

THE EFFECT OF THE HYDROGEN ION CONCENTRATION ON THE
RATE OF EXCHANGE BETWEEN THE ALPHA HYDROGEN OF
MALONIC ACID AND TRITIATED WATER, AND THE
EQUILIBRIUM ISOTOPE EFFECT OF THE
REACTION

by

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INTRODUCTION

Much valuable and pertinent information has been gained recently through the use of radioisotopes. Isotope effects can be very important in organic chemistry in the determination of organic mechanisms. Theoretical calculations of equilibrium isotope effects are usually mathematically simple, and the mathematics involved in the treatment of a transition state are avoided. Because of the differences in the masses of the three hydrogen isotopes, protium, deuterium and tritium, kinetic and equilibrium isotope effects should be greater than those for the isotopes of heavier elements, where the mass ratio differences are much lower. Tritium is approximately three times heavier than protium, with the highest isotopic mass ratio, and it is also naturally radioactive, thereby giving a convenient tool by which the reaction may be followed.

The objectives of this problem are as follows:

1. To measure the rate of exchange of the alpha hydrogen atoms of the dicarboxylic acids with the tritium atoms of water-t.
2. To compare these rates at different pH values, and to compare them also at different temperatures.
3. To find the equilibrium isotope effect, and to compare it with the theoretical effect.

HISTORICAL

Isotopic molecules do not react at identical rates, especially when a bond to the isotopic atom is broken during the reaction (2). The difference in reaction rates is called the isotope effect, and it is generally agreed that this effect will be shown only when the bond to the isotopic atom is broken or formed during the rate-determining step in a reaction. In much of the early work, the assumption was made that the effect of the isotopic substitution on the reaction rate was negligible. This assumption, while probably justifiable for the heavier elements, introduced a few discrepancies for the lighter elements, regarding both equilibrium distribution and specific reaction rate (1, 12). Since the isotopes of hydrogen should show the largest isotope effect, in this case, the following work was to be concerned with the rate of exchange between the protium and tritium isotopes of hydrogen, and also the equilibrium isotope effect that would be induced.

Tritium is produced in the atomic pile through the bombardment of lithium with neutrons. It has a half-life of 12.2 years, disintegrating into helium-3 and a beta particle. The energy of the beta particle is 0.0189 Mev., which makes assay of the radioactivity a little difficult, since this low energy particle cannot penetrate even a thin mica window. A method of assay for tritium by Wilzbach, Kaplan, and Brown, (14) was to be used. This method

involves the reduction of the sample into tritium gas (or a combination of gases such as methane- t , etc.) at a temperature of 650° , the gas is then introduced into an ionization chamber, and the radioactivity is measured by the radiation-induced ionization of the gas (15).

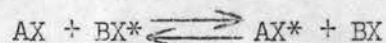
The reactivity of the alpha hydrogen atoms of the monocarboxylic acids has been studied under many and varied conditions. It is well known and easily demonstrable that the hydrogen atoms directly adjacent to the carboxyl group are much more reactive than are hydrogen atoms elsewhere on the chain. Karrer (8) states that the alpha hydrogen atoms are so reactive that they can be replaced at some definite rate, and that the reaction may be followed by some means.

In the case of the dicarboxylic acids, the proximity of another carboxyl group should greatly enhance an effect upon the rate of exchange of the alpha hydrogen atoms. As the length of the intervening chain increases, the effect of the second carboxyl group should decrease, until all effect from this second group is lost in the chain, and only the immediately adjacent carboxyl group affects the alpha hydrogen atoms.

An equilibrium exchange reaction will follow a first order equation if the following conditions are fulfilled; 1) that there be no chemical reaction to disturb the system, 2) that there be no isotope effect, and 3) that the exchanging atoms be chemically

equivalent to each other, no matter which substance they may reside within. Harris (6) and Melander (9) and Burr (2) have shown that exchange kinetics approximate first order reactions even when these conditions are not completely fulfilled, if the relative concentration of the distinguishable isotope is small.

Friedlander and Kennedy (4) and others (6, 9, 13) have shown that the rate, R, can be evaluated in a dynamic equilibrium such as



where the starred atoms represent the radioactive component, from the equation

$$Rt = \frac{ab}{a+b} - \ln(1-F)$$

where $a = [AX + AX^*]$

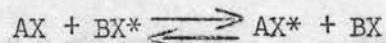
$b = [BX + BX^*]$

$t = \text{time}$

$F = \text{activity of AX at time } t / \text{activity of AX at equilibrium.}$

R is found from the slope of the line when $\ln(1-F)$ is plotted versus t .

The reaction by which isotopic molecules approach equilibrium may be expressed as follows (3, 5, 9, 10, 12):



The equilibrium constant K can be expressed as

$$K = \frac{Q_2}{Q_1} / \frac{Q_4}{Q_3}$$

where Q represents the complete partition function of each molecule and the subscripts 1 and 2 refer to AX and AX* respectively, the subscripts 3 and 4 to BX and BX* respectively. The Q for each

molecule comprises the translational energy, the vibrational energy, the rotational energy, the electronic energy, and the energy from nuclear spin of that molecule. These different energy contributions are difficult to calculate individually. However, fortunately only the ratios are necessary, not the actual values.

In the following ratios, all subscripts will refer to the equation above, and will have the same meaning. The translational energy contribution ratio is

$$\left(\frac{M_2}{M_1}\right)^{3/2}$$

where M signifies the molecular weight.

The vibrational partition function ratio reduced to

$$\prod \frac{1 - \exp(-hcw_1/kT)}{1 - \exp(-hcw_2/kT)}$$

where h is Planck's constant

c is the speed of light

w is the characteristic frequency in wave numbers (cm^{-1})

k is Boltzman's constant

T is the absolute temperature

The rotational partition function ratio becomes

$$\frac{\sigma_1}{\sigma_2} \left(\frac{I_{A2} I_{B2} I_{C2}}{I_{A1} I_{B1} I_{C1}} \right)^{1/2}$$

where σ is a symmetry number, and I represents the moments of inertia.

