to be constant to within ±0.1%. The alcohol contained 0.00360 mole of water per ml., and the water in the acetic acid was negligible. The essential data and results of the study are given in Table I. The graph shows the relation between the apparent equilibrium constant as calculated and the mole per cent. of perchloric acid present in the equilibrium mixtures. To save space the moles of ethyl alcohol and acetic acid at equilibrium have been omitted from the table. These values may be found for each experiment by subtracting the values of column 5 from 0.03190 for alcohol and 0.03456 for acetic acid in experiments 1 to 7, and from half these numbers for the others. These were the respective quantities of these substances introduced in making up the reaction mixtures.

A search of the literature indicates that perchloric acid will not oxidize any of the constituents of these mixtures, or react with alcohol to form an ester under the conditions of these experiments. This conclusion was borne out by suitable tests which were performed.

The relation of the apparent equilibrium constant to the mole per cent. of perchloric acid present is well expressed by the equation $K = 3.45 + 0.68\ M$ up to about $M = 11$. Calculation shows that the variation of this constant with concentration of the catalyst cannot be explained as due to combination of a part of the water with it to form a definite hydrate, as has been proposed by Jones and Lapworth.[3]

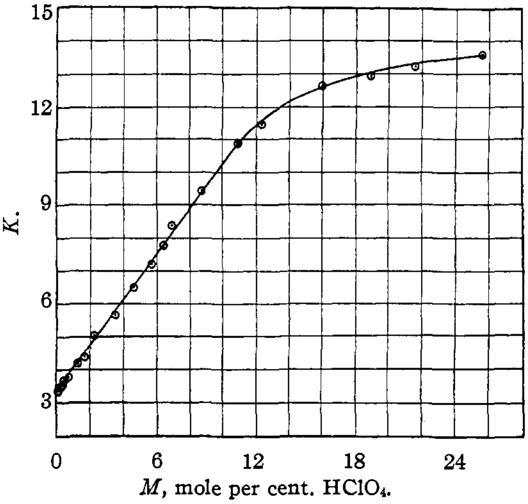

Fig. 1.—Relation of apparent equilibrium constant to mole per cent./$HClO_4$.

## Summary

The results of a study of the apparent equilibrium constant for the reaction

$$CH_3COOH + C_2H_5OH \rightleftarrows CH_3COOC_2H_5 + H_2O$$

in the presence of perchloric acid as catalyst, at concentrations up to 25.79 mole per cent., are presented.

STILLWATER, OKLAHOMA RECEIVED JANUARY 2, 1940

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[3] Jones and Lapworth, *J. Chem. Soc.*, **99**, 1427 (1911).

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF COLUMBIA UNIVERSITY]

# The Kinetics of Isotopic Exchange between Carbon Dioxide, Bicarbonate Ion, Carbonate Ion and Water[1]

BY G. ALEXANDER MILLS AND HAROLD C. UREY

## Introduction

The important role of carbon dioxide in nature and in industry, as well as its intrinsically interesting properties, have made it the subject of intensive study.[2] These investigations have resulted in the belief that in aqueous solution less than 1% of the carbon dioxide present exists in combination with water. The rather strong metacarbonic acid so formed is highly ionized due to its small concentration. The first dissociation constant ordinarily determined is therefore not a true dissociation constant. Usually called the apparent dissociation constant it is nevertheless a real constant.

The differentiation between free and combined carbon dioxide has been possible through the circumstance, first noticed in 1912 by McBain,[3] that carbon dioxide does not react instantaneously with water. The effect of various reagents on the rate of reaction has been studied in detail.[4] The maximum amount of alkali instantaneously neutralized by a solution of carbon dioxide corresponds to the equilibrium amount of carbonic acid, ionized and un-ionized, if dissociation of carbonic acid is assumed to be very rapid. From conductivity data the ionized portion is known. The true first dissociation constant was therefore estimated to be $4 \times 10^{-4}$. The reaction also has

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[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] Quinn and Jones, "Carbon Dioxide," The Reinhold Publishing Corp., New York, N. Y., 1936.

[3] McBain, *J. Chem. Soc.*, **101**, 814 (1912).

[4] Vorlander and Strube, *Ber.*, **46**, 172 (1913); Thiele, *Ber.*, **46**, 867 (1913); Thiele and Strohecker, *ibid.*, **47**, 1061 (1914); Strohecker, *Z. Nahr.-Genussm.*, **31**, 121 (1916); Wilke, *Z. anorg. Chem*,, **119**, 365 (1921); Thiele, *ibid.*, **121**, 211 (1922).

been followed by studying the rate of change of conductivity.[5]

Faurholt[6] in 1924 was first to recognize that the reaction process was determined by the *p*H of the solution. When the *p*H is less than 8 only simple hydration is important

$$CO_2 + H_2O \rightleftarrows H_2CO_3$$

When the *p*H is greater than 10 a bimolecular reaction predominates

$$CO_2 + OH^- \rightleftarrows HCO_3^-$$

Between these limits both determine the rate of reaction. By an ingenious method depending on the difference in rates of reaction between carbon dioxide and bicarbonate ion with amines Faurholt established approximately forward and backward reaction velocity constants for both reactions.

