24 hours	Complete exch. (F)
Acetone	25	24 hours	No exch. (F)
	100	24 hours	Partial exch. (F)
Urea	25	54 hours	No exch. (F)

in water is negligible under these conditions.⁹ Whether the difference in the behavior of butyric acid and trichloroacetic acid is to be ascribed to the difference in acidity must be ascertained by further experiments. As a result of these qualitative experiments it can be seen that, in general, the oxygen of the hydroxyl group and the carboxyl group (except chloroacetic acids) does not exchange with water, but the oxygen of the carbonyl group in both acetone and acetaldehyde does exchange with water, the latter more readily than the former. The difference in the reaction of the C=O group in the carbonyl group and the carboxyl group is not surprising and is evidenced in other reactions as well.¹⁰

In order to make a more detailed study of the exchange between water and the carbonyl group, we decided to investigate the kinetics of the reaction quantitatively. From the viewpoint of kinetic studies, this type reaction has great advantages. Like racemization reactions and inversion reactions, there is no change occurring in the medium during the course of the reaction. This factor simplifies the experimental procedure as well as the interpretation of the results.

Kinetics of the Acetone-Water Exchange Reaction

Preliminary Investigation.—From the qualitative results, it was thought that the rate of the acetone-water exchange reaction could be measured conveniently at 100°. The reaction mixture containing 1.5 cc. of water and an equimolar quantity

(9) Kappana, *Z. physik. Chem.*, **158**, 355-364 (1932).

(10) Smedley, *J. Chem. Soc.*, **95**, 231 (1909); Watson, *Chem. Rev.*, **7**, 173 (1930).

of acetone was sealed in an ampoule and placed in a 100° thermostat. After a given time, the reaction mixture was cooled and approximately 0.7 cc. of water recovered from it by vacuum distillation at 0°. The results of the analyses of the isotopic water thus recovered from a number of trial experiments were both inconsistent and irreproducible.

An attempt to find the source of the irreproducibility by checking on each step of the procedure led to the following set of experiments in which each ampoule was kept for one half-hour at 100°. In order to check on the mass spectrometer method of analysis, one sample, treated in the usual manner, was divided into three parts, M₁, M₂, M₃; the first two were analyzed on one day and the third one another day. It also was necessary to check on the method of preparation of the samples. The reaction mixture was frozen in liquid air and the ampoule was sealed under vacuum to avoid the formation of products of decomposition of acetone, which might be produced in the usual sealing process, as well as to remove the air which was present. After reaction this sample, which contained twice the usual quantity of the reaction mixture, was divided into two parts, A₁ and A₂. In order to find the effects of incomplete separation of the acetone and water, 1.2 cc. of water was recovered by vacuum distillation from A₁ and 0.4 cc. of water from A₂. For the purpose of checking the effect of surface, one ampoule (S) was filled with glass beads. To find the effect of acid and base, two samples (Acid 1 and 2) were prepared containing 0.002 *N* hydrochloric acid and one (Base) containing 0.005 *N* sodium hydroxide. The results are tabulated in Table IV.

TABLE IV

Sample	%O ¹⁸
Initial water	0.086
M ₁	.118
M ₂	.118
M ₃	.117
A ₁	.107
A ₂	.096
S	.141
Acid 1	.141
Acid 2	.141
Base	.140

From these results, it can be seen that the reaction is catalyzed by hydrochloric acid, sodium hydroxide, and glass beads (S). To a lesser extent the reaction is catalyzed by either carbon dioxide of the air, which may remain when the reaction

vessel is not evacuated before sealing off, or by products formed during the sealing process (*cf.* M and A). If it is assumed in the case of A_1 that 0.4 cc. of the total 1.22 cc. recovered as water was actually acetone which subsequently reacted to completion, the value becomes 0.096. It is further evident that the analyses on the mass spectrometer are reproducible within 1%. Two additional experiments with hydrochloric acid and sodium hydroxide, at the same concentration as above, showed that the reaction went to completion in one hour at 25° under those conditions.

