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The Decarboxylation of Methylmalonic Acid and *n*-Octadecylmalonic Acid in Normal Alkanols

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Abstract

Rate constants and activation parameters are reported for the decarboxylation of methylmalonic acid and *n*-octadecylmalonic acid in three normal alkanols (hexanol-1, octanol-1, and decanol-1). Enthalpies of activation for both substrates in the various solvents are found to be a linear function of the number of carbon atoms or methylene groups in the hydrocarbon chain of the solvent. For both reaction series the isokinetic temperature is found to be equal to the melting point of the substrate. The free energy of activation at the isokinetic temperature in kcal/mole is 29.0 for *n*-octadecylmalonic acid and 29.4 for methylmalonic acid. Based on the results of the present investigation as well as on previously reported data in the case of malonic acid and *n*-butylmalonic acid, an empirical method of calculating the rate of reaction for the decarboxylation of malonic acid and its *n*-alkyl derivatives in normal alkanols is proposed. As a further test of the method of calculation the decarboxylation of *n*-dodecylmalonic acid in heptanol-1 at 110.30°C was studied. The calculated value of the pseudo-first-order specific reaction velocity constant of the reaction agreed with the experimental value to within about 0.1 percent.

Introduction

Malonic acid and its *n*-alkyl derivatives readily undergo decarboxylation when warmed in polar solvents. The number of malonic acid derivatives which are capable of reaction is extensive, and so is the number of potential nucleophilic catalysts [1]. Highly accurate rate measurements of these reactions are possible by virtue of the fact that one of the products of the reaction is a gas. These circumstances serve as the basis for a detailed investigation of the effect of substituents and structure on chemical reactivity.

Experimental rate constants and activation parameters have already been reported on the decarboxylation of malonic acid [2] and *n*-butylmalonic acid [2] in a series of normal alkanols. In these investigations two interesting results were noted, (a) The enthalpies of activation of the reactions appeared to be a linear function of the number of carbon atoms or methylene groups in the hydrocarbon chain of the solvent, and (b) The free energy of activation at the melting point of the substrate appeared to be a constant, the same for both substrates. In view of the novelty of these results it was deemed worthwhile to extend the investigation of the decarboxylation reaction to include additional members of the series of *n*-alkyl malonic acid derivatives in this group of homologous solvents. In order to cover as large a spectrum as possible, two extreme members of the series of straight-chain monoalkyl derivatives of malonic acid were selected for this investigation, namely, methylmalonic acid and *n*-octadecylmalonic acid. Careful rate measurements were carried out on the decarboxylation of these two compounds in three normal alkanols (hexanol-1, octanol-1, and decanol-1) at several different temperatures in order to accurately evaluate activation parameters for the purpose of comparison with data previously reported. Kinetic data on the noncatalyzed decarboxylation of methylmalonic acid and *n*-octadecylmalonic acid have been published [3]. The results of this investigation are reported herein.

Experimental

Reagents

Methylmalonic acid, mp 123.5°C, obtained from Aldrich Chemical Company, and *n*-octadecylmalonic acid, mp 123.0°C, obtained from Eastman Kodak Company, were used as purchased. The alkanols were reagent grade. Approximately 90-ml samples of each solvent were distilled directly into the dried reaction flask immediately before the beginning of each decarboxylation experiment.

Apparatus and Technique

Details of the apparatus and technique have been described previously [4]. A fragile glass capsule containing a weighed sample of the acid was introduced in the usual manner into the 100 ml r.b. three-neck s.t. reaction flask containing solvent connected by a standard taper joint to the reflux condenser. The condenser in turn was connected via flexible tubing to a water-jacketed buret (calibrated by the U.S. Bureau of Standards) equipped with a leveling bulb and filled with the entraining liquid. The reaction flask was immersed in a constant-temperature oil bath, the temperature of which was controlled to within ±0.005°C, by the use of a transistorized temperature-control unit equipped with a sensitive thermistor probe. The temperature of the oil bath was measured by means of a thermometer (graduated in tenths of a degree Celsius) which had been calibrated by the U.S. Bureau of Standards. A constant-temperature Lauda-K/2R water circulator controlled the temperature of the water in the water jacket to within ±0.05°C. The experiments were carried out in an atmosphere of dried CO_2 gas. Samples of methylmalonic acid weighing 0.2122 g, or samples of *n*-octadecylmalonic acid weighing 0.6506 g, were used in the individual experiments. These are the weights of methylmalonic acid or of *n*-octadecylmalonic acid, respectively, required to furnish 40.00 ml of CO_2 at NTP on complete reaction, based upon the actual molar volume of CO_2 at NTP, namely, 22,264 ml. In the rate experiments decarboxylations were generally carried out only to about 75% completion.