The electronic partition function and the nuclear spin partition function are ignored.

The energy zero partition function is

$$\exp \sum (hcw_1 - hcw_2) / 2kT$$

All of the above have been for the partition function ratios

$$\frac{Q_2}{Q_1} . \text{ A similar set of calculations could be considered for } \frac{Q_4}{Q_3}$$

but need not be derived here. All functions would be the same, only the subscripts would change.

For each Q we have the following: (Q_2 will be used as an example.)

$$Q_2 = (M_2)^{\frac{3}{2}} \frac{1}{U_2} (I_{A2} I_{B2} I_{C2})^{\frac{1}{2}} \prod \frac{\exp(-hcw_2)/2kT}{1 - \exp(-hcw_2)/kT}$$

substituting $\mu = hcw/kT$

$$\frac{Q_2}{Q_1} = \left(\frac{M_2}{M_1} \right)^{\frac{3}{2}} \frac{U_1}{U_2} \left(\frac{I_{A2} I_{B2} I_{C2}}{I_{A1} I_{B1} I_{C1}} \right)^{\frac{1}{2}} \prod \frac{1 - \exp(-\mu_1)}{1 - \exp(-\mu_2)} \frac{\exp(-\mu_2/2)}{\exp(-\mu_1/2)}$$

similarly

$$\frac{Q_4}{Q_3} = \left(\frac{M_4}{M_3} \right)^{\frac{3}{2}} \frac{U_3}{U_4} \left(\frac{I_{A2} I_{B2} I_{C2}}{I_{A1} I_{B1} I_{C1}} \right)^{\frac{1}{2}} \prod \frac{1 - \exp(-\mu_3)}{1 - \exp(-\mu_4)} \frac{\exp(-\mu_4/2)}{\exp(-\mu_3/2)}$$

and finally

$$K = \frac{Q_2}{Q_1} / \frac{Q_4}{Q_3} = \left(\frac{M_2 M_3}{M_1 M_4} \right)^{\frac{3}{2}} \frac{U_1 U_4}{U_2 U_3} \left(\frac{I_{s2} I_{s3}}{I_{s1} I_{s4}} \right)^{\frac{1}{2}}$$

$$\frac{1 - \exp(-\mu_1) \cdot 1 - \exp(-\mu_4) \cdot \exp(-\mu_2/2) \cdot \exp(-\mu_3/2)}{1 - \exp(-\mu_2) \cdot 1 - \exp(-\mu_3) \cdot \exp(-\mu_1/2) \cdot \exp(-\mu_4/2)}$$

The above equation can be simplified by application of a theorem of Teller and Redlich,

$$\left(\frac{M_2}{M_1}\right)^{\frac{3}{2}} \left(\frac{I_{A2} I_{B2} I_{C2}}{I_{A1} I_{B1} I_{C1}}\right)^{\frac{1}{2}} \left(\frac{m_1}{m_2}\right)^{\frac{3n}{2}} \prod_i \frac{\mu_{1i}}{\mu_{2i}} = 1$$

where m_1 and m_2 are the atomic weights of the isotopic atoms being considered, and n is the number of isotopic atoms exchanged. If the right sides of the above equations are multiplied by μ_2/μ_1 and $\prod_i \mu_{2i}/\mu_{1i}$, respectively, it is possible to simplify these expressions and define new partition functions which are in fact the equilibrium constants for exchange reactions between the compound considered and the separated atoms. A like expression could be derived for $\frac{Q_4}{Q_3}$ also. The finished equation is:

$$K = \frac{Q_2}{Q_1} \frac{Q_4}{Q_3} \frac{\sigma_1 \sigma_4}{\sigma_2 \sigma_3} \prod_i \frac{\mu_{2i} \mu_{3i} (1 - \exp(-\mu_{1i})) (1 - \exp(-\mu_{4i})) \exp(-\mu_{2i}/2) \exp(-\mu_{3i}/2)}{\mu_{1i} \mu_{4i} (1 - \exp(-\mu_{2i})) (1 - \exp(-\mu_{3i})) \exp(-\mu_{1i}/2) \exp(-\mu_{4i}/2)}$$

From the above equation, theoretical values for the equilibrium constant were calculated.

DISCUSSION OF PROCEDURE

The procedure followed can be outlined very simply as 1) background and theoretical considerations, 2) methods and performance of the reaction, 3) reduction of the products of the reaction to the gaseous state, 4) assay of the sample for radioactivity.

In order to study the outlined objectives, the following attributes were necessary for the acid:

1. Good water solubility. The exchange conditions and also the mathematics of the reaction could be greatly simplified if the reaction could be performed directly in "hot" water, since there would be no further need for any other solvent.

2. Nonformation of anhydrides. The intention was to keep the reaction temperature low, and since this was accomplished, no difficulty was encountered.

3. Low volatility. The dicarboxylic acids are practically non-volatile.

4. No decarboxylation. Again, it was hoped that the low reaction temperature would exclude this possibility.

5. A solid acid. All of the dicarboxylic acids are solids.

Malonic acid fitted these attributes very nicely, and it was also suspected that the reactivity of the alpha hydrogen atoms of malonic acid would be high. The activity of the water-t was to be held low enough to exclude the formation of any doubly substituted alpha carbon atoms.

Temperature can be of great importance in a reaction of this type. The higher the reaction temperature, the less the isotope effect, since the excitation of the reacting molecules is greater at higher temperatures, and consequently the reacting molecules are less discriminating. It was hoped that the reaction could be run at 50° or less.