Measuring the rate of absorption and evolution of carbon dioxide by a buffered solution Brinkman, Margaria and Roughton[7] obtained data consistent with those of Faurholt. The use of two phases possibly introduces some uncertainty as to the interpretation of the results. However, the manometric measurements are much more precise. Stadie and O'Brien[8] have studied the reaction in physiological media. The catalyst, carbonic anhydrase, which occurs in blood, accelerates the reaction very considerably. Measuring the rate of reaction also by a "boat and manometer" method Roughton and Booth[9] have found an increase in the reaction rate in the presence of buffer solutions usually employed over that in pure water. They have incorporated their results in the form of a catalytic function and have evaluated this for several inorganic salts.

The rate of absorption of gaseous carbon dioxide by solutions is in part determined by the rate of chemical reaction. The effect of various substances on this rate was studied by Riou *et al.*[10] More recently a great deal of industrial work has been done using packed columns.[11]

The reaction between carbon dioxide and water results in an isotopic fractionation rather favorable for separation.[12] Experimental results[13] were lower than predicted, due, no doubt, to the slowness of the chemical reaction.

## Method of Isotopic Exchange

The chemical identity of isotopes makes possible an investigation of reaction kinetics. The rate of establishment of isotopic equilibrium is measured in a system in a steady state except for the distribution of isotopes. This rate depends on the chemical reactions normally occurring. The chemical equilibrium ordinarily considered, which we may call *elementic* equilibrium, is concerned with the number of ions and molecules present. Isotopic equilibrium is concerned with the distribution of isotopes in the various ions and molecules. This latter equilibrium, except in the case of hydrogen and deuterium, results in a uniform distribution of isotopes in all compounds, since the constants for isotopic equilibrium are unity within a few per cent. The time necessary to reach isotopic equilibrium is greater than that necessary to reach ordinary equilibrium. This is true because in the former case each ion or molecule must come to equilibrium with all other ions and molecules. For example in the case of the oxygen exchange between carbon dioxide and water if the $O^{18}$ content is not the same originally the hydration reaction must occur many times in order that there be isotopic equilibrium. Carbon dioxide dissolved in water will establish the half equilibrium concentration of carbonic acid in the order of one second. The half time necessary for oxygen exchange is about 1000 seconds.

A solution of carbon dioxide mixed with a solution of sodium bicarbonate will establish elementic equilibrium fairly quickly. If the $C^{13}$ content of the carbon dioxide is not the same as that of the sodium bicarbonate there will be a comparatively slow change tending to establish a uniform distribution of the carbon isotopes. By drawing off samples of carbon dioxide from the solution at various times and making an isotopic analysis, the rate of change of $C^{13}$ in the carbon dioxide can be measured. This can then be related to the rate of reaction of carbon dioxide with water.

Exchange occurs between the oxygen of carbon

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(5) Pusch, *Z. Elektrochem.*, **22**, 206 and 293 (1916); Thiele, *ibid.*, **22**, 423 (1916); Eucken and Grützner, *Z. physik. Chem.*, **125**, 363 (1927); Saal, *Rec. trav. chim.*, **47**, 264 (1928).

(6) Faurholt, *Z. anorg. Chem.*, **120**, 85 (1922); *J. Chim. Phys.*, **21**, 400 (1924). Values of rate constants given must be multiplied by 2.303.

(7) Brinkman, Margaria and Roughton, *Phil. Trans. Roy. Soc.*, **A232**, 65 (1933).

(8) Stadie and O'Brien, *J. Biol. Chem.*, **103**, 521 (1933); *ibid.*, **112**, 723 (1936).

(9) Roughton and Booth, *Chem. and Ind.*, **66**, 1053 (1937); *J. Physiol.*, **92**, 36P (1938); *Biochem. J.*, **32**, 2049 (1938).

(10) Riou *et al.*, *Compt. rend.*, **174**, 1463 (1922); *ibid.*, **186**, 1546 (1928).

(11) See, for example: Hitchcock and Cadot, *Ind. and Eng. Chem.*, **27**, 728 (1935); Comstock and Dodge, *ibid.*, **29**, 520 (1937).

(12) Urey and Greiff, THIS JOURNAL, **57**, 321 (1935); Weber, Wahl and Urey, *J. Chem. Phys.*, **3**, 129 (1935).

(13) Urey, Aten and Keston, *ibid.*, **4**, 622 (1936).

dioxide, bicarbonate ion, carbonate ion and water. Carbon dioxide with an atom fraction of $O^{18}$ different from ordinary may be dissolved rapidly in water. Samples of carbon dioxide extracted from portions of this solution at various times will have different $O^{18}$ contents. The rate of oxygen exchange in solutions of carbonates and bicarbonates can be measured by studying the rate of change of $O^{18}$ content in the carbon dioxide liberated at various times. All these results can be interpreted in terms of the kinetics of the reactions normally occurring.

The reversible hydration of carbon dioxide takes place quite rapidly. Investigation of the slower isotopic reactions is therefore of advantage. This is particularly true in the case of oxygen exchange. The correction for the effect of the back reaction is easily and quantitatively made and the effect of changing *p*H is eliminated. By studying the reaction in the liquid phase only, uncertainties due to rates of diffusion and solution are avoided.

## Experimental

**Preparation of Isotopic Material.**—Employing a countercurrent method the reaction between carbon dioxide and bicarbonate ion has been used to obtain some concentration of $C^{13}$.[13] The carbonate solution so produced was first boiled with sodium hydroxide to drive off excess amines. Sulfuric acid liberated carbon dioxide which was then sublimed at liquid nitrogen temperatures. The $C^{13}$ atom fraction of this carbon dioxide was 0.0140, the natural abundance being taken as 0.0106.