Results

Kinetics experiments were carried out in each solvent at several temperatures over a 10–15-degree interval. Two or more parallel experiments were conducted at each temperature in the various solvents. No evidence of a secondary esterification reaction was noted at the temperatures used in this research. Measured volumes of CO_2 were converted to NTP, taking into account the water-jacket temperature, the corrected barometric pressure, and the calculated vapor pressure of the entraining liquid. The pseudo-first-order rate constants of the various reactions were calculated in the usual manner from the slopes of log $(V_\infty - V_t)$ versus time plots. Average values thus obtained are shown in Tables I and II. Enthalpies and entropies of activation of the various reactions were calculated according to the absolute rate equation [5, p. 41]

$$k = \frac{\kappa T}{h} e^{\Delta S^{\ddagger}/R} e^{-\Delta H^{\ddagger}/RT} \tag{1}$$

TABLE I. Pseudo first-order rate constants for the decarboxylation of methylmalonic acid in normal alkanols.

Solvent	Temperature	$k_{obs.} \times 10^4$ (sec^{-1})	$k_{calc.} \times 10^4$ (sec^{-1})
Hexanol-1	115.31	2.60	2.547
	117.22	3.02	3.020
	119.96	3.868	3.854
	125.10	6.00	5.996
	129.73	9.00	8.860
Octanol-1	115.40	2.65	2.651
	120.04	4.00	3.925
	125.15	6.00	5.984
	128.33	7.74	7.739
Decanol-1	117.17	3.14	3.160
	118.20	3.48	3.434
	119.72	3.82	3.878
	120.81	4.20	4.230
	121.81	4.55	4.579
	123.00	5.00	5.028
	125.20	5.84	5.971
	127.59	7.20	7.181
	128.08	7.475	7.456
	128.18	7.51	7.513

TABLE II. Pseudo first-order rate constants for the decarboxylation of *n*-octadecylmalonic acid in normal alkanols.

Solvent	Temperature °C.	$k_{obs.} \times 10^4$ (sec^{-1})	$k_{calc.} \times 10^4$ (sec^{-1})
Hexanol-1	113.16	2.81	2.816
	114.18	3.16	3.203
	122.90	8.10	8.160
Octanol-1	112.96	2.91	2.910
	115.06	3.51	3.524
	123.50	8.70	8.710
Decanol-1	113.24	3.10	3.105
	114.83	3.67	3.664
	122.90	8.10	8.160

assuming a transmission coefficient of unity. These data are collected in Tables III and IV.

The maximum fractional error in the experimental rate constants shown in Tables I and II is believed to be about 0.005. This was approximately the reproducibility of the parallel experiments. An error in k of this magnitude, in the case of measurements extending over a 15-degree interval, may be expected to lead to an error in $\Delta H^{\ddagger}$ of approximately ±150 cal/mole, and to an error in $\Delta S^{\ddagger}$ of approximately ±0.3 eu/mole [6]. These values may therefore be taken to represent approximately the limits of error in the derived values shown in Tables III and IV.

Discussion

It is interesting to compare the data for the decarboxylation of methylmalonic acid in normal alkanols with those previously reported for the decarboxylation of

TABLE III. Activation parameters for the decarboxylation of methylmalonic acid in normal alkanols.

Solvent	$\Delta H^{\ddagger}$ (kcal/mole)	$\Delta S^{\ddagger}$ (eu/mole	$\Delta G^{\ddagger}_{123.5°}$ (kcal/mole)
Hexanol-1	26.1	-8.32	29.4
Octanol-1	24.9	-11.345	29.4
Decanol-1	23.7	-14.37	29.4

TABLE IV. Activation parameters for the decarboxylation of *n*-octadecylmalonic acid in normal alkanols.

