

[CONTRIBUTION FROM THE CHEMISTRY DIVISION OF OAK RIDGE NATIONAL LABORATORY]

A Comparison of the Magnitudes of the Isotope Intermolecular Effects in the Decarboxylations of Malonic-1-C¹⁴ Acid and Malonic-2-C¹⁴ Acid¹ at 154°

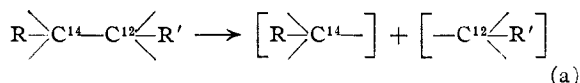
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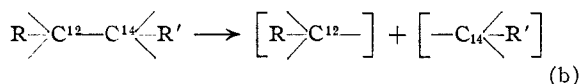
By a method involving measurement of the rate of change with time of the logarithm of the specific activity of unchanged malonic acid, the isotope effect, k_{14}/k_{12} , in the decarboxylation of malonic-2-C¹⁴ acid at 154° has been shown to have a value of 0.929. For decarboxylation of malonic-1-C¹⁴ acid under the same conditions the value of k'_{14}/k_{12} was found to be 0.939.

I. Introduction

A number of studies involving isotope effects in reactions of isotopically labeled carbon compounds have recently appeared in the chemical literature.² The principal objective of the work described in the present paper was the comparison of the two carbon-14 isotope effects in a pair of bond breaking reactions of the types



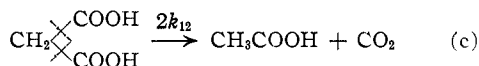
and



where the reactions differ only in that the label appears in one case at the carbon bonded to the groups collectively represented by R and in the other case at the carbon bonded to the groups collectively represented by R'. It seemed probable that isotope substitution in one of the two units, $\text{R} \begin{array}{c} \nearrow \\ \searrow \end{array} \text{C}$ and $\text{R}' \begin{array}{c} \nwarrow \\ \swarrow \end{array} \text{C}$, might have a different influence on the vibrations involving the labeled atom and consequently on the ratio of the reaction rate constants, k_{14}/k_{12} , from that of isotope substitution in the other fragment³ particularly if the bonds to the labeled carbon were of different types in the two units. Such a case was found in the first-order decarboxylations⁴ of malonic-1-C¹⁴ acid and malonic-2-C¹⁴ which were investigated as to the extent of isotope fractionation in each.

Here $\text{R} \begin{array}{c} \nearrow \\ \searrow \end{array} \text{C}$ represents the carboxyl group and $\text{R}' \begin{array}{c} \nwarrow \\ \swarrow \end{array} \text{C}$ the group $-\text{CH}_2\text{COOH}$.

In spite of complications caused by the fact that carboxyl-labeled malonic acid molecules can decarboxylate by two paths, one producing carbon-14 dioxide and the other producing carbon-13 dioxide, it was possible to estimate the relative values of the rate constants involved

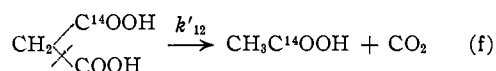
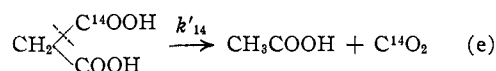
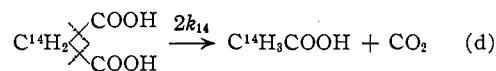


(1) This document is based upon work performed under Contract Number W-7405-eng.26 for the Atomic Energy Commission at the Oak Ridge National Laboratory.

(2) G. A. Ropp and O. K. Neville, *Nucleonics*, **9**, 22 (1951). A brief general discussion of carbon isotope effects was presented in this review.

(3) K. S. Pitzer, *J. Chem. Phys.*, **17**, 1341 (1949).

(4) (a) P. Yankwich and M. Calvin, *ibid.*, **17**, 109 (1949); (b) J. Bigeleisen, *ibid.*, **17**, 425 (1949); (c) A. Roe and M. Hellman, *ibid.*, **19**, 660 (1951).



These equations define the rate constants so that k_{12} and k'_{12} each refer to the breaking of a single C¹² bond, and k_{14} and k'_{14} each refer to the breaking of a single C¹⁴ to C¹² bond. The comparison desired was therefore that between k_{14} and k'_{14} .