Water having an $O^{18}$ atom fraction of 0.00500 compared to 0.00200 for ordinary has been produced by the fractional distillation of water.[14] This water was purified by refluxing and distilling from alkaline permanganate at least twice and once from chromic acid. The first and last portions were not used. Carbon dioxide with an $O^{18}$ value greater than ordinary was prepared by shaking pure carbon dioxide with this water for at least ten hours.[15] Heavy oxygen sodium carbonate was prepared by dissolving pure sodium bicarbonate in the heavy oxygen water and allowing the solution to stand a week or more. The water was distilled off, the residue ground fine and heated at 300° for three hours.

**Exchange Reactions with $C^{13}$.**—A solution of carbon dioxide with a $C^{13}$ content greater than ordinary was mixed rapidly with a solution of ordinary sodium bicarbonate. The temperature was maintained at 0.00 ± 0.03°. Liquid samples were withdrawn from time to time into evacuated vessels. The carbon dioxide first to come off was collected. It was assumed that this was representative of the carbon dioxide existing as such in solution. Carbon dioxide was obtained from the solution remaining by addition of acid. A rough estimation was thereby obtained of the combined carbon dioxide. The samples were analyzed on a Bleakney type mass spectrograph.[16] The error in analysis is about 1% of the $C^{13}$ present. Typical results are given in Table I and in Fig. 1. $\alpha$ and $\beta$ are the atom fractions of $C^{13}$ in the carbon dioxide and bicarbonate ion, respectively.

TABLE I

Run 9; 0.00 ± 0.03°; $k_1[H_2O] = 0.0038$ sec.$^{-1}$; $[CO_2] = 0.021$ *M;* $[NaHCO_3] = 0.021$ *M.*

| Time in sec. | $\beta$ | $\alpha$ | log $(\alpha - \alpha_\infty)$ |
|---|---|---|---|
| 0 | 0.01060 | 0.01393 | −2.79 |
| 35 | .01175 | .01341 | −2.95 |
| 70 | .01176 | .01326 | −3.02 |
| 265 | .01199 | .01253 | −3.63 |
| ∞ | .01230 | .01230 | |

Run 9-B; 25.00 ± 0.02°; $k_1[H_2O] = 0.021$ sec.$^{-1}$; $[CO_2] = 0.021$ *M;* $[NaHCO_3] = 0.021$ *M.*

| Time in sec. | $\alpha$ | log $(\alpha - \alpha_\infty)$ |
|---|---|---|
| 0 | 0.01352 | −2.73 |
| 20 | .01246 | −3.09 |
| 58 | .01171 | |
| 95 | .01164 | |

For the *p*H range studied only simple hydration occurs. The possible reactions may be represented as

$$C^{13}O_2 + H_2O \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} H_2C^{13}O_3 \rightleftharpoons H^+ + HC^{13}O_3^-$$

$$C^{12}O_2 + H_2O \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} H_2C^{12}O_3 \rightleftharpoons H^+ + HC^{12}O_3^-$$

It is assumed that the ionization of carbonic acid is rapid. The rate of decrease of $C^{13}$ in carbon dioxide is given by the expression

$$-\mathrm{d}[C^{13}O_2]/\mathrm{d}t = k_1[H_2O][C^{13}O_2] - k_{-1}[H_2C^{13}O_3]$$
$$-[CO_2]\mathrm{d}\alpha/\mathrm{d}t = k_1[H_2O][CO_2]\alpha - k_{-1}[H_2CO_3]\beta$$

However, since elementic equilibrium has been established quickly

$$k_1[H_2O][CO_2] = k_{-1}[H_2CO_3]$$

and so

$$-\mathrm{d}\alpha/\mathrm{d}t = k_1[H_2O](\alpha - \beta)$$

The amount of $C^{13}$ is constant. Therefore, at any time

$$([CO_2] + [H_2CO_3] + [NaHCO_3])\alpha_\infty = \alpha[CO_2] + \beta([H_2CO_3] + [NaHCO_3])$$

$$-\frac{\mathrm{d}\alpha}{\mathrm{d}t} = k_1[H_2O]\left\{1 + \frac{[CO_2]}{[H_2CO_3] + [HCO_3^-]}\right\}(\alpha - \alpha_\infty)$$

The exchange reaction is of the first order, as is true in general.[17] The value of $k_1[H_2O]$ was obtained from the slope of the plot of log $(\alpha - \alpha_\infty)$ against time, Fig. 1.

The precision is low because the reaction is so fast, being substantially complete in a few min-

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[14] Huffman and Urey, *Ind. Eng. Chem.*, **29**, 531 (1937).

[15] Cohn and Urey, THIS JOURNAL, **60**, 679 (1938).

[16] Bleakney, *Phys. Rev.*, **40**, 496 (1932).

[17] McKay, *Nature*, **142**, 997 (1938).

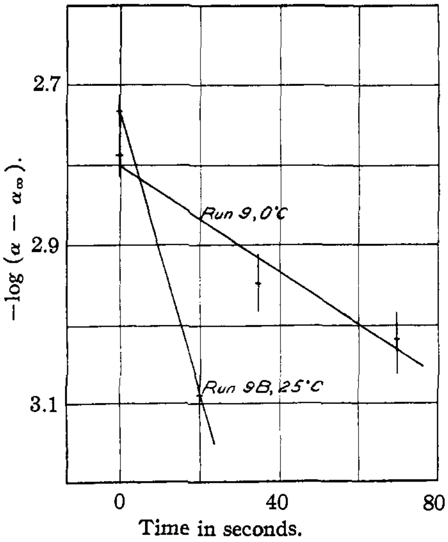

Fig. 1.

utes. Several seconds were necessary to take a sample. Also the low $C^{13}$ atom fraction makes accurate analysis difficult. A number of experiments showed qualitatively the effect of added substances upon the reaction rate. Ethyl alcohol and basic solutions accelerated the rate while iron sol decreased it to some extent.