A temperature of 50° was merely an arbitrary starting point, but it became necessary to determine whether or not there was any decarboxylation at this temperature. A constant-temperature bath set at 50° was constructed, and a large sample of malonic dissolved in water was placed therein. The acid titer of aliquot proportions of this solution were then determined. At this temperature there was no decarboxylation, even after an extended period of time. Decarboxylation would have been a very serious matter, and it was satisfying that none was found.

The method of handling the reaction was to be very simple. A weighed amount of malonic acid was dissolved in a known amount of ordinary water, the pH was adjusted with sodium hydroxide of known concentration and amount, the tritiated water was added, and the resulting solution was divided into 1-cc portions, which were placed in vials, sealed, and put into the constant temperature bath. At various intervals, a vial was removed from the bath, opened, and the water was distilled from the acid and/or salt through the use of a vacuum line.

Once the acid and/or salt was dry, ordinary water was used to flush the dried sample, to remove the carboxyl tritium. The difference in the rate of exchange between the carboxyl tritium, which was known to be very rapid, and the rate of exchange of the alpha carbon tritium was expected to be great enough to allow this method of handling. The solution was then redistilled as before, and the solid acid and/or salt remaining was assayed.

However, the solution did not stay completely frozen once the freezing mixture was removed, and the equilibrium value could not be reproduced. Since no good equilibrium value could be obtained, this method of handling the sample was abandoned. In fact, if the acid and/or salt were washed enough times the activity disappeared completely. An attempt was made to flush the sample with alcohol instead of water, since the alcohol distilled much faster than water under vacuum, but the results were no better.

In order to overcome this difficulty, a modification, involving the precipitation of the acid and/or sodium salt of the acid with barium ions was attempted, with much greater success. The precipitated salt was dried under vacuum desiccation, and as was determined experimentally with Carl Fisher reagent, the salt could be dried to an extremely low water content, thereby eliminating any activity that might have come from included radioactive water molecules. The vial was treated exactly as before, except that upon removal from the constant temperature bath, the sample was

immediately precipitated with barium hydroxide. Barium malonate will precipitate from solution at about a pH of 4.5, and the addition of excess barium hydroxide insured a very complete precipitation. The precipitate formed upon the addition of the barium hydroxide was removed with suction filtration, the precipitate washed with water, and the salt immediately put into the desiccator. After a sufficient length of time (determined by experimentation to be 12 to 24 hours) the sample was dry enough to reduce to the gaseous state and assay.

Precipitation with barium ions accomplished more than just the separation of the acid and/or salt from solution. Precipitation eliminated the need for vacuum distillation, which was by far the most time-consuming portion of the operation. It also removed any need to flush the sample, since the dimalonate formed removed any carboxyl tritium which was present. Naturally, the removal of a step in the reaction, i.e. the necessity of removal of the carboxyl tritium, also cut down considerably on the handling time.

EXPERIMENTAL RESULTS

There was no concern over a solvent, since tritiated water was readily available in the laboratory from a method perfected by Hodnett, Feldman and Flynn (7). In essence, the method is to pass tritium gas over copper oxide at 300° and collect all the water formed in a trap immersed in liquid nitrogen. The system is then flushed with protium, and the tritiated water formed is removed from the line. Ordinary water is added to dilute it. The water formed was placed in a ground glass stoppered flask to await assay, and, of course, use in the experiment.

The water-t that was to be used was assayed by filling the water ampules with a weighed amount of the radioactive water, and then handled in exactly the same manner as a solid sample. A value of 3360 $\mu\text{c./g.}$ was obtained, which converted to 60.48 $\mu\text{c./mmole.}$ This value was important, since this water was used in all experiments that were done.

Run 1.

Data for run 1 are given in Table 1. This run was abandoned when it was discovered that the samples of acid were not completely dry, and therefore had probably exchanged further with the water.

TABLE 1
Run 1

		<u>mmoles</u>
pH	normal (approx. 1.00)	
Temperature	50°	
Malonic Acid	1.0406 g.	10.006
Water- <u>t</u>	1.0155 g.	56.36
Water	to make 5 ml.	

Run 2.

Data for run 2 are given in Table II. The samples were dried, flushed, dried again, and assayed. From the standpoint of actual useful data, no good equilibrium value could be found. However, the data were quite encouraging, despite the lack of a good equilibrium value, for they definitely showed that there was an exchange. The lack of a good equilibrium value was due to the fact that this method of handling (i.e. flushing the sample with ordinary water to remove the carboxyl tritium) was unsatisfactory. If the flushing was repeated often enough, the activity completely disappeared. The reactivity of the alpha hydrogen atoms of malonic acid very nearly turned out to be too great.

TABLE II
Run 2

		<u>mmoles</u>	<u>mmoles of H</u>
pH	normal		
Temperature	50		
Malonic Acid	1.0412	10.06	40.02
Water-t	1.0612	58.96	117.92
Water	3.1925	177.36	354.72

<u>Sample No.</u>	<u>Time (hr)</u>	<u>Activity ($\mu\text{c}/\text{mmole}$)</u>	<u>of Reaction</u>
1.	4	3.40	0.4985
2.	8	5.73	0.8402
3.	20	6.99	1.0000
4.	30	6.52	1.0000
5.	96	6.45	1.0000
6.	120	6.01	1.0000
7.	144	7.36	1.0000
8.	173	6.78	1.0000

Run 2-A.

Run 2-A was used as a check upon the method of flushing. If acid were flushed enough times radioactivity disappeared. Flushing with alcohol was tried also, since alcohol will distil much faster than water, but the results were no better.