Solvent	$\Delta H^{\ddagger}$ (kcal/mole)	$\Delta S^{\ddagger}$ (eu/mole)	$\Delta G^{\ddagger}_{123^{\circ}}$ (kcal/mole)
Hexanol-1	32.1	7.83	29.0
Octanol-1	30.9	4.80	29.0
Decanol-1	29.7	1.77	29.0

the parent compound, malonic acid, in the various solvents [2] (see Table V). In both cases it will be observed that each additional methylene group added to the hydrocarbon chain of the solvent lowers $\Delta H^{\ddagger}$ in the amount of 0.6 kcal/mole. The same effect is observed in the case of the decarboxylation of *n*-octadecylmalonic acid in these solvents (see Table IV). If we compare heats of activation for the two substrates, malonic acid and methylmalonic acid, in identical solvents, it will be noted that the presence of the methyl group on the methylene carbon atom of malonic acid results in a slight decrease in the value of $\Delta H^{\ddagger}$.

Figure 1 is a plot of $\Delta H^{\ddagger}$ versus the number of carbon atoms or methylene groups in the hydrocarbon chain of the normal alkanols in the case of the decarboxylation of the three substrates (malonic acid, methylmalonic acid, and *n*-octadecylmalonic acid) in the various solvents. It is a matter of some interest that the three lines are parallel inasmuch as each carbon atom in the structure of the solvent molecule lowers $\Delta H^{\ddagger}$ by the same amount for each substrate, namely,

TABLE V. Comparison of heats of activation for the decarboxylation of malonic acid and methylmalonic acid in normal alkanols.

Solvent	$\Delta H^{\ddagger}$ (kcal/mole)		
	Malonic Acid[a]	Methylmalonic Acid[b]	$d\Delta H^{\ddagger}$
Butanol-1	27.6		
Pentanol-1	27.0		
Hexanol-1	26.4	26.1	-0.3
Heptanol-1	25.8		
Octanol-1	25.2	24.9	-0.3
Nonanol-1	24.6		
Decanol-1	24.0	23.7	-0.3

[a] From [2].
[b] Table III.

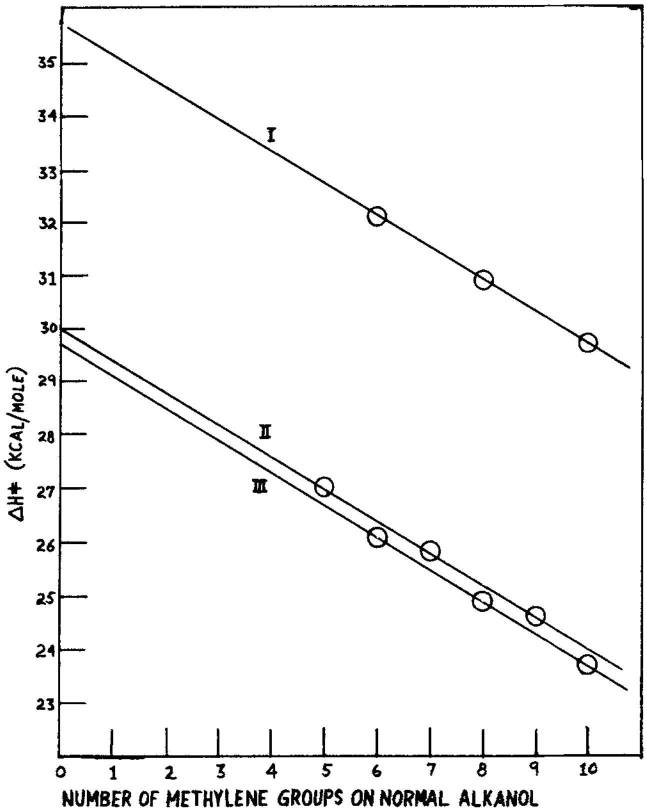

Figure 1. Decarboxylation of malonic acid and its derivatives in normal alkanols. Plot of $\Delta H^\ddagger$ vs. the number of methylene groups on the normal alkanol. I—*n*-octadecylmalonic acid, II—malonic acid, III—methylmalonic acid.

by 600 cal/mole per methylene group. The graph shows clearly the close proximity of the parameters for malonic acid and methylmalonic acid. The three lines in Figure 1 may be represented by the following equations:

(2) line I (*n*-octadecylmalonic acid): $\Delta H^\ddagger = -600n + 35{,}700$ cal/mole

(3) line II (malonic acid): $\Delta H^\ddagger = -600n + 30{,}000$ cal/mole

(4) line III (methylmalonic acid): $\Delta H^\ddagger = -600n + 29{,}700$ cal/mole

where n is the number of carbon atoms or methylene groups in the normal alkanol. The constant in each of the above equations corresponds to the value of $\Delta H^\ddagger$ in the case of the reaction taking place in an alkanol in which n is zero. This, of course, is pure water, since the alkanols may be regarded as derivatives of water, an alkyl group being substituted for one of the hydrogen atoms on the water molecule.