For the purpose of determining whether the effect of glass beads was due to a heterogeneous reaction, the usual mixture was allowed to react (1) in a quartz vessel and (2) in a quartz vessel filled with broken quartz. The percentage reaction after one hour at 100° was the same in both cases. The existence of a heterogeneous reaction also was eliminated by studying the reaction in a series of buffered solutions, in one case filling the reaction vessel with glass beads. This series of phthalate buffers was prepared in acetone-water mixtures containing 10% water by volume in the manner described by Cray and Westrip.¹¹ The neutral point in such a solution corresponds to pH 9.7. In these experiments, the initial concentration of the O^{18} in the water was 0.092%, and Table V shows the final concentration of O^{18} in the water after ten hours at 25°.

TABLE V

Expt.	Cc. of aqueous $M/80$ disodium phthalate in 100 cc. soln.	Cc. of aqueous $M/80$ phthalic acid in 100 cc. soln.	pH	% O^{18} in water after 10 hours at 25°
1st stage dissociation of acid				
1	8.65	1.35	11.9	0.106
2 (glass beads)	8.65	1.35	11.9	.106
3	5.40	4.60	10.3	.098
2nd stage dissociation of acid				
4	4.45	5.55	7.05	0.122
5	1.00	9.00	5.55	.146

The absence of the heterogeneous reaction, as well as the presence of a catalytic effect due to hydrogen and hydroxyl ions, is evident from this series. An attempt to determine the catalytic effect solely of the hydrogen ion in 0.0001 *N* hydrochloric acid at 25° was unsuccessful because the reaction is too sensitive to hydrogen ion catalysis. As for hydroxyl ion, the same was found to be true for 0.001 *N* sodium hydroxide. The only possible

(11) Cray and Westrip, *Trans. Faraday Soc.*, **21**, 326 (1925).

method of determining the catalytic constants was therefore to study the rate of reaction in buffered solutions.

Experimental Procedure

Purification of Materials.—The water was purified in the manner described earlier in the paper. C. P. grade of acetone was dried with Drierite for several days and 500 cc. was fractionally distilled twice; the initial and final 75 cc. was discarded in each distillation. C. P. salicylic acid was recrystallized from water three times and c. P. sodium salicylate was dissolved in alcohol and precipitated with ether three times.

Preparation of the Reaction Mixture.—Since the course of the reaction was followed by the change in the isotopic concentration of the water, it follows that the greater the percentage of acetone in the reaction mixture, the greater the change in the observed quantity; therefore a solution containing 90% acetone and 10% water by volume was used. In the experiments in which the buffer concentration was sufficiently low (experiments 1, 2, 4), the buffer solution was prepared in the isotopic water, 10 cc. of this solution at 25° was then placed in a 100-cc. flask, and sufficient acetone was added to make a total volume of 100 cc. The flask was then placed in a thermostat ($T = 25.02 \pm 0.01^\circ$), and the first sample was withdrawn after three minutes. In the other experiments the concentration of the buffer was too high to dissolve in water, but it could dissolve in the acetone-water mixture, so that the salt and acid were weighed out for each experiment. Since it was found that too much reaction took place during the mixing of acetone and water, it became necessary to change the procedure and add about 90 cc. of acetone to the solid salt and acid, cool to 0°, then add 10 cc. of water at 25° and mix. After the mixture was allowed to come to temperature equilibrium in the thermostat, sufficient acetone was added to compensate for the contraction and make the volume 100 cc. at 25.02°. The first sample (14.2 cc.) was withdrawn after three minutes and immediately frozen with a mixture of solid carbon dioxide and acetone. In each experiment seven samples were withdrawn. Tests showed that vaporization of the reaction mixture during the time necessary to withdraw a sample was negligible.

Separation of Acetone and Water.—In the first two experiments, the acetone and water were separated by vacuum distillation at 0°. This method, however, did not prove wholly satisfactory because the amount of water recovered was not constant and the water was sometimes contaminated with acetone. The method used thereafter was to keep the mixture at dry-ice temperature and to draw off the acetone through a fritted glass filter. The water then remaining was washed twice with 10-cc. portions of benzene to remove any remaining acetone. In this way, from 0.5 to 0.7 cc. of water was recovered from a 14-cc. sample of the mixture containing 10% water.