A search was now instituted to find a heavy metal that would precipitate the malonate ion out of solution, instead of depending on the distillation method. The literature lacks data on malonate salts, and a check of the literature and experimentation soon proved that the best possibility for this precipitation would occur with barium salts. However, the only barium malonates described were hydrates. These salts would naturally give erroneous results, since there was the possibility of the inclusion of radioactive water molecules. Several samples of barium malonate were precipitated and placed under vacuum desiccation. Experimentation showed that the salt could be dried to a constant weight, and that the amount of water present in the dried salt was negligible. Calculations of the concentration of barium ion necessary to precipitate the malonate showed that the precipitation would be very complete upon the addition of a reasonable amount of barium ion. Accordingly, a saturated solution of barium hydroxide was prepared, and the samples were precipitated as the barium salt from this point on. Barium hydroxide has sufficient solubility to give the necessary concentration of barium ions, and since barium malonate precipitates in basic solution but not in highly

acid solution, barium hydroxide seemed the best choice.

Run 3.

Data for run 3 are given in Table III. An assay value of approximately 8.50 $\mu\text{c.}/\text{mmole}$ was obtained for each of the different samples, showing that the run was already at equilibrium after only 18 hours. The method of determining equilibrium was to run samples until the difference between successive samples was indistinguishable.

TABLE III
Run 3

			<u>mmoles</u>	<u>mmoles of H</u>
pH	2.3			
Temperature	50 ^o			
Malonic Acid	1.0443 g.		1.003	40.14
Water-t	1.0154 g.		56.411	112.82
Water	3.1039 g.		172.439	344.88
<u>Sample No.</u>	<u>Time (hr)</u>	<u>Activity ($\mu\text{c}/\text{g}$)</u>	<u>Activity ($\mu\text{c}/\text{mmole}$)</u>	<u>Fraction of Reaction</u>
1.	18	35.89	8.59	1.000
2.	29	35.40	8.47	1.000
3.	40	35.51	8.50	1.000
4.	53	-----	-----	-----

Run 3-A.

Run 3-A was begun as a supplement to run 3 since the first sample in run 3 was already at equilibrium. An assay value of 8.50 $\mu\text{c.}/\text{mmole}$ was again obtained when the values were adjusted so that the two runs were regarded under the same conditions. Equilibrium was reached at or before 8 hours.

Run 3-B.

As a consequence of the results of run 3-A, a run was made in

which the samples were removed from the bath at very short intervals after their introduction. The corrected value obtained for the first sample was 8.50 $\mu\text{c./mmole}$ at 0.5 hours. This equilibrium value was very good, but the rate of the reaction could not be calculated. The reaction proceeded so fast that errors in time, due to handling, outweighed the handling efforts that could be made at times faster than 0.5 hours. In other words, the time involved in handling these samples at such short intervals could not be trusted.

Run 4.

Data for run 4 are given in Table IV. Since the rate of the reaction was so fast at a pH of 2.0 and 50° , run 4 was adjusted to a pH of 7.0. The temperature remained at 50° . The results were a little erratic, but subsequent runs corroborated the validity of these data.

TABLE IV
Run 4

		<u>mmoles</u>	<u>mmoles of H</u>
pH	7.0		
Temperature	50		
Malonic Acid	1.0513 g.	10.102	40.41
Water-t	1.0326 g.	57.367	114.74
Water	3.3114 g.	183.967	367.94
NaOH (N=5.922)	4.4157 g.		21.53 H from NaOH
			394.88 H from H ₂ O
			1303.21 Total

<u>Sample No.</u>	<u>Time (hr)</u>	<u>Activity ($\mu\text{c./mmole}$)</u>	<u>Fraction of Reaction</u>
1.	2	2.23	0.5646
2.	4	2.59	0.6557
3.	6	3.10	0.7848
4.	10	3.38	0.8557
5.	24	3.95	1.0000
6.	123	3.34	1.0000

Run 5.

A single solution was made which was split into two portions, from which both run 5 and run 5-A were taken. Precision was poor, and values were obtained which were both confusing and mystifying. Samples coming off after long reaction times had lower activities than samples that had been removed after only a short reaction time. It is easy to understand now, with the use of hindsight, that the vibrating reed electrometer was beginning to fail, but at the time there was no known reason for these results. Run 5 was assayed, but abandoned when results were so poor.

Run 5-A.

Run 5-A showed the same lack of precision and accuracy that appeared in run 5. This run was also abandoned.

Run 6.

Data for run 6 are given in Table V. Run 6 was considered a moderate success. An equilibrium value was obtained which was considered to be accurate.

TABLE V
Run 6

		<u>mmoles</u>	<u>mmoles of H</u>
pH	7.0		
Temperature	30		
Malonic Acid	1.1043 g.	10.612	42.45
Water-t	1.0248 g.	56.933	113.87
Water	2.9508 g.	163.933	327.87
NaOH (N = 5.922)	3.2188 g, 3.41 ml.		15.70 H from NaOH 288.02 H from NaOH's H ₂ O
			787.91 Total

<u>Sample No.</u>	<u>Time (hr)</u>	<u>Activity (μc/mmole)</u>	<u>Fraction of Reaction</u>
1.	4	1.34	.2543
2.	8	1.16	.2201
3.	18	1.95	.3700
4.	24	2.58	.4896
5.	30	3.02	.5731
6.	49	4.00	.7590
7.	149	5.27	1.0000

Run 7.

Run 7 was abandoned after assay of the first few samples. There was no trend in the results whatever. The samples at the beginning of the run were apparently more radioactive than the samples at the end of the run. The vibrating reed evidently had its ups and downs during this period. Some concern was also expressed at this time that the mass action of the acid was displacing the equilibrium. However, the amount taken out as radioactive acid was so small that we believe that this had no marked effect.

Run 8.