II. Methods of Evaluating the Isotope Effects

A. Derivation of the Equation Used to Evaluate the Isotope Effect for Decarboxylation of Malonic-2-C¹⁴ Acid.—For equation (d) let

n^{14} = number of moles of malonic-2-C¹⁴ acid left unreacted at time t

n_0^{14} = number of moles of malonic-2-C¹⁴ acid at time, $t = 0$

Since the reaction is first order

$$n^{14} = n_0^{14}e^{-2k_{14}t}$$

Similarly for equation (c)

$$n^{12} = n_0^{12}e^{-2k_{12}t}$$

$$\therefore n^{14}/n^{12} = n_0^{14}/n_0^{12}e^{2(k_{12}-k_{14})t}$$

and

$$2.303 \log (n^{14}/n^{12}) = 2.303 \log (n_0^{14}/n_0^{12}) + 2(k_{12} - k_{14})t$$

Since at tracer level (n^{14}/n^{12}) is proportional to the specific activity of the malonic acid remaining at time, t , $2(k_{12} - k_{14})$ may be obtained from the slope of a plot of log specific activity of remaining malonic acid vs. time. Dividing by $2k_{12}$, the experimentally measured first order kinetic rate constant, gives a value of $2(k_{12} - k_{14})/2k_{12}$ from which the ratio k_{14}/k_{12} is calculated.

B. Evaluation of the Isotope Effect for the Decarboxylation of Malonic-1-C¹⁴ Acid.—For equations (e) and (f) let

N^{14} = the number of moles of malonic-1-C¹⁴ acid left unreacted at time, t

N_0^{14} = the number of moles of malonic-1-C¹⁴ acid at time $t = 0$

then

$$N^{14} = N_0^{14}e^{-(k'_{12} + k'_{14})t}$$

Since Roe and Hellman^{4c} have shown that the ratio, k'_{12}/k'_{14} , has the value 1.06, the previous equation may be rewritten

$$N^{14} = N_0^{14}e^{-2.06k'_{14}t}$$

Dividing by the corresponding relation from equation (c) gives

$$N^{14}/n^{12} = \frac{N_0^{14}e^{-2.06k'_{14}t}}{n_0^{12}e^{-2k_{12}t}} = N_0^{14}/n_0^{12}e^{2(k_{12}-1.03k'_{14})t}$$

$$\therefore 2.303 \log (N^{14}/n^{12}) = 2.303 \log (N_0^{14}/n_0^{12}) + \frac{2(k_{12} - 1.03k'_{14})t}{1.03k'_{14}}$$

Thus at tracer level the slope of the plot of log specific activity of the unreacted malonic acid *vs.* time determines $2(k_{12} - 1.03k'_{14})$. Division by the kinetic rate constant establishes the relations

slope/measured rate constant =

$$\frac{2(k_{12} - 1.03k'_{14})}{2k_{12}} = 1 - 1.03k'_{14}/k_{12}$$

$$\therefore k'_{14}/k_{12} = (1 - \text{slope/measured rate constant})/1.03$$

C. Use of the Flow-Method of Evaluation of the Isotope Effect in the Decarboxylation of Malonic-1-C¹⁴ Acid.—Since decarboxylation of malonic-1-C¹⁴ acid produces the labeled gas, carbon-C¹⁴ dioxide, the isotope effect was further checked by application of the flow method previously used for studying the dehydration of formic-C¹⁴ acid.⁵ The equation was slightly more complex than in the case of formic acid because the malonic-1-C¹⁴ acid decomposed by two paths represented by equations (e) and (f) instead of one path as in the formic acid case. The relation becomes

$$2.303 \log S = 2.303 C \log \left[\frac{k'_{14}N_0^{14}}{2k_{12}n_0^{12}} \right] + 2(k_{12} - 1.03k'_{14})t$$

where *C* is a constant whose value is dependent upon the units chosen for *S*, the instantaneous specific activity of the carbon-C¹⁴ dioxide produced at time, *t*. Therefore at tracer level the relationship of k'_{14}/k_{12} to the slope of the plot of log of the instantaneous specific activity of the carbon dioxide *vs.* time is the same as that derived under B, the difference being that the specific activity of malonic-1-C¹⁴ acid remaining is replaced by the instantaneous specific activity of the carbon dioxide.