Method of Analysis.—The mass spectrometer was used throughout.

Experimental Results

All the experiments were done with salicylate buffers. The values of the hydrogen-ion concen-

tration were determined from a series of pH measurements of these solutions. The measurements were made on a Klett-Beaver colorimeter,¹² and picramic acid was used as the indicator, because it had been found in this medium that there was no salt effect on the *pK* of the indicator.¹¹ The average values for *K_A* of salicylic acid in a 10% water-acetone solution determined in this manner are precise to 5%.

TABLE VI

Concentration of sodium salicylate	<i>K_A</i> × 10 ³
0.01	10.3
.005	8.9
.001	7.6
.00013	6.0

The over-all rate constant for the reaction was determined from the usual bimolecular equation

$$dx/dt = k[(A - x)(B - x) - (C + x)(D + x)]$$

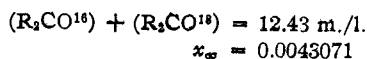
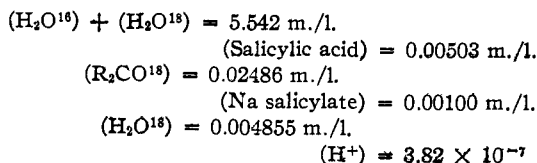
$$kt = \frac{1}{A + B + C + D} \ln \frac{x_{\infty}}{x_{\infty} - x}$$

where *A* = [H₂O¹⁶], *B* = [R₂CO¹⁸], *C* = [H₂O¹⁸], *D* = [R₂CO¹⁶] initially, and *x* = concentration of H₂O¹⁸ formed after time *t*. The values of *k* for the forward and reverse reactions are assumed identical, since from the experimental data, the value of the equilibrium constant cannot be distinguished from 1.

A typical set of data is shown in Table VII, and is plotted (experiment 6) in Fig. 2, *i. e.*, $-\log(x_{\infty} - x)$ is plotted against time, and the length of the vertical lines indicates the error in each point due to a probable error of 1.4% in analysis. The slope of the line gives the value *k/c*, where *c* = 2.303/(*A* + *B* + *C* + *D*).

TABLE VII

Time, min.	Vol. H ₂ O, cc.	CO ₂ ¹⁸ /CO ¹⁶ O ¹⁸	%O ¹⁸ in CO ₂	%O ¹⁸ in H ₂ O	<i>x</i>	<i>x_∞</i> - <i>x</i>	$-\log(x_{\infty} - x)$
0	0.52	493.1	0.1014	0.0990	0.0006318	0.0036753	2.4347
30	.61	437.4	.1143	.1119	.0013467	.0029604	2.5286
60	.51	382.2	.1308	.1276	.0022168	.0020903	2.6798
90	.63	372.7	.1342	.1315	.0024052	.0019019	2.7208
120	.63	356.4	.1403	.1375	.0027655	.0015416	2.8120
180	.64	339.3	.1474	.1445	.0031534	.0011537	2.9779
240	.55	318.3	.1571	.1535	.0036522	.0006549	3.1838



(12) Beaver, *J. Opt. Soc. Am.*, **18**, 41 (1929).

The concentrations of water and acetone were determined experimentally in conjunction with the calibration of the volumetric apparatus. The contraction of volume of the solution agrees very well with that previously measured.¹³ The concentration of O¹⁸ in acetone was assumed to be normal.