Run 8 also gave erratic results. The vibrating reed now began to show a very definite variation in the results. A check of the

electronic tubes showed nothing unusual, however, further runs were held off until the machine could be overhauled.

Run 9.

Data for run 9 are not given. Samples of run 9 were assayed on the Packard Tri-Carb, a liquid scintillation apparatus. There was apparently some activity; however, the solubility of malonic acid in the scintillation solution proved to be too small.

Run 9-A.

Data for run 9-A are also not given. This run was begun before the results of run 9 were definitely known, but the same results were obtained. This method was abandoned, not without some regret, since the method was easy and fascinating.

Run 10.

Data for this run are given in Table VI. The vibrating reed was overhauled, and values were sharp and clear. As will be seen in the data table, a good equilibrium value was obtained. The last sample of this run was divided, and a portion of the water was distilled and assayed to obtain the equilibrium value of the water. The other portion was precipitated as usual, and a value was obtained for the equilibrium value of the acid. Good values were obtained in each case.

TABLE VI
Run 10

pH	7.0	<u>mmoles</u>	<u>mmoles of H</u>
Temperature	30°		
Malonic Acid		9.017	36.07
Water-t	1.0254 g.	56.967	113.93
Water	2.8841 g.	160.228	320.46
NaOH (N=6.4505)	3.9909 g.	20.917	20.92 (NaOH)
		175.244	350.49 (H ₂ O)
			1841.87 Total
Sample No.	Time (hr)	Activity ($\mu\text{c.}/\text{mmole}$)	Fraction of Reaction
1.	12	1.30	.4377
2.	17	1.71	.5758
3.	24	1.27	.4276
4.	36	1.94	.6531
5.	48	2.26	.7609
6.	72	2.59	.8721
7.	192		
8.	7,360	2.97	
Water	7,360	4.03	

Run 11.

Data for run 11 are given in Table VII. Run 11 was taken from a stock solution made to give enough for the rest of the runs. The last sample was split again to obtain a value for both the water of the reaction and the precipitated sale. The last sample was removed after 6,720 hours. Good values were obtained for both of the last samples, and for the reaction time.

TABLE VII
Run 11

		<u>mmole</u>	<u>mmoles of H</u>
pH	7.0		
Temperature	30°		
Malonic Acid	.9173 g.	8.815	35.260
Water-t	1.0254 g.	56.967	113.93
Water	2.8252 g.	156.956	313.91
NaOH (N=6.4505)	4.0717 g.	21.339	21.34 (NaOH)
		178.794	357.59 (H ₂ O)
			842.03 Total

Sample No.	Time (hr)	Activity ($\mu\text{c.}/\text{mmole}$)	Fraction of Reaction
1.	10	1.43	.3844
2.	22	1.72	.4624
3.	40	2.64	.7097
4.	168	3.10	.8333
5.	260	3.75	-----
6.	380	4.07	-----
7.	6,720	3.72	-----
Water	6,720	5.29	

Run 12.

Data for run 12 are given in Table VIII. Run 12 was taken from a second aliquot of the same stock solution that was used for run 11. Run 12 was also split, however, no precipitate was obtained from the solution, due to faulty handling methods. A good value for the water was obtained, however, and with the reactivity of the solution (run 12 was run at 50°), a good value for the equilibrium of the precipitate was obtained from the previous sample.

TABLE VIII
Run 12

		<u>mmole</u>	<u>mmoles of H</u>
pH	7.0		
Temperature	50°		
Malonic Acid	1.0543 g.	10.132	40.53
Water-t	1.2702 g.	70.566	141.13
Water	3.2662 g.	181.455	362.91
NaOH (N=6.4505)	3.9871 g.	34.83 (NaOH)	34.83
	.8357 g. NaOH	175.08 (H ₂ O)	350.16
	3.1514 g. H ₂ O		
		Total	929.56

<u>Sample No.</u>	<u>Time (hr)</u>	<u>Activity</u> <u>(μc/mmole)</u>	<u>Fraction</u> <u>of Reaction</u>
1.	4	1.86	.5981
2.	5	2.12	.6817
3.	18	3.16	-----
4.	48	3.11	-----
5.	144	2.42	-----
Water	7,421	5.65	-----

DISCUSSION OF RESULTS

A study of the graphs shows a half life of approximately three hours for the runs made at 50^o, and a half life of twenty-four hours for the runs made at 30^o.

For the experimentally determined value of the equilibrium isotope effect, if, at some infinite time, we let

x_0 = the radioactivity of the acid salt at equilibrium, and

x_1 = the radioactivity of the water at equilibrium,

then the equilibrium isotope effect of the exchange is the

ratio: $K = x_0/x_1$. Where there is no isotope effect,

$x_0/x_1 = 1$. From the data obtained,

at 30^o $K = 0.7201$

and at 50^o $K = 0.5504$

These deviations from $x_0/x_1 = 1$ show the presence of the isotope equilibrium distribution.

Calculation of the theoretical isotope effect is done from the equation mentioned in the Historical section. From Schmelz, Nakagawa, Mizushima, and Quagliano (11) values were obtained for the frequencies necessary to calculate the theoretical data for the acid salt. These data are not readily available, especially for the malonate salts of barium, however, the assumption was made that the sodium and potassium malonate values would suffice. Also, there are no data for the C-T frequency values of these salts. These

latter frequencies were calculated from Hooke's Law for harmonic oscillators, which is the inverse ratio of the square root of the reduced masses:

$$\frac{\sqrt{C-T}}{\sqrt{C-H}} = \sqrt{\frac{\mu_{C-H}}{\mu_{C-T}}}$$

This equation gives a value of $\sqrt{C-T} = 0.620173 \times \sqrt{C-H}$.