**Exchange Reactions with $O^{18}$.**—The rate of oxygen exchange between water and carbon dioxide depends upon the acidity of the solution.[18] The experiments made may be divided conveniently into three groups: (a) those in which the solution was acid enough so that substantially all the carbon dioxide remained in that state; (b) experiments in which the bicarbonate ion concentration was considerable; (c) reactions in basic solution where the carbonate ion was predominant. Carbon dioxide with an $O^{18}$ content greater than ordinary was dissolved rapidly in water by shaking in a closed vessel. This solution was then placed in the reaction chamber, A, Fig. 2. From time to time a 10-cc. sample of this solution was withdrawn through the capillary manifold, B, into one of the evacuated bulbs, C. The carbon dioxide liberated was separated quickly from the water vapor by passage through an efficient trap, D, immersed in a dry-ice-bath. It was condensed in one of the sample tubes, E, by means of liquid nitrogen. The sample tube was sealed off and later analyzed for $O^{18}$. Frequent tests using a mass spectrograph showed that all but negligible amounts of water vapor were removed. The total time necessary to take a sample was ten seconds, though most of the carbon dioxide came off in the first part of this period. The liquid withdrawn from A was replaced with clean mercury from the reservoir, F, in order to prevent the formation of a gas phase above the liquid. Tests showed that the presence of mercury had no apparent effect on the reaction. When the time between samples was one minute or less, each sampling bulb was separately evacuated and equipped with an individual trap.

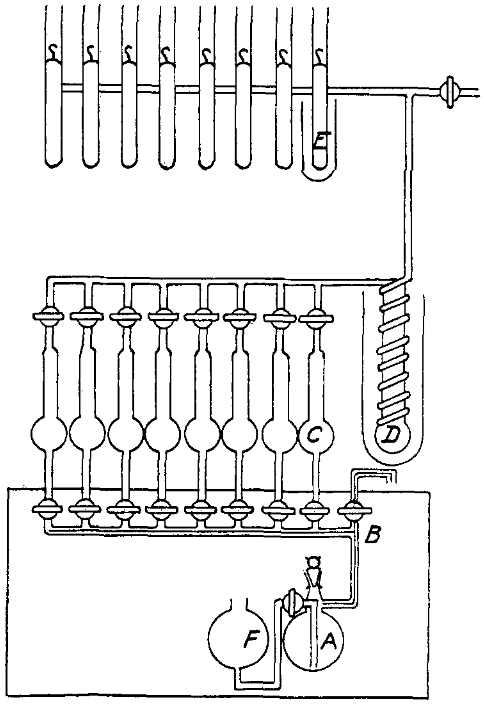

Fig. 2.

The rate of oxygen exchange between carbonate ion and water was studied. Sodium carbonate having an $O^{18}$ content greater than ordinary was dissolved in ordinary water. Samples of this solution were withdrawn as before. In this case each sample bulb, C, contained 5 cc. of 0.3 *M* sulfuric acid. In a similar manner the oxygen exchange of various mixtures was studied. These were prepared by dissolving a known amount of heavy oxygen sodium carbonate in ordinary water and adding a known amount of standard acid, salt or phosphate buffer.

Details of typical experiments are shown in Tables II and III and in Fig. 3. $\alpha$ is the atom fraction of $O^{18}$ in the liberated carbon dioxide. A summary of the results obtained in this way is given in Tables IV, V and VI.

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(18) Mills and Urey, This Journal, **61**, 534 (1939).

TABLE II

Run B-15; $T = 0.00 \pm 0.03°$; $k_1[H_2O] = 0.00204$ sec.$^{-1}$; [NaCl] = 0.0452 *M*; [$CO_2$] = 0.0226 *M*; [HCl] = 0.0224 *M*.

| Time in minutes | $\alpha$ | Log ($\alpha$ − 0.00210) |
|---|---|---|
| 0 | 0.00498 | −2.540 |
| 6 | .00429 | −2.660 |
| 12 | .00390 | −2.770 |
| 20 | .00330 | −2.921 |
| 25 | .00308 | −3.009 |
| 30 | .00292 | −3.086 |
| 36 | .00276 | −3.180 |
| 42 | .00261 | −3.292 |

TABLE III

Run B-22; $T = 0.00 \pm 0.03°$; *A*, observed rate, min.$^{-1}$ = 0.00969; $k_1[H_2O]$, sec.$^{-1}$ = 0.00210; $Na_2CO_3$ = 0.3034 g.; $H_2O$ = 39.13 cc.; HCl = 80.87 cc., 0.05250 *M*.

| Time in minutes | $\alpha$ | Log ($\alpha$ − 0.00210) |
|---|---|---|
| 0 | 0.00483 | −2.564 |
| 10 | .00425 | −2.668 |
| 20 | .00380 | −2.770 |
| 30 | .00350 | −2.854 |
| 40 | .00317 | −2.971 |
| 50 | .00300 | −3.046 |
| 60 | .00282 | −3.145 |
| 70 | .00266 | −3.252 |