The value of the constant in eq. (3) in the case of the decarboxylation of malonic acid in water (30,000 cal/mole) has been confirmed [7].

Equations (2)–(4) may be used to calculate the heats of activation in the case of the decarboxylation of the various substrates in members of the homologous series of alkanols which have not yet been investigated.

Each group of reactions reported in this research, namely, the decarboxylation of methylmalonic acid and *n*-octadecylmalonic acid in normal alkanols, constitutes a reaction series, each series showing an isokinetic temperature equal to the melting point of the substrate (123°C for *n*-octadecylmalonic acid, 123.5°C for methylmalonic acid) (see Tables III and IV). In the case of the decarboxylation of *n*-octadecylmalonic acid the free energy of activation at the isokinetic temperature ($\Delta G^{\ddagger}_0$) is 29.0 kcal/mole.

The decarboxylation of malonic acid in normal alkanols, previously reported, likewise was found to constitute a reaction series with an isokinetic temperature equal to the melting point of the substrate (135°C) in which the free energy of activation ($\Delta G^{\ddagger}_0$) was likewise equal to 29.0 kcal/mole [2]. The decarboxylation of *n*-butylmalonic acid in normal alkanols, previously reported, yielded similar results [2]. The melting point of *n*-butylmalonic acid is 102.5°C. This was also the isokinetic temperature of the reaction series. For this series the $\Delta G^{\ddagger}_0$ value was also 29.0 kcal/mole.

The results in the case of the decarboxylation of methylmalonic acid in normal alkanols (Table III) are divergent from those of the other members of the series of malonic acid derivatives thus far investigated. The melting point of methylmalonic acid is 123.5°C. The isokinetic temperature of the reaction series is equal to the melting point of the substrate. However, in the case of methylmalonic acid, the free energy of activation at the isokinetic temperature ($\Delta G^{\ddagger}_0$) turns out to be 29.4 kcal/mole. These results are summarized in Table VI.

TABLE VI. Decarboxylation of malonic acid and its derivatives in normal alkanols—Free energy of activation at the isokinetic temperature.

Substrate	Melting Point °C.	Isokinetic Temperature °C.	$\Delta G^{\ddagger}_0$ (kcal/mole)
Malonic Acid[a]	135.0	135.0	29.0
Methylmalonic Acid[b]	123.5	123.5	29.4
n-Butylmalonic Acid[c]	102.5	102.5	29.0
n-Octadecylmalonic Acid[d]	123.0	123.0	29.0

[a] From [2].
[b] Table III.
[c] From [3].
[d] Table IV.

The larger value of $\Delta G^{\ddagger}_0$ in the case of the decarboxylation of methylmalonic acid in normal alkanols means that the rate of reaction of this substrate in polar solvents is substantially lower than that of other members of the malonic acid family of *n*-alkyl derivatives.

The mechanism of the decarboxylation of malonic acid in polar solvents proposed by Fraenkel and coworkers [8] postulates the formation prior to cleavage of an intermediate compound, the unshared pair of electrons on the nucleophile coordinating with the polarized carbonyl carbon atom of malonic acid. According to this proposed mechanism an electron-releasing substitutent (such as a methyl group) on the methylene carbon atom of malonic acid should reduce the effective positive charge on the polarized carbonyl carbon atom. This should tend to *increase* the activation energy or the heat of activation. It would be expected, therefore, that the enthalpy of activation for the decarboxylation of methylmalonic acid in normal alkanols would be greater than that of the parent compound, malonic acid. The actual experimental fact, however, is exactly the opposite—heats of activation for the decarboxylation reaction are higher in the case of malonic acid than in that of methylmalonic acid in the three solvents studied (Table V). This circumstance raises some doubts as to the validity of the mechanism proposed by Fraenkel and coworkers [8].

An Empirical Technique for Predicting Rates of Reaction

Using the results of the present investigation as well as previously published data for the decarboxylation of malonic acid [2] and of *n*-butylmalonic acid [2] in normal alkanols, the author has developed an empirical technique for predicting rate constants in the case of the decarboxylation of malonic acid and its *n*-alkyl derivatives in this type of solvent. The rationale of the various steps involved in this technique for predicting rate constants is outlined below.