Values were obtained, or calculated from Hooke's Law for $\sqrt{(CH)}$ stretching, CH_2 bending, CH_2 wagging, and CH_2 rocking. Values for H_2O and HTO were obtained from Urey (12). These values were inserted in the equation in the necessary places to determine each function, Q_i , where i represented the total number of frequencies that had to be taken into consideration.

For the theoretical isotope exchange value of K , the following was found:

$$\text{At } 30^\circ \quad K = \frac{Q_2/Q_4}{Q_1/Q_3} = \frac{35.658}{59.846} = 0.5958$$

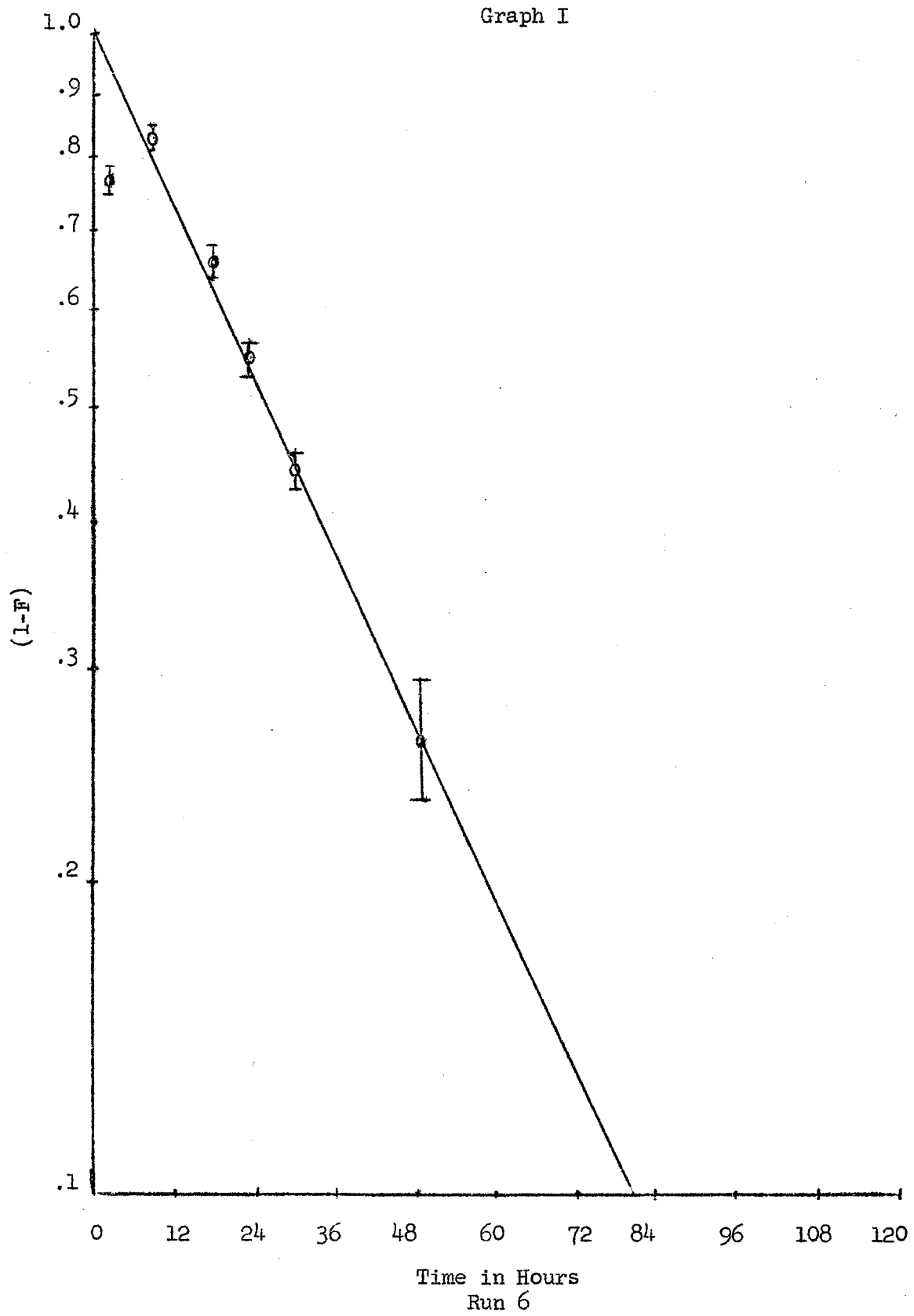
$$\text{and at } 50^\circ \quad K = \frac{Q_2/Q_4}{Q_1/Q_3} = \frac{23.546}{57.450} = 0.4099$$