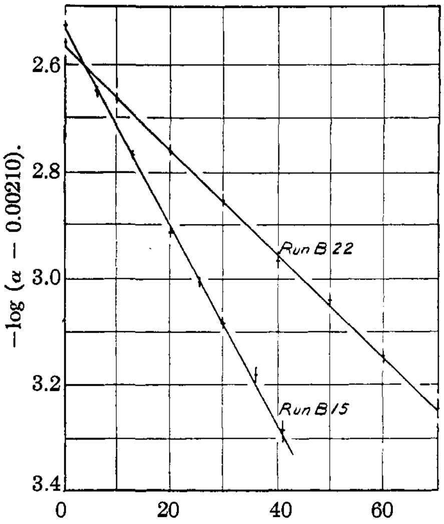

Fig. 3.

Sodium carbonate with an $O^{18}$ atom fraction equal to 0.00500 was dissolved in ordinary water. At 25° the time of half exchange was approximately twenty-eight hours. The presence of 0.04 *M* sodium hydroxide so inhibited the reaction that no exchange could be detected after seventy-four hours. The results are shown in Table VII.[19]

TABLE IV

AT 0.00 ± 0.03°

| Expt. | Solutions, molar concentrations: $CO_2$ | $NaHCO_3$ | NaCl | HCl | KCl | HAc | NaAc | $\frac{(NaHCO_3)}{(CO_2)}$ | *A*, obsd. rate, min.$^{-1}$ | $k_1(H_2O)$, sec.$^{-1}$ |
|---|---|---|---|---|---|---|---|---|---|---|
| B-10 | 0.0131 | | | | | | | 0 | 0.0170 | 0.00195 |
| B-15 | .0226 | | 0.0452 | 0.0224 | | | | 0 | .0177 | .00204 |
| B-19 | .0242 | | .0485 | .3010 | | | | 0 | .0169 | .00195 |
| B-21 | .0127 | | | | | 0.0803 | 0.0237 | 0 | .0182 | .00221 |
| B-16 | .0100 | 0.0100 | .0300 | | | | | 1.00 | .00912 | .00191 |
| B-20 | .0100 | .0100 | .0300 | | 0.1100 | | | 1.00 | .0101 | .00212 |
| B-22 | .01153 | .01232 | .03538 | | | | | 1.07 | .00969 | .00210 |
| B-23 | .00633 | .01899 | .03165 | | | | | 3.00 | .00419 | .00181 |
| B-14 | .00460 | .01840 | .02756 | | | | | 4.00 | .00318 | .00173 |
| B-29 | .00232 | .02600 | .03064 | | | | | 11.2 | .000684 | .00093 |
| B-27 | .00013 | .02650 | .02676 | | | | | 204 | .000130 | .00303 |
| B-26 | .00917 | .01669 | .03503 | $Na_2HPO_4 + KH_2PO_4$ *M*/30 | | | | 1.82 | .00699 | .00212 |
| B-24 | .00662 | .01376 | .02700 | $Na_2HPO_4 + KH_2PO_4$ *M*/15 | | | | 2.08 | .00827 | .0027 |

TABLE V

AT 25.00 ± 0.02°

| Expt. | Solutions, molar concentrations: $CO_2$ | $NaHCO_3$ | NaCl | HCl | $\frac{(NaHCO_3)}{(CO_2)}$ | *A*, obsd. rate, min.$^{-1}$ | $k(H_2O)$, sec.$^{-1}$ |
|---|---|---|---|---|---|---|---|
| C-4 | 0.0208 | | 0.0416 | 0.0086 | 0 | 0.220 | 0.0253 |
| C-5 | .0213 | | .0426 | .0100 | 0 | .256 | .0294 |
| C-1 | .00636 | 0.01654 | .02926 | | 2.60 | .0323 | .0124 |
| C-2 | .00686 | .01930 | .03302 | | 2.81 | .0349 | .0142 |
| C-3 | .00114 | .01864 | .02092 | | 16.4 | .0114 | .0225 |

TABLE VI

AT 40.00 ± 0.02°

| Expt. | Solutions, molar concentrations: $CO_2$ | $NaHCO_3$ | NaCl | $\frac{(NaHCO_3)}{(CO_2)}$ | *A*, obsd. rate, min.$^{-1}$ | $k_1$ ($H_2O$) sec.$^{-1}$ |
|---|---|---|---|---|---|---|
| D-5 | 0.0023 | 0.0205 | 0.0251 | 8.91 | 0.130 | 0.128 |
| D-3 | .00058 | .01742 | .01858 | 30.0 | .0417 | .147 |
| D-4 | .00044 | .01607 | .01695 | 36.5 | .0377 | .153 |

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[19] In one experiment heavy oxygen sodium carbonate was heated in an evacuated pyrex container to the softening point of the glass. The carbon dioxide obtained was found to have a lower $O^{18}$ content than the original sodium carbonate. Apparently exchange occurs with glass at this temperature.