III. Results

A. Experimentally Measured First Order Rate Constants (Values of $2k_{12}$) at 154°.—min.⁻¹ × 10²: 6.13, 6.72, 6.10, 6.44, 6.86; mean value: 6.45 ± 0.31 (95% confidence interval).

B. Isotope Effect for Decarboxylation of Malonic-2-C¹⁴ at 154°.—

Time (minutes)	8	12	16	20	24	28	32
Sp. act., μc./mg. × 10 ²	1.995	2.021	2.085	2.097	2.165	2.178	2.207

$$2(k_{12} - k_{14}) = 2.303 \times \text{slope} = 0.00455 \text{ (Fig. 1a); } (k_{12} - k_{14})/k_{12} = 0.0706; k_{14}/k_{12} = 0.929.$$

C. Isotope Effect for Decarboxylation of Malonic-1-C¹⁴ Acid at 154°. (1) **By Following the Variation of the Specific Activity of the Remaining Malonic-1-C¹⁴ Acid.**—

Time, minutes	4	8	12	16	20	24	28	31.5
Sp. act., μc./mg. × 10 ³	5.14	5.22	5.24	5.31	5.35	5.37	5.43	5.52

$$2.303 \times \text{slope} = 0.00225 \text{ (Fig. 1b); } 1.03k'_{14}/k_{12} = (1 - 0.00225/0.0645) = 0.965; k'_{14}/k_{12} = 0.937.$$

(5) G. A. Ropp, A. J. Weinberger and O. K. Neville, *THIS JOURNAL*, **73**, 5573 (1951).

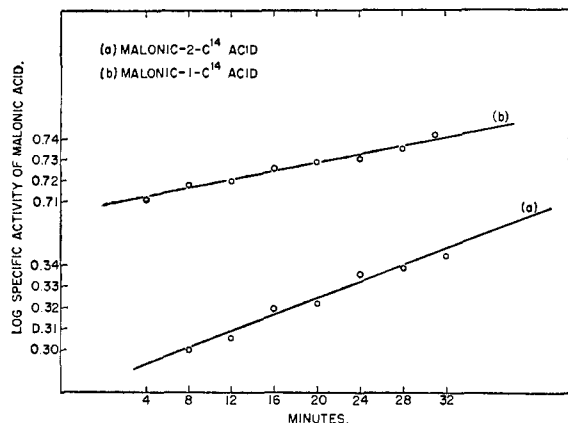


Fig. 1.—Relation of specific of malonic acid to time of sampling in the first-order decarboxylation at 154°.

(2) **By Following the Variation of Specific Activity of Carbon-C¹⁴ Dioxide Evolved by the Flow System.**—

First run: millivolt readings taken from Brown Recorder Chart at regular intervals

Time, minutes	0	3	6	9	12	15	18	21	24	27
Millivolts (proportional to sp. act.)	287	290	292	293	294	295	297	298.5	301.5	304

$$2.303 \times \text{slope} = 0.00194 \text{ (Fig. 2a); rate constant determined simultaneously} = 0.0610 \text{ min.}^{-1}; 1.03k'_{14}/k_{12} = (1 - 0.00194/0.0610) = 0.968; k'_{14}/k_{12} = 0.940.$$

Second run:

Time, minutes	0	3	6	9	12	15	18	21	24	27
Millivolts (proportional to sp. act.)	289	293	294	296	298	297.5	300	302.5	304	307.5

$$2.303 \times \text{slope} = 0.00214 \text{ (Fig. 2b); rate constant determined simultaneously} = 0.0644 \text{ min.}^{-1}; 1.03k'_{14}/k_{12} = (1 - 0.00214/0.0644) = 0.967; k'_{14}/k_{12} = 0.939$$

D. Summary of Results.—

k'_{14}/k_{12}	k_{14}/k_{12}	k'_{14}/k_{14}
0.937		
.940		
.939		
Av. .939	0.929	1.01