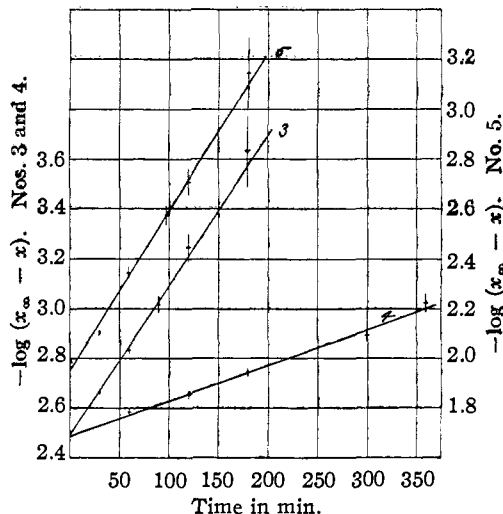


Fig. 1.—Effect of buffer concentration at constant ionic strength.

The data for all the experiments are summarized in Table VIII.

Experiments 1 and 2 were identical in all conditions except that the zero points were taken at slightly different times. The values of the constants are 1.49 × 10⁻⁴ and 1.50 × 10⁻⁴, respectively. When the concentrations of both the acid and the salt were increased (experiment 3) approximately by a factor of 8, the constant increased to

7.87 × 10⁻⁴. In order to determine how much of this increase was due to an increase in ionic strength, experiment 4 was run with the same concentrations of salicylic acid and sodium salicylate as were used in experiments 1 and 2, but enough potassium chloride was added to make the total salt concentration identical with that of experi-

(13) Reilly, *Proc. Roy. Soc., Dublin*, **15**, 597 (1919).

TABLE VIII

Expt.	Initial (H ₂ O ¹⁸) _{m./l.}	c _{acid} × 10 ³	c _{salt} × 10 ³	c _{H⁺} × 10 ⁷	k/c × 10 ³	k × 10 ⁴
1	0.005259	1.25	0.125	6.00	1.16	1.49
2	.005259	1.25	.125	6.00	1.17	1.50
3	.005388	9.93	1.04	7.26	6.13	7.87
4 ^a	.005233	1.25	0.125 ^a	7.60	1.40	1.80
5	.02486	10.38	1.01	7.81	6.31	8.08
6	.004855	5.03	1.00	3.82	3.06	3.92
7	.004855	10.08	5.15	1.74	5.31	6.80
8	.004855	1.97	0.975	1.54	1.17	1.50
9	.04059	1.99	9.92	0.21	1.11	1.43

^a Concentration of KCl, 0.873×10^{-3} .

ment 3. The rate constant in experiment 4 was 1.80×10^{-4} as compared with 1.50×10^{-4} for experiments 1 and 2 and 7.87×10^{-4} for experiment 3; this comparison indicates that the primary salt effect is relatively small, if not zero. Experiment 5 was a check on experiment 3; the initial (H₂O¹⁸) concentrations were 0.02486 and 0.005233 m./l., respectively. Since the percentage of O¹⁸ in the water in experiment 5 was greater than in the acetone, the net reaction proceeded in the opposite direction from the previous experiments. The results for these runs have been plotted in Fig. 1.

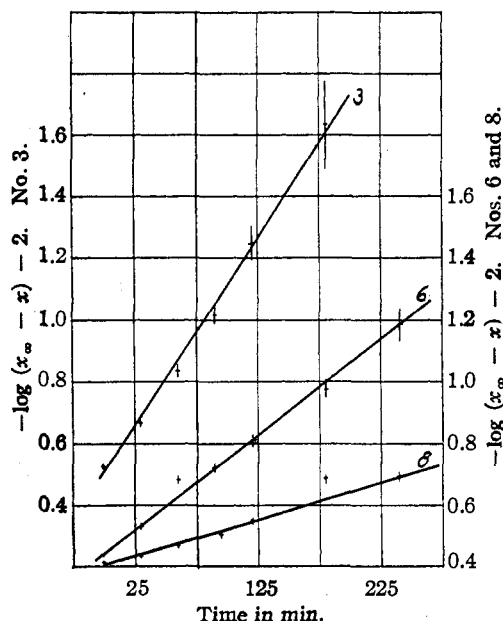


Fig. 2.—Effect of salicylate acid concentration.