TABLE VII

OXYGEN EXCHANGE BETWEEN SODIUM CARBONATE AND WATER AT 25.00 ± 0.02°

| Time in hours | $O^{18}$ atom fraction<br>$[Na_2CO_3] = 0.02\ M$ | <br>$[Na_2CO_3] = 0.02\ M$<br>$[NaOH] = 0.04\ M$ |
|---|---|---|
| 0 | 0.00513 | |
| 23.5 | .00383 | 0.00465 |
| 46 | .00310 | .00461 |
| 73.8 | .00264 | .00465 |

## Discussion of Experimental Results

For the *p*H range in which only hydration occurs the reactions possible may be represented as follows, assuming that the equilibrium between carbonic acid and its ions is rapid

$$\begin{array}{l}
CO^{16}O^{16} + H_2O^{16} \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} H_2CO^{16}O^{16}O^{16} \\
CO^{16}O^{16} + H_2O^{18} \rightleftarrows H_2CO^{16}O^{16}O^{18} \\
CO^{16}O^{18} + H_2O^{16} \rightleftarrows H_2CO^{16}O^{16}O^{18} \\
CO^{16}O^{18} + H_2O^{18} \rightleftarrows H_2CO^{16}O^{18}O^{18} \\
CO^{18}O^{18} + H_2O^{16} \rightleftarrows H_2CO^{16}O^{18}O^{18} \\
CO^{18}O^{18} + H_2O^{18} \rightleftarrows H_2CO^{18}O^{18}O^{18}
\end{array}$$

Then for the rate of change of $O^{18}$ content in the carbon dioxide, carbonic acid and water

$$\begin{aligned}
-\frac{dO^{18}(CO_2)}{dt} = {} & k_1[CO^{16}O^{18}]\{[H_2O^{16}] + [H_2O^{18}]\} + \\
& 2k_1[CO^{18}O^{18}]\{[H_2O^{16}] + [H_2O^{18}]\} - \\
& {}^2/_3k_{-1}[H_2CO^{16}O^{16}O^{18}] - {}^4/_3k_{-1}[H_2CO^{16}O^{18}O^{18}] - \\
& 2k_{-1}[H_2CO^{18}O^{18}O^{18}]
\end{aligned}$$

$$\begin{aligned}
-\frac{dO^{18}(H_2CO_3)}{dt} = {} & k_{-1}\ [H_2CO^{16}O^{16}O^{18}] + \\
& 2k_{-1}[H_2CO^{16}O^{18}O^{18}] + 3k_{-1}[H_2CO^{18}O^{18}O^{18}] - \\
& k_1[H_2O^{16}]\{[CO^{16}O^{18}] + 2[CO^{18}O^{18}]\} - \\
& k_1[H_2O^{18}]\{[CO^{16}O^{16}] + 2[CO^{16}O^{18}] + 3[CO^{18}O^{18}]\}
\end{aligned}$$

$$\begin{aligned}
-\frac{dO^{18}(H_2O)}{dt} = {} & \frac{k_{-1}}{3}\ [H_2CO^{16}O^{16}O^{18}] + \\
& {}^2/_3k_{-1}[H_2CO^{16}O^{18}O^{18}] + k_{-1}[H_2CO^{18}O^{18}O^{18}] - \\
& k_1[H_2O^{18}]\{[CO^{16}O^{16}] + [CO^{16}O^{18}] + [CO^{18}O^{18}]\}
\end{aligned}$$

Let $\alpha$, $\beta$ and $\gamma$ be the atom fractions of $O^{18}$ in the carbon dioxide, water and carbonic acid, respectively. That is

$$\alpha = \frac{2[CO_2{}^{18}] + [CO^{16}O^{18}]}{2[CO_2]}$$

with similar expressions for $\beta$ and $\gamma$. Substituting for the concentrations of the molecules present in terms of the atom fractions leads to the following equations. The same result is obtained if each molecule is assumed to be present in the proportion expected, if statistical equilibrium exists between all the isotopic varieties of each compound.

$$2[CO_2]\frac{d\alpha}{dt} = k_1[H_2O][CO_2]2(\gamma - \alpha)$$

$$3\{[H_2CO_3] + [HCO_3{}^-]\}\frac{d\gamma}{dt} = k_1[H_2O][CO_2](2\alpha + \beta - 3\gamma)$$

$$[H_2O]\frac{d\beta}{dt} = k_1[H_2O][CO_2][\gamma - \beta]$$

When $\{[H_2CO_3] + [HCO_3{}^-]\}$ is very small we may set $3\gamma = 2\alpha + \beta$. The $O^{18}$ content of the carbonic acid is thus between that of the water and the carbon dioxide.

In solutions acid enough so that only carbon dioxide exists to any extent

$$-\frac{d\alpha}{dt} = \frac{k_1[H_2O]}{3}(\alpha - \beta)$$

The $O^{18}$ content of the water remains effectively the same so that $\beta$ may be taken as constant. The integrated expression is of the form

$$At + B + \log(\alpha - \beta) = 0$$

where $A = k_1[H_2O]\ 2.303/60$ and is the slope of the least square line determined experimentally and $k_1[H_2O]$ is in sec.$^{-1}$. The values of $A$ and $k_1[H_2O]$ are given in Tables IV and V.