It is well known that many reactions taking place in solution are complicated by the tendency of both substrate and solvent molecules to associate and co-associate resulting in an aggregate of substrate molecules intermingled with an aggregate of catalyst or solvent molecules (see [6, p. 493]). Hammett has used the term "polymolecular" to describe this kind of reaction [9]. For lack of a better description we can name this aggregation of molecules the substrate–catalyst complex. It is a principle of kinetic theory that the rate of a chemical reaction is greater in the medium which favors the association of reactants (see [6, p. 505]).

It has been shown that the decarboxylation of malonic acid in quinoline is first order in quinoline [8,2], indicating that the rate-determining step in this reaction involves a single molecule of the amine. We can infer from this that the substrate–catalyst complex giving rise to this particular reaction probably consists of one solvent molecule plus an unknown number of substrate molecules. In the case of the decarboxylation of malonic acid in aniline and its *N*-alkyl derivatives it has been shown that the heat of activation of the reaction decreases in the amount of 300 cal/mole for each additional methylene group added to the alkyl moiety of the solvent [10,2]. If we make the assumption that these reactions (like the one in quinoline) are also first order with respect to the solvent, the conclusion is reached that each methylene group added to the substrate–catalyst complex by solvent molecules lowers the heat of activation of the reaction in the amount of 300 cal/mole. If the substrate–catalyst complex contains two molecules of catalyst, it would be expected that the heat of activation of the reaction in this case would be lowered by twice this amount, or by 600 cal/mole, for each additional methylene group making up the alkyl moiety of the solvent molecule. The occurrence of this event in the case of the decarboxylation of malonic acid, methylmalonic acid, and *n*-octadecylmalonic acid in normal alkanols (see Fig. 1) suggests that in these reactions two catalyst molecules are involved in the formation of the substrate–catalyst complex. Other kinds of evidence have been adduced indicating that certain reactions in solution involving hydroxylic solvents are second order with respect to the solvent. Examples include the hydrolysis of acid chlorides in aqueous solution [11,12], the ethanolysis of methyl-*p*-nitrobenzenesulfonate in ethanol [13,14], and the alcoholysis of isopropylbenzenesulfonate in isopropanol [15].

If it is true that, in the case of the decarboxylation of malonic acid and its *n*-alkyl derivativs in normal alkanols, every methylene group or carbon atom on each solvent molecule that is involved in the formation of the substrate–catalyst complex has the effect of lowering the heat of activation of the reaction in the amount of 300 cal/mole, it may be inferred that every methylene group or carbon atom in each substrate molecule that is involved in the formation of the complex will also have this effect, namely, will lower the heat of activation of the reaction in the amount of 300 cal/mole. In other words, every methylene group or carbon atom present in the complex, regardless of source, whether contributed by solvent or by substrate molecules, should lower the $\Delta H^{\ddagger}$ of the reaction by 300 cal/mole. Furthermore, inasmuch as an oxygen atom (atomic weight 16) differs only slightly in physical characteristics from a methylene group (formula weight 14), it may be deduced that these atoms also should manifest approximately the same effect on the heat of reaction as do the methylene groups.

Assuming the correctness of the inferences described above we may propose a working hypothesis that, in the case of the decarboxylation of malonic acid and its *n*-alkyl derivatives in normal alkanols, every atom involved in the formation of the substrate–catalyst complex (except hydrogen) contributed by both substrate and catalyst molecules will lower the $\Delta H^{\ddagger}$ of the reaction in the amount of 300 cal/mole. The foregoing statement may be expressed mathematically as follows:

$$\Delta H^{\ddagger} = -300n + \text{constant} \tag{5}$$

where $\Delta H^{\ddagger}$ is the experimentally observed heat of activation and n is the total number of atoms (exclusive of hydrogen) in the substrate–catalyst complex contributed by both substrate and solvent molecules. The constant in eq. (5) represents a limiting maximum value of $\Delta H^{\ddagger}$ in the case of a reaction in solution involving zero number of atoms. A suggested value for this constant has been determined by an iterative process on the basis of the data for the decarboxylation of malonic acid, methylmalonic acid, *n*-butylmalonic acid, and *n*-octadecylmalonic acid in normal alkanols. The complete equation is

$$\Delta H^{\ddagger} = -300n + 66{,}300 \text{ cal/mole} \tag{6}$$

Equation (6) implies that every atom constituting the substrate–catalyst complex (hydrogens excepted) contributed by both substrate and solvent molecules, in the case of the decarboxylation of malonic acid and its *n*-alkyl derivatives in normal alkanols, lowers the heat of activation of the reaction in the amount of 300 cal/mole from a maximum value of 66,300 cal/mole. By substituting in eq. (6) the experimentally determined value of $\Delta H^{\ddagger}$ for a given reaction, the total number of atoms n in the complex can be readily determined. Provided the number of molecules of catalyst in the complex is known, eq. (6) enables the calculation of the number of molecules of substrate involved in the formation of the substrate–catalyst complex. This procedure can be illustrated by means of an example.