In experiments 3, 6, and 8 (see Fig. 2), the salt concentration was held constant, and the acid concentration was varied approximately in the ratio 10:5:2. In experiments 3 and 7, the acid concentration was held constant, and the salt concentration was varied in the ratio of 1:5. The

effect of varying the salt concentration is even more obvious in experiments 8 and 9 (see Fig. 3). In these experiments the contribution of the hydrogen ion catalysis is small, the acid concentration is held constant, and the salt concentration is varied from 1 to 10 and the rate changes from 1.50×10^{-4} to 1.43×10^{-4} .

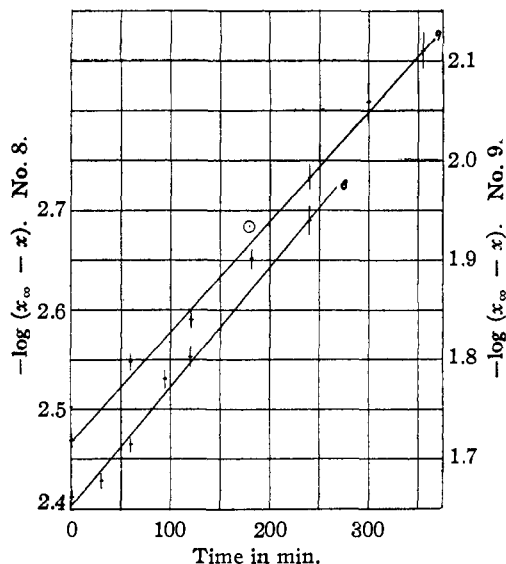


Fig. 3.—Effect of salicylate ion concentration.

If all these results are combined and the values of the catalytic coefficients, k_a , k_b , and k_{H^+} , for the acid, base and hydrogen ion, respectively, are determined by the method of least squares from the nine equations of the form $k = c_a k_a + c_{H^+} k_{H^+} + c_b k_b$ where k is the observed over-all reaction rate constant, each result being weighted to give a minimum percentage error, the following values are obtained: $k_a = 0.0682$, $k_b = 0.000150$, $k_{H^+} = 116.8$. It is obvious that the catalytic constant for the salicylate ion is negligible, and on the assumption that k_b is zero, the values become: $k_a = 0.0683$, $k_{H^+} = 116.5$. The calculated and observed values are compared in Table IX.

TABLE IX

$$k_{\text{calcd.}} = 0.0682c_a + 0.00015c_b + 116.8c_{\text{H}^+}$$

$$k'_{\text{calcd.}} = 0.0683c_a + 116.5c_{\text{H}^+}$$

Expt.	$k_{\text{calcd.}} \times 10^4$	$k'_{\text{calcd.}} \times 10^4$	$k_{\text{obsd.}} \times 10^4$
1	1.55	1.55	1.49
2	1.55	1.55	1.50
3	7.64	7.64	7.87
4	1.74	1.74	1.80
5	7.99	8.00	8.08
6	3.88	3.88	3.92
7	7.08	7.08	6.80
8	1.52	1.52	1.50
9	1.40	1.39	1.43

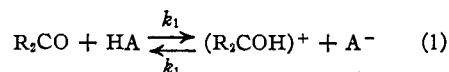
It has been established that the exchange reaction between acetone and the oxygen of water is catalyzed by hydrogen ion, hydroxyl ion, and the salicylic acid molecule, but not by salicylate ion. The fact that salicylate ion does not catalyze the reaction does not, of course, exclude the possibility of observing basic catalysis if stronger bases than salicylate ion were used. However, the preliminary investigation showed that in the presence of secondary phthalate ion, a much stronger base, the catalysis is very small, if not zero (the preliminary results cannot be used to distinguish between hydroxyl ion catalysis and secondary phthalate ion catalysis). Further experimental work is necessary to determine the existence of general basic catalysis.