When considerable bicarbonate ion is present the rate of exchange is much slower, being proportional to the ratio $[CO_2] : \{[H_2CO_3] + [HCO_3{}^-]\}$. The three differential equations still represent the changes taking place. The solutions will be of the form

$$\alpha = a_1e^{-\lambda_1t} + a_2e^{-\lambda_2t} + a_3e^{-\lambda_3t} \qquad (1)$$

with similar expressions for $\beta$ and $\gamma$. It then turns out that

$$\lambda_1 = 0$$

$$\lambda_{2,3} = \frac{p + q \pm \sqrt{p^2 + q^2 + r^2 - 2pr - \frac{2qr}{3} + \frac{2pq}{3}}}{2}$$

where

$$p = k_1[H_2O],\ q = k_1\frac{[H_2O][CO_2]}{[H_2CO_3] + [HCO_3{}^-]} \text{ and } r = k_1[CO_2]$$

However, $r$ is of the order of $^1/_{1000}$ of $p$ or $q$ and can be neglected. Using the boundary conditions, when

$$t = 0,\ \alpha = \beta = \alpha_0,\ \beta = \beta_0$$

and when

$$t = \infty,\quad \alpha = \beta = \gamma = \alpha_\infty$$

it turns out that the second term on the right in equation (1) for the atom fraction becomes unimportant soon after the reaction begins. During this time the $O^{18}$ content of the carbonic acid and bicarbonate ion adjusts itself to a value less than that of the carbon dioxide. After this initial period

$$\alpha = \alpha_\infty + a_3e^{-\lambda_3t}$$
$$\gamma = \alpha_\infty + c_3e^{-\lambda_3t}$$

where

$$c_3\left[\frac{p}{p - \lambda_3} - \frac{p}{p - \lambda_2}\right] = (\alpha - \alpha_\infty)\left[1 - \frac{p}{p - \lambda_2}\right]$$

and

$$a_3 = \frac{p}{p - \lambda_3}c_3$$

The values of $a_3$ and $c_3$ are only a few per cent. different from unity, which they approach as the ratio $[CO_2]$ : $[HCO_3^-]$ decreases. The value of $[H_2CO_3]$ is so small in these cases that it can be neglected.

Since the carbon dioxide liberated in the sample bulbs by sulfuric acid is representative of the carbon dioxide and sodium bicarbonate, we may represent its $O^{18}$ fraction by

$$\delta = \frac{\alpha[CO_2] + \gamma[HCO_3^-]}{[CO_2] + [HCO_3^-]}$$

Making the proper substitutions

$$d \ln(\delta - \alpha_\infty)/dt = -\lambda_3$$

From the measured rate of the reaction obtained by evaluating $A$ in the expression $At + B + \log(\delta - \alpha_\infty) = 0$, we obtain the value of the constant

$$p = k_1[H_2O]\text{sec.}^{-1}$$
$$= A \times \frac{2.303}{60} \times$$
$$\left\{ \frac{2}{1 + \frac{[CO_2]}{[HCO_3^-]} - \sqrt{1 + \frac{2}{3}\frac{[CO_2]}{[HCO_3^-]} + \left(\frac{[CO_2]}{[HCO_3^-]}\right)^2}} \right\}$$

The concentrations of $[CO_2]$ and $[HCO_3^-]$ were obtained from the weight of heavy oxygen sodium carbonate and the amounts of water and standard acid used. In an unsatisfactory attempt to determine the ratio $[CO_2]:[HCO_3^-]$ in another way the $p$H of the solution was determined at the reaction temperature by two opposing quinhydrone half cells. One contained the $CO_2$–$HCO_3^-$ solution and the other a Sørensen phosphate buffer. The ratio $[CO_2]:[HCO_3^-]$ was calculated from the equation

$$\log \frac{[CO_2]}{[HCO_3^-]} = pK_a - pH + \log f_{HCO_3^-}$$

where $-0.5\sqrt{\mu}$ was substituted for $\log f_{HCO_3^-}$.[20] However, using standard solutions and carefully guarding against loss of carbon dioxide, e. m. f. values were obtained which yield $p$H values other than those calculated. A junction potential may account for this discrepancy. Keller[21] has reported a difference between the calculated $p$H and the observed $p$H for such solutions using a colorimetric method. At 40° the e. m. f. measurements were unsteady and the $p$H was determined using a Beaver colorimeter[22] with phenol red as indicator. The $pK_a$ value was taken as 7.70 for these solutions whose ionic strength was about 0.05. The ratio $[CO_2]:[HCO_3^-]$ calculated from these measurements was in agreement with those obtained from weighings.

The values of $A$ have been determined by the method of least squares from the experimental data and then $k_1[H_2O]$ evaluated. The results are given in Tables IV, V and VI.

Oxygen exchange between carbon dioxide and water takes place very slowly compared with the time necessary to establish elementic equilibrium. This is true because the carbon dioxide must come to equilibrium with all the water. When the solution was acid enough so that all the carbon dioxide remained as such in solution the values of the rate constant for the velocity of hydration have a constant value. The rate is not affected by addition of sodium chloride, sodium acetate or high concentrations of hydrochloric or acetic acid. In this range it appears that only simple hydration occurs. The results of this and other work are compared in Table VIII.

TABLE VIII

Reaction rate constants for the velocity of hydration of carbon dioxide = $k_1[H_2O]\text{sec.}^{-1}$. Those in parentheses were determined in buffer solutions. All values at 38° were obtained by extrapolation.

| Reference | 0° | 18° | 25° | 38° |
|---|---|---|---|---|
| Faurholt, 1924, multiplied by 2.303 | (0.0030) | (0.025) | | (0.23) |
| Brinkman, Margaria and Roughton, 1933 | ( .0026) | ( .024) | | ( .26) |
| Stadie and O'Brien, 1933 | ( .0027) | | | |
| Roughton and Booth, 1938 | ( .0027)<br>.0021 | | | |
| This paper | ( .0027)<br>.00205<br>± .00005 | | 0.0275<br>± .0015 | .10 |

At 0° the rate of oxygen exchange is just that found by direct kinetic measurement for the rate of hydration of carbon dioxide. This agreement indicates that there is no rapid reversible reaction of carbon dioxide with water which could result in oxygen exchange as has been sometimes supposed. At 25° the value of the rate constant is considerably lower than that previously established. The fact that at elevated temperatures the reaction is so rapid that direct kinetic measurements are less precise probably accounts for this difference. The average energy of activation between 0 and 25° is 16,800 ± 400 calories.