Let us take for this purpose data for the decarboxylation of methylmalonic acid in decanol-1. Let us assume that two molecules of catalyst are involved in the formation of the complex. The experimental value of $\Delta H^{\ddagger}$ for this reaction is 23,700 cal/mole (see Table III). Substituting this value of $\Delta H^{\ddagger}$ in eq. (6) and solving for n, we find

$$n = (66{,}300 - 23{,}700)/300 = 142$$

This result tells us that in the case of the decarboxylation of methylmalonic acid in decanol-1 there are a total of 142 atoms in the substrate–catalyst complex. Each catalyst molecule (decanol-1) contributes 11 atoms (10 carbon atoms plus 1 oxygen atom). Each substrate molecule (methylmalonic acid) contributes 8 atoms (4 carbon atoms plus 4 oxygen atoms). We now have all the information needed in order to determine the number of substrate molecules in the complex assuming that two molecules of catalyst are present.

We may write

$$n = ab + yz \tag{7}$$

where a is the number of molecules of substrate in the complex, b the number of atoms per molecule of substrate, y the number of molecules of catalyst in the complex, and z the number of atoms per molecule of catalyst. Solving eq. (7) for a and substituting the above-mentioned values for the remaining symbols, we find

$$a = (142 - 2 \times 11)/8 = 15$$

These results indicate that, in the case of the decarboxylation of methylmalonic acid in decanol-1, the substrate catalyst complex consists of an aggregation of 15 molecules of substrate associated with 2 molecules of catalyst. The number of molecules of substrate present in the substrate–catalyst complex in the case of the decarboxylation of malonic acid, *n*-butylmalonic acid, and *n*-octadecylmalonic acid in normal alkanols, calculated by the procedure outlined above, turns out to be 17, 11, and 4, respectively. These results are summarized in Table VII.

TABLE VII. Decarboxylation of malonic acid and its derivatives in decanol-1—Number of molecules of substrate in the transition state.[a]

Substrate	$\Delta H^{\ddagger}$ (kcal/mole)	n	ab	b	a
Malonic acid	24.0	141	119	7	17
Methylmalonic acid	23.7	142	120	8	15
n-Butylmalonic acid	26.7	132	121	11	11
n-Octadecylmalonic acid	29.7	122	100	25	4

[a] *n*—Total number of atoms in the transition state contributed by both substrate and catalyst molecules (excluding H); *a*—number of molecules of substrate in the transition state; *b*—number of atoms in one molecule of substrate (excluding H).

The data in Table VII indicate that the number of molecules of substrate in the substrate–catalyst complex decreases as the molecular weight increases. A straight line is produced when the number of molecules of substrate in the complex (as given in Table VII) is plotted versus the reciprocal of the molecular weight (Fig. 2). The closed circles in Figure 2 correspond to the results shown in Table VII in the case of the four substrates which have been investigated. The open circles represent predicted coordinates in the case of the remaining straight-chain monoalkyl derivatives of malonic acid through *n*-octadecylmalonic acid based on the assumption that, in each case, the complex contains a discrete number of molecules. The equation of the line in Figure 2 as given by a least squares treatment of the data is as follows:

$$(8) \qquad a = 1912.3M^{-1} - 1.20 \pm 0.27$$

where a is the number of molecules of substrate in the complex and M is the molecular weight. Equation (8) may be used to calculate the number of molecules of substrate in the substrate–catalyst complex in the case of the decarboxylation of any straight-chain monoalkyl derivative of malonic acid in any normal alkanol by substituting the appropriate molecular weight for M. The same information may be gleaned also by reference to Figure 2. This item will enable the calculation of n, the total number of atoms in the complex, from which the heat of activation may be calculated by use of eq. (6).