Errors.—The error in each value of x and x_{∞} , due solely to the method of analysis, is of the order of 1.4%, 1% in each analysis and 1% in the standard. The consequent error of each point in the graph is indicated in the figures. Another source of error in x may be the incomplete separation of the acetone and water. Under the influence of the carbon dioxide added to the water for analysis, the residual acetone would react to completion, thus changing the isotopic composition of the water. Such errors would be largest when the isotopic composition of the water and acetone differ most, *i. e.*, at the beginning of the experiment, and always would cause the points to lie above the curve. It can be seen easily from the figures that this is actually the case for those points which lie considerably outside the limit of error imposed by the method of analysis. It will be noted that in Fig. 3 the circled point of experiment 8 is considerably outside the normal error. The analysis of this point was exactly the same as that of the last point, and it seemed likely that some unusual error had occurred. Since the last point coincided with the first five points, it was considered justifiable to neglect the sixth point.

The fact that the concentration of the hydrogen ion is known only within 5% introduces a considerable error only in those experiments in which the contribution of the hydrogen ion catalysis is large compared to the total rate. This is true in experiments 1, 2, and 4 in which approximately 50% of the total rate is due to hydrogen ion catalysis and the calculated value of k is therefore in error by 2.5% due to this factor alone. In all other experiments the contribution of the hydrogen ion catalysis to the total rate is 10% or less. In general the calculated value of k does not differ from the observed value by more than 4%.

Mechanism of the Reaction

The existence of general acid catalysis indicates essentially that the rate determining step in the acid catalyzed reaction must be a prototropic one, that is, either the addition or the removal of a proton. The first step, in accord with the general scheme of acid catalysis, is



This first step is exactly the same as that postulated by Pedersen¹⁴ for the acid catalyzed enolization of acetone. In the latter reaction, the rate determining step is not the addition of the proton, but rather the removal of a proton from the methyl group. This mechanism has received very convincing confirmation from the work of Bonhoeffer and Reitz¹⁵ on the rate of bromination of light and heavy acetone in light and heavy water as well as the rate of deuterium exchange.

A direct comparison between the rates of enolization (or bromination) and of the oxygen exchange reaction is, unfortunately, not possible, because the rate of enolization has never been studied in a 10% water-90% acetone medium. In dilute aqueous solution, Dawson¹⁶ has found $k_{\text{H}^+} = 0.00172$ per mole of acetone, and in 80% alcohol water solution, $k_{\text{H}^+} = 0.00314$; the corresponding k_{H^+} measured in this reaction would be 168.3. The effect of the medium on the rate of bromination has been studied,¹⁷ and it is found that the reaction is inhibited by water. Even in pure acetone, however, the hydrogen-ion catalyzed enolization reaction is slower than the oxygen ex-

(14) Pedersen, *J. Phys. Chem.*, **38**, 581-800 (1934).

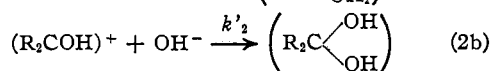
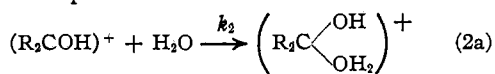
(15) O. Reitz, *Z. physik. Chem.*, **A179**, 119 (1937); Bonhoeffer and Reitz, *ibid.*, 135.

(16) Dawson and Hall, *Proc. Leeds Phil. Lit. Soc., Sci. Sect.*, **2**, 289 (1932).

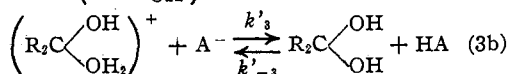
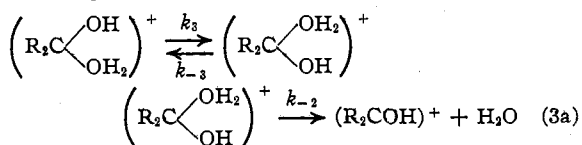
(17) T. Tomanari, *Z. physik. Chem.*, **B32**, 222 (1936).

change reaction by a factor of 500. The most striking difference between the enolization and exchange reactions is the apparent absence of general basic catalysis in the latter. For an acid with K_A of the order of 10^{-7} (such as salicylic acid is in this medium), the ions would be much more effective as catalysts than the acid molecules in the enolization of acetone, but the contrary is true in the case of the oxygen interchange. All this evidence proves that the formation of the enol form is not a necessary step in the exchange between acetone and the oxygen of water.