This 1% difference between k'_{14} and k_{14} is probably not significant in view of the broad interval (1.06 ± 0.02) reported^{4c} for the value, 1.06, of k'_{12}/k'_{14} . The conclusion is therefore, that only a very slight increase in the isotope effect, if any change at all, results from moving the carbon-14 label from the carboxyl group to the methylene group. It is worthy of note that the isotope effects calculated here are not in agreement with certain previously reported values.^{4a} A further approximate calculation may be made to demonstrate that k'_{12} is essentially equal to k_{12}

$$k'_{12}/k_{12} = \frac{k'_{12}/k'_{14} = 1.06}{k_{12}/k'_{14} = 1/0.939} = 0.995$$

Since three of the isotope effect ratios depend upon the value of k'_{12}/k'_{14} used in their calculation, and since the value of k'_{12}/k'_{14} reported by Roe and Hellman^{4c} is considered by some to be too low, these isotope effect ratios have also been calculated using a value of 1.10 as an upper limit for k'_{12}/k'_{14} . The new ratios calculated become: $k'_{14}/k_{12} = 0.921$, $k'_{14}/k_{14} = 0.992$, and $k'_{12}/k_{12} = 1.02$. The conclusion that k'_{14} and k_{14} are very nearly equal re-

mains the same; the fact that the ratio k'_{12}/k_{12} becomes greater than one suggests that the value, 1.10, for k'_{12}/k'_{14} may be too high.

IV. Experimental

A. Synthesis of Malonic-2-C¹⁴ Acid and Malonic-1-C¹⁴ Acid.—By conventional procedures malonic-2-C¹⁴ acid was prepared by the reaction of chloroacetic acid-2-C¹⁴ with potassium cyanide followed by hydrolysis of the resulting cyanoacetic-2-C¹⁴ acid, and malonic-1-C¹⁴ acid was prepared from a corresponding series of reactions beginning with chloroacetic acid and potassium cyanide-C¹⁴. Both acids were carefully purified by crystallization from ether and acetone to remove radioactive impurities. The malonic-C¹⁴ acid was also sublimed at 90–100° at a pressure of less than 1 mm.

B. Determination of the First-order Rate Constant for the Decarboxylation of Malonic Acid at 154°.—Decarboxylations of 4-g. samples of molten malonic acid were carried out in a 7-ml. glass vessel heated by the vapors of refluxing anisole. The evolved carbon dioxide was passed through a small U-tube cooled with solid Dry Ice to remove entrained acetic acid. The carbon dioxide was collected over 85% phosphoric acid where its volume was noted at regular time intervals. The calculated first order rate constants were in fair agreement with the values estimated by Hinshelwood⁶ at 153.2°.

C. Decarboxylation of Malonic-2-C¹⁴ Acid at 154°.—Using the same reaction vessel described under B, 2 g. of malonic-2-C¹⁴ acid was decomposed at the temperature of refluxing anisole. No attempt was made to collect the carbon dioxide or to prevent escape of acetic acid. At four-minute intervals small samples were drawn from the reaction mixture with a pipet and quenched in cold ligroin. The ligroin and acetic acid were allowed to evaporate and the malonic acid samples were purified by sublimation at 90–100° at less than 1 mm. pressure. A weighed portion of each sample was burned⁷ using Van Slyke solution and the resulting carbon dioxide was swept into an ion chamber and assayed using the vibrating-reed electrometer.⁷

D. Decarboxylation of Malonic-1-C¹⁴ Acid at 154°. (1) **Following the Specific Activity of the Remaining Malonic-1-C¹⁴ Acid.**—Eight 500-mg. samples of malonic-1-C¹⁴ acid in test-tubes prepared from 3-inch lengths of 7-mm. tube were bathed in the vapors of refluxing anisole in an all-glass apparatus designed to ensure the same rate of heating of all eight tubes. Carbon-C¹⁴ dioxide and acetic-1-C¹⁴ acid escaped at will. At the end of each four-minute interval one tube was withdrawn and quenched by cooling in liquid nitrogen. The malonic-2-C¹⁴ acid was recovered from each tube, purified, and assayed as previously described.