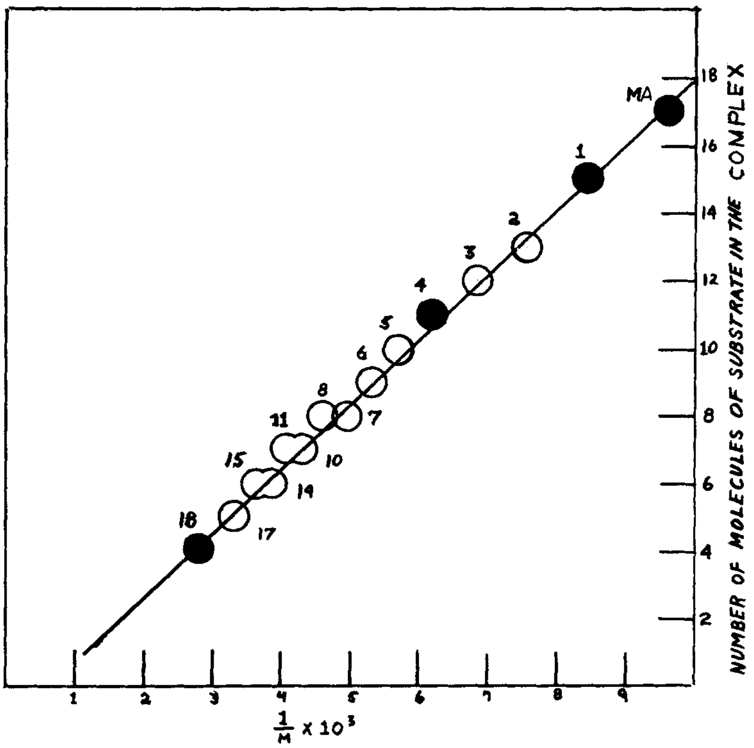

Figure 2. Decarboxylation of malonic acid and its derivatives in normal alkanols. Plot of the number of molecules of substrate in the complex vs. the reciprocal of the molecular weight of the substrate. MA—malonic acid; the numerals 1, 2, 3, . . . designate the number of methylene groups in the hydrocarbon moiety of the malonic acid derivative (e.g., 1—methylmalonic acid; 2—ethylmalonic acid, 3—*n*-propylmalonic acid, 4—*n*-butylmalonic acid, . . . 18—*n*-octadecylmalonic acid).

The specific reaction velocity constant of a chemical reaction is related to the free energy of activation through the ART equation [5, p. 41]

$$(9) \qquad k = \frac{\kappa T}{h} e^{-\Delta G^\ddagger/RT}$$

assuming a transmission coefficient of unity. The logarithmic form of eq. (9) is

$$(10) \qquad \log k = \log \kappa/h + \log T - \Delta G^\ddagger/2.303RT$$

Substituting in eq. (10) currently accepted values of the fundamental physical constants [16], we obtain

$$(11) \qquad \log k = \log T + 10.3188244783 - \Delta G^\ddagger/4.57567936T$$

Equation (11) is a general equation which may be used to determine the rate constant k for any reaction at any temperature if the free energy of activation of the reaction is known, or it can be used to calculate the free energy of activation of the reaction if the rate constant is known.

The free energy of activation of a reaction is related to the parameters $\Delta H^\ddagger$ and $\Delta S^\ddagger$ by the equation [5, p. 195]

$$\Delta G^\ddagger = \Delta H^\ddagger - T\Delta S^\ddagger \tag{12}$$

In the case of the decarboxylation of malonic acid and any of its straight-chain monoalkyl derivatives in any normal alkanol the heat of reaction $\Delta H^\ddagger$ can be easily calculated by use of equations (6), (7), and (8). For each reaction series in the case of most of the compounds investigated the free energy of activation at the isokinetic temperature—which is also the melting point of the substrate—is 29.0 kcal/mole (in the case of methylmalonic acid it is 29.4 kcal/mole). The entropy of activation for any particular reaction can be predicted by use of the isokinetic temperature relationship. These relationships provide a basis for the prediction of the specific reaction velocity constant at any specified temperature in the case of the decarboxylation of malonic acid and any of its *n*-alkyl derivatives in any normal alkanol. The various steps involved in carrying out such a calculation may be illustrated by means of a specific example.

Let us select for this purpose the decarboxylation of *n*-octadecylmalonic acid in decanol-1 at 113.24°C. We first of all determine the number of molecules of *n*-octadecylmalonic acid present in the substrate–catalyst complex undergoing reaction by substituting in eq. (8) the molecular weight of the substrate, namely, 356.5476 g, as follows:

$$\begin{aligned} a &= 1912.3M^{-1} - 1.20 \pm 0.27 \\ &= 1912.3/356.5476 - 1.20 \pm 0.27 = 4 \end{aligned} \tag{8}$$

The above result indicates that in this reaction the complex contains four substrate molecules. Exclusive of hydrogens each molecule of *n*-octadecylmalonic acid contains 25 atoms (21 carbon atoms plus 4 oxygen atoms). We will assume that the complex contains two molecules of catalyst. Each solvent molecule contains 11 atoms (10 carbon atoms plus 1 oxygen atom) exclusive of hydrogen.