Since the first step, the addition of a proton to the acetone, is not followed by the conversion to the enolic form, it must be followed directly by the addition of a water molecule or a hydroxyl ion to the complex



If we consider (2a), we find that it may be followed by either of two steps to result in the oxygen exchange

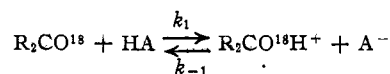


In reaction (3a), the complex formed in reaction (2a) undergoes an intramolecular shift of the H from one O to the other, followed by the reverse of reaction (2a). The intramolecular shift of H is highly improbable because all known cases of apparent intramolecular shifts have always been found actually to be prototropic changes. In reaction (3b) the complex reacts with a base to remove a proton and form the acetone hydrate. All the reactions must then be reversed in order to return to acetone with an exchanged oxygen.

If we now consider (2b), we find that the hydrate is formed directly. The hydrate thus formed may yield the acetone and water by the same steps as the hydrate formed in (3b). The restriction imposed by the fact that the reaction is subject to general acid catalysis, eliminates step (2a) or (2b) as the rate determining step. If k_2 were rate determining, only specific hydrogen ion catalysis would exist and similarly, if k'_2 were

rate determining, no catalysis would exist for the total reaction. The existence of general acid catalysis cannot help to distinguish between the occurrence of reactions (2a) and (2b).

We may conclude that in either case the rate determining step must be (1) or (3). If we assume first that the rate determining step is (1), it will be seen that the succeeding steps which bring the R_2COH^+ ion to equilibrium with the water will be rapid so that at any time the isotopic composition of the R_2COH^+ is that of the water. If then including the isotopic composition of the reactants, we rewrite equation (1)



acetone containing O^{18} can only disappear or appear as a result of this reaction. Setting up the usual expression for the velocity of this reaction, and substituting for

$$[\text{R}_2\text{CO}^{18}\text{H}^+] \text{ the value } [\text{R}_2\text{COH}^+] \frac{[\text{H}_2\text{O}^{18}]}{[\text{H}_2\text{O}]}$$

$$\text{and for } [\text{R}_2\text{CO}^{18}] \text{ the value } [\text{R}_2\text{CO}] \frac{[\text{R}_2\text{CO}^{18}]}{[\text{R}_2\text{CO}]}$$

it is possible to express the kinetic equation in the form

$$\frac{d[\text{R}_2\text{CO}^{18}]}{dt} = k_1[\text{R}_2\text{CO}][\text{HA}] \frac{[\text{R}_2\text{CO}^{18}]}{[\text{R}_2\text{CO}]} - k_{-1}[\text{R}_2\text{COH}^+][\text{A}^-] \frac{[\text{H}_2\text{O}^{18}]}{[\text{H}_2\text{O}]}$$

The acetone of all isotopic varieties must be in equilibrium with the acetonium ion of all isotopic varieties, since the concentration of the latter must be very small, and, hence, this kinetic expression reduces to the form of the bimolecular equation, but

$$k_1 = [\text{H}_2\text{O}] k [\text{HA}]$$

where k is the constant obtained from consideration of a bimolecular reaction between R_2CO^{18} and H_2O^{16} as given in the tables.

On the other hand, if (3) is the rate determining step, a corresponding derivation gives

$$-\frac{d[\text{R}_2\text{CO}^{18}]}{dt} = \frac{1}{2}k_3 K_1 K_2 [\text{HA}] \{ [\text{R}_2\text{CO}^{18}][\text{H}_2\text{O}^{18}] - [\text{R}_2\text{CO}^{16}][\text{H}_2\text{O}^{18}] \}$$

where K_1 and K_2 are the equilibrium constants for reactions (1) and (2), respectively. In this case

$$k_3 = 2k/K_1 K_2$$

We have not varied the total concentration of water and hence cannot distinguish between the two possibilities from our experimental data. In order to change the water concentration without introducing unknown medium effects it would be

necessary to measure the reaction rates in dilute solutions; this would be very difficult to do experimentally.