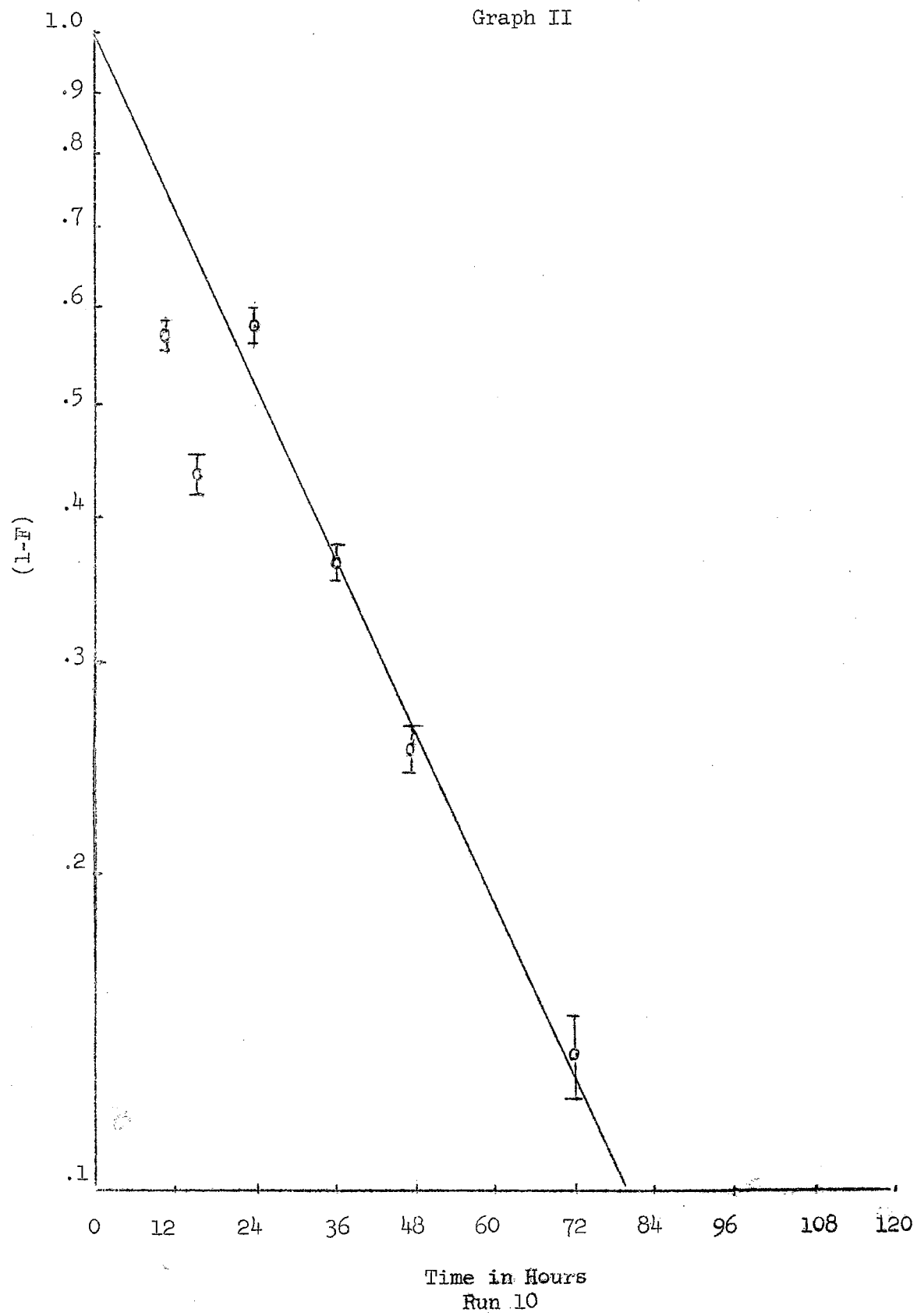
It is immediately apparent that the data from the experimentally determined values do not match the data from the theoretically determined values. However, the theoretically determined values were calculated from data that are both incomplete and not well determined as yet. It is with some surprise that a lower value (i. e. a greater isotope effect) was obtained at 50° than at 30° . It was assumed that as the temperature increased that the

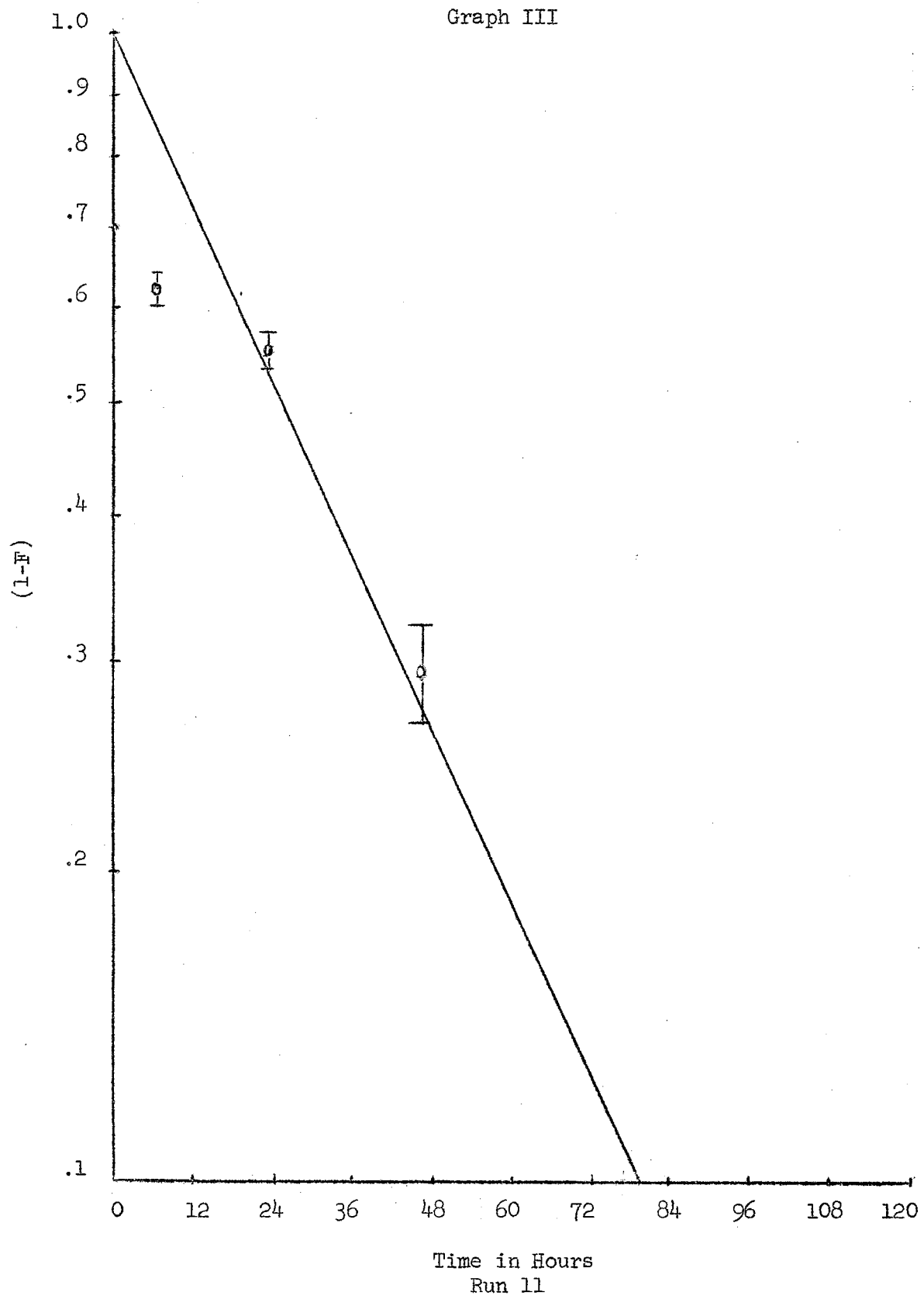
isotope effect would be less noticeable.