The velocity constant for dehydration can be determined from a knowledge of the true dissociation constant of carbonic acid. Taking this as $4 \times 10^{-4}$, then at 0°

$$k_{-1} = \frac{[CO_2]}{[HCO_3^-]} k_1[H_2O] = \frac{K(\text{true})}{K(\text{apparent})} \times 0.0020 = 4 \text{ sec.}^{-1}$$

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[20] Hastings and Sendroy, *J. Biol. Chem.*, **65**, 445 (1925); Stadie and Hawes, *ibid.*, **77**, 265 (1928).

[21] Keller, *Z. anal. Chem.*, **113**, 8 (1938).

[22] Beaver, *J. Optical Soc.*, **18**, 41 (1929).

When considerable amounts of bicarbonate ion are present, the rate of oxygen exchange is much slower, being dependent on the ratio $[CO_2]:[HCO_3^-]$. As is shown in Table IV, the value of $k_1[H_2O]$ remains constant until very small values of carbon dioxide concentration are reached. Then the inaccuracy in concentration satisfactorily accounts for the deviation. Actually as shown for run B-27 the ratio has varied some 200-fold while $k_1[H_2O]$ changes by only 50%. In Table V the rate constants in run C-1 and C-2 are low. It is thought that this is due to loss of carbon dioxide, a circumstance which occurs more easily at higher temperatures and which would explain the low values. A comparison of runs B-16 and B-20 shows that increasing the salt concentration considerably does not affect the rate. Therefore it seems that under these conditions the bicarbonate ion exchanges oxygen with water only through the reversible formation of carbon dioxide by simple hydration

$$CO_2 + H_2O \rightleftharpoons H_2CO_3 \rightleftharpoons H^+ + HCO_3^-$$

In the presence of $M/15$ phosphate buffer an increase of about 30% in the rate is observed. This is exactly in agreement with the recent data of Roughton and Booth,[9] who have found that the presence of the phosphate buffer, usually heretofore employed, accelerates the reaction to this extent.

Sodium carbonate exchanges all its oxygen slowly with water. It is not feasible to calculate a rate constant since the purity of the sodium carbonate so affects the concentration of carbon dioxide. However, even if one-fourth the sodium carbonate were sodium bicarbonate, it can be shown that the rate of exchange is 1000 times greater than can be accounted for by simple hydration. The rapidity apparently is due to the reaction of carbon dioxide with hydroxyl ion. When the solution has been made more basic by addition of sodium hydroxide, the exchange becomes very slow due to the extremely small amount of carbon dioxide present. The slow exchange of carbonate ion[18] has been studied also by Titani and Goto.[23,24] Our more precise analytical means allow observation of smaller changes.

Oxygen exchange of other inorganic ions has been studied.[24,25] It has appeared that anhydride formation would in some cases account for exchange in acid solutions. Exchange with the sulfate ion is strongly catalyzed by hydroxyl ions.[26] No such effect was observed for carbonate ion.

## Summary

The rate of carbon exchange between carbon dioxide and bicarbonate ion has been studied. Approximate rate constants were determined which are consistent with those established independently for the rate of hydration of carbon dioxide.

The rate of oxygen exchange between carbon dioxide, bicarbonate ion, carbonate ion and water has been investigated. The exchange between carbon dioxide and water is due to the reversible hydration only. The addition of salts or acids did not affect this rate. The rate constant at 0° agrees with that found recently by Roughton and Booth, being one-fourth lower than the previously accepted value which was established in the presence of buffer solutions. At higher temperatures the rate found is considerably less than that previously established. The average energy of activation between 0 and 25° is 16,800 ± 400 calories.

Oxygen exchange of bicarbonate ion occurs only through the reversible formation of carbon dioxide by simple hydration when the $p$H is less than 8. The rate is not affected by the addition of sodium or potassium chloride. In the presence of phosphate buffer the reaction is accelerated.

Carbonate ion slowly exchanges its oxygen with water. The rate is faster than for simple hydration of the carbon dioxide present. This increase is presumably due to the reaction of carbon dioxide with hydroxyl ion. A high concentration of hydroxyl ion retards the exchange, since then only very small concentrations of carbon dioxide are present.

NEW YORK, N. Y. RECEIVED JANUARY 25, 1940

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(23) Titani, Morita and Goto, *Bull. Chem. Soc. Japan*, **13**, 329 (1938).

(24) Titani and Goto, *ibid.*, **14**, 77 (1939).

(25) Blumenthal and Herbert, *Trans. Faraday Soc.*, **33**, 849 (1937); Datta, Day and Ingold, *J. Chem. Soc.*, 1968 (1937); Titani and Morita, *Bull. Chem. Soc. Japan*, **13**, 667 (1938).

(26) Winter, Carlton and Briscoe, *J. Chem. Soc.*, 131 (1940), have shown that sulfate ion is not hydroxyl-catalyzed, and that at high concentration of hydroxyl ion reaction with the glass container may account for the exchange reported by Datta, Day and Ingold.