The general problem of uniquely determining the rate-determining step in general acid catalyzed reactions has been much discussed, and only in a few reactions has it been possible to settle the problem experimentally, for example, in the case of the enolization of acetone. However, from the data in the oxygen exchange reaction between acetone and water, it can be concluded that the rate of ionization of acetone as a base is not slower than the rate of oxygen exchange.

It would be of some interest to measure the rate of exchange of oxygen between acetone and water in D_2O . The experimental work of Reitz¹⁵ on the enolization of both light and heavy acetone in both light and heavy water gives the change in the equilibrium constant of the ionization of acetone in light and heavy water. If the oxygen exchange reaction involves the same equilibrium, this would tend to increase the rate of reaction in D_2O . On the other hand, if equilibrium were not attained in the first step, and the rate of ionization were rate determining, there would be a decided decrease in the rate of D_2O .

We are indebted to Dr. Marvin Fox for the analyses of many of our samples, and also to Prof. L. P. Hammett for many valuable discussions and suggestions in regard to this work.

Summary

1. The existence and the approximate rates of exchange for reactions between oxygen in water in some typical organic compounds have been investigated, with the use of waters ranging from 0.080 to 0.750% O^{18} .

2. It was found that the oxygen of hydroxyl and carboxyl groups (except chloroacetic acids) does not exchange with water, but the oxygen of the carboxyl group in both acetone and acid aldehyde does exchange with water, the latter more rapidly than the former.

3. A detailed kinetic study of the reaction between acetone and water revealed that the reaction was catalyzed by hydrogen ions, by hydroxyl ions, and by salicylic acid molecules, but not by salicylate ions.

4. The catalytic coefficients of the hydrogen ion and salicylic acid molecule for a bimolecular reaction between water and acetone in a 10% water-90% acetone medium were 116.5 and 0.0683 (m./l.)⁻¹ min.⁻¹, respectively.

5. The difference between these rates and the rates of the enolization of acetone shows that the exchange of the oxygen does not proceed through the enolic form although it has been shown that the exchange with hydrogen does. The rate of ionization of acetone as a base cannot be slower than the rate of oxygen interchange.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, WASHINGTON SQUARE COLLEGE, NEW YORK UNIVERSITY]

The Oxidation of Iodide Ion by Persulfate Ion. V. The Rate at Low Ionic Strength

BY ORAN M. KNUDSEN AND CECIL V. KING

Measurements of the rate of the persulfate-iodide ion reaction in aqueous solutions of low ionic strength reported in paper IV of this series¹ indicated the primary salt effect to be in good agreement with the predictions of the Brönsted theory.² These earlier measurements were made by adding small, known amounts of thiosulfate to the reaction mixtures and noting the time of appearance of iodine photoelectrically, without the aid of starch or other indicator.

New measurements of the rate were published in 1933 by Soper and Williams,³ with significantly

different results. While at the ionic strength 0.025 some of their results agreed well with those of other workers, as will be discussed later, their values at lower ionic strengths fell off in such a way that the slope of the $\log k$ vs. $\sqrt{\mu}$ curve became about 2.5 rather than the theoretical 2.0 to 2.08 at 25°.

Soper and Williams made up their solutions in 500- or 1000-cc. flasks, withdrew samples from time to time and titrated with 0.002 *N* thiosulfate while bubbling nitrogen through the solution to exclude oxygen.⁴ While exact details are not given, no mention is made of any unusual precautions in titrating the exceptionally dilute

(1) King and Jacobs, *THIS JOURNAL*, **53**, 1704 (1931).

(2) Brönsted, *Z. physik. Chem.*, **102**, 169 (1922).

(3) Soper and Williams, *Proc. Roy. Soc. (London)*, **A140**, 59 (1933).

(4) Soper, *J. Chem. Soc.*, **125**, 1899 (1924).