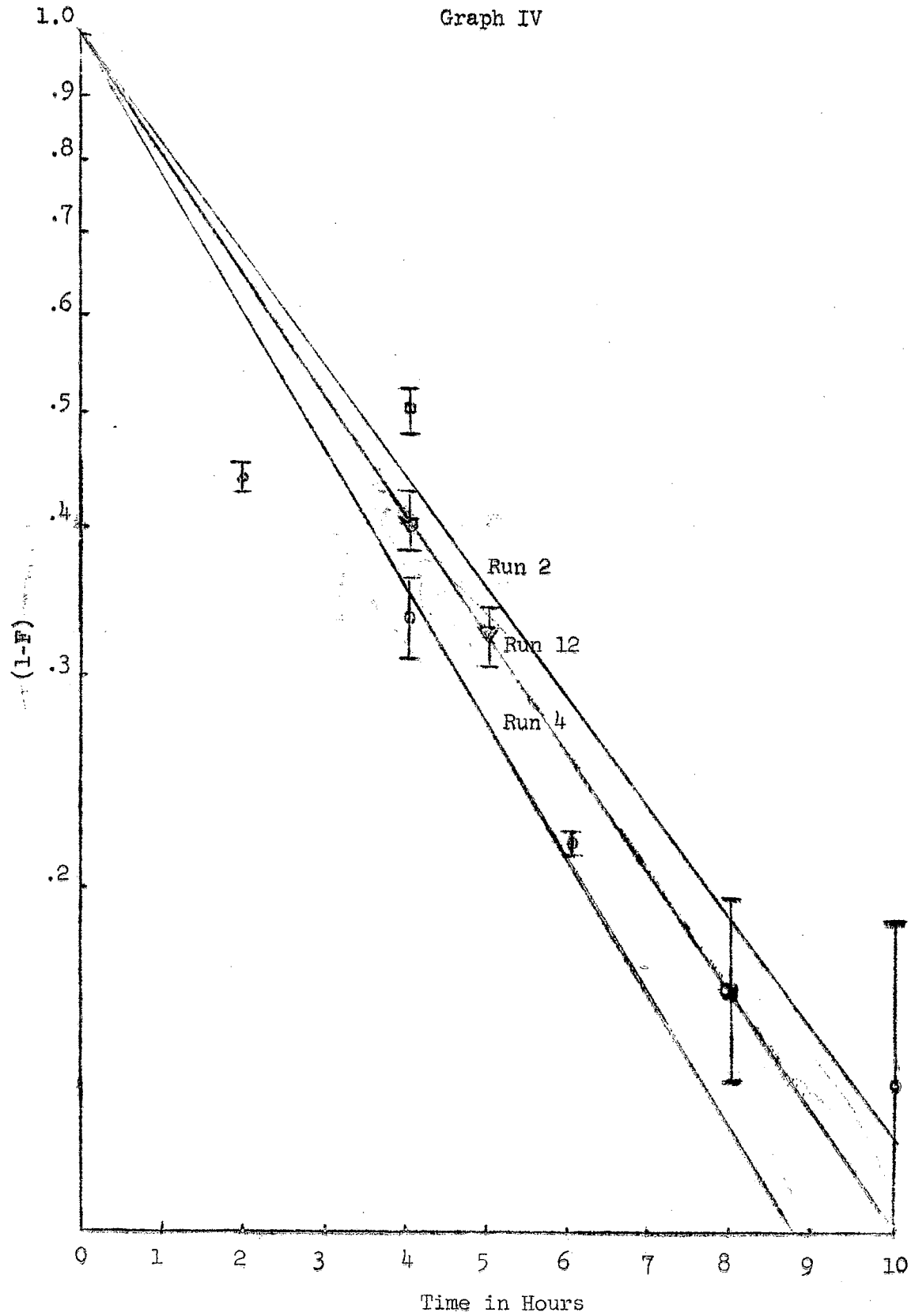
Exchange at low pH values was extremely rapid. As the pH was shifted to neutral, the rate of exchange was slowed. From these indications, it is apparent that the assumption that the free acid would exchange more quickly than the sodium salt of the acid was correct.

Graph I









SUMMARY

The rate of exchange between the alpha hydrogen atoms of malonic acid and water-t has been measured. The reaction is very fast at low pH values, and tends to slow down as the pH approaches 7. Indications are that the reaction is almost impossible to measure at pH values other than neutral. It is not surprising that the rate of exchange is faster at higher temperatures. The equilibrium isotope effect has been determined. Isotope effects for the reaction have been calculated from the theoretical, and these values have been compared with the experimental values.

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