(2) **Using the Flow System.**—Four grams of malonic-1-C¹⁴ acid was decomposed exactly as described under B. The evolved carbon-C¹⁴ dioxide was passed first through a small U-tube cooled with solid Dry Ice, then through a 9-inch length of 7-mm. copper tube to ensure equilibration with the temperature of the room. The gas then passed through

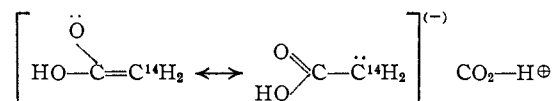
the 10-ml. stainless steel ion chamber⁸ where its instantaneous specific activity was measured and plotted on the chart of a Brown recorder as a function of time. Gas leaving the ion chamber was collected over 85% phosphoric acid to permit simultaneous measurement of the first order rate constant. Specific activities (millivolts) were taken at 3-minute intervals from the Brown recorder plot. Logarithms of these values were plotted as shown in Fig. 2.

V. Discussion of the Results

Bigeleisen⁸ has shown that according to the theory of absolute reaction rates, the isotope effect on reaction rates is made up of at least two factors the reduced mass effect and the zero-point energy effect. It has also been stated⁹ that the reduced mass effect may be calculated from the masses of the two atoms connected by the bond which breaks during the reaction. Therefore, so far as the reduced mass effect is concerned, the two isotope effects—*i.e.*, in decarboxylation of malonic-1-C¹⁴ acid and in decarboxylation of malonic-2-C¹⁴ acid—should have the same value. However, the theory would predict that the second factor—the zero point energy effect could have different values for these two isotope effects, and for this reason that the isotope effects would probably differ to some degree for the two types of malonic acid. The theory has been applied to the decarboxylation of malonic-1-C¹⁴ acid by Bigeleisen^{4b} and by Pitzer³ using different models. For the sake of comparison with the mean value of the malonic-1-C¹⁴ isotope effect measured in the present work, their theoretical values have been listed in terms of the constants defined in this paper:

k'_{14}/k_{12}	Bigeleisen (400°K.)	Pitzer (400°K.)	Reported here (427°K.)
	0.960	0.877	0.939

It is apparent that the theoretical calculations differ considerably from each other and that neither calculation gives results agreeing with the value reported in this paper. Since lack of knowledge about the vibrational frequencies in the malonic acid molecule may be mainly responsible for this lack of agreement, any theoretical estimation of the isotope effect in the decarboxylation of malonic-2-C¹⁴ would probably be unreliable. There would also be an additional uncertainty in setting up a model for the activated complex in the case of the decarboxylation of malonic-2-C¹⁴ acid: the experimentally observed fact that β -keto acids decarboxylate much more readily than α - or γ -keto acids suggests a rather large degree (but an unknown degree) of contribution to the activated complex of resonance stabilized forms such as



Thus this lack of knowledge about the character of the bonds to the labeled carbon atom would add to the uncertainties involved in estimating the vibrational frequencies of the activated complex and cast more doubt on any theoretically estimated value for k_{14}/k_{12} .

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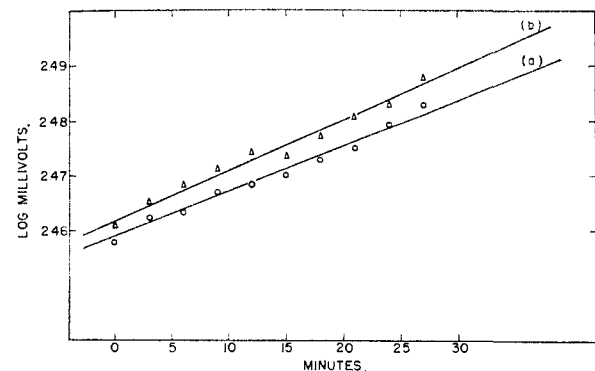


Fig. 2.—Use of the flow system in following the relation of specific activity of C¹⁴O₂ to time in the decarboxylation of malonic-1-C¹⁴ acid.

(6) C. N. Hinshelwood, *J. Chem. Soc.*, 156 (1920).
(7) O. K. Neville, *This Journal*, **70**, 3501 (1948).

(8) J. Bigeleisen, *J. Chem. Phys.*, **17**, 675 (1949).
(9) J. Bigeleisen, *ibid.*, **17**, 344 (1949).