We now calculate the total number of atoms n contributed by both substrate and catalyst molecules, present in the substrate–catalyst complex, by substituting the above values in eq. (7) as follows:

$$n = 4 \times 25 + 2 \times 11 = 122 \text{ atoms}$$

The enthalpy of activation of the reaction can now be calculated by use of eq. (6) as follows:

$$\begin{aligned} \Delta H^\ddagger &= -300n + 66{,}300 \text{ cal/mole} \\ &= -300 \times 122 + 66{,}300 \text{ cal/mole} \\ &= 29{,}700 \text{ cal/mole} \end{aligned} \tag{6}$$

Knowing (a) that the melting point of *n*-octadecylmalonic acid is 123°C, (b) that the isokinetic temperature of the reaction series is equal to the melting point of the substrate, and (c) that the free energy of activation at the isokinetic temperature is 29.0 kcal/mole, the entropy of activation for this particular reaction may be readily calculated by use of eq. (12) as follows:

$$\begin{aligned} \Delta G^{\ddagger} &= \Delta H^{\ddagger} - T\Delta S^{\ddagger} \\ \Delta S^{\ddagger} &= (\Delta H^{\ddagger} - \Delta G^{\ddagger})/T \\ &= (29{,}700 - 29{,}000)/396.15 = 1.767 \text{ eu/mole} \end{aligned} \tag{12}$$

Knowing both the enthalpy of activation and the entropy of activation of the reaction, we can now calculate the free energy of activation of this particular reaction at the specified temperature, namely, 113.24°C (386.39°K), by substituting these values in eq. (12) as follows:

$$\begin{aligned} \Delta G^{\ddagger}{}_{113.24^\circ} &= \Delta H^{\ddagger} - T\Delta S^{\ddagger} \\ &= 29{,}700 - 1.767 \times 386.39 \\ &= 29{,}017 \text{ cal/mole} \end{aligned} \tag{12}$$

The specific reaction velocity constant k for the decarboxylation of *n*-octadecylmalonic acid in decanol-1 at 113.24°C can now be calculated by substituting the above value of $\Delta G^{\ddagger}{}_{113.24^\circ}$ in eq. (11) as follows:

$$\begin{aligned} \log k &= 2.5870259 + 10.3188244783 - 29{,}017/4.57679 \times 386.39 \\ &= -3.5027 \end{aligned}$$

Taking the antilogarithm, we obtain $k = 0.0003143 \text{ sec}^{-1}$ (calculated). The value of the rate constant for this particular reaction thus calculated compares with the experimentally observed value of $0.000310 \text{ sec}^{-1}$ (see Table II).

Summary

The various steps involved in the prediction of rates of reaction in the case of the decarboxylation of any straight-chain monoalkyl malonic acid derivative in any normal alkanol at any specified temperature may be summarized as follows.

(1) Determination of the number of molecules of substrate in the substrate–catalyst complex [Fig. 2 or eq. (8)];

(2) Determination of the number of molecules of catalyst bound to substrate in the complex [2,17];

(3) Determination of the total number of atoms in the complex [eq. (7)];

(4) Calculation of the heat of activation [eq. (6)];

(5) Calculation of the entropy of activation [eq. (12)];

(6) Calculation of the free energy of activation at the specified temperature [eq. (12)];

(7) Calculation of the specific reaction velocity constant at the temperature of the reaction [eq. (11)].

Application of the Empirical Technique for Predicting Rate Constants

Rate constants calculated by the technique outlined above in the case of the decarboxylation of methylmalonic acid and *n*-octadecylmalonic acid in the various solvents, at each temperature which was experimentally investigated, are shown in the last columns of Tables I and II. The excellent agreement between observed and calculated values attests to the validity of the assumptions on which the calculations were based.

As a further test of the predictive power of the technique outlined herein an additional experiment was conducted employing a malonic acid derivative other than the four already investigated. It was decided to study the decarboxylation of *n*-dodecylmalonic acid in heptanol-1 at 110.30°C. This compound was prepared by the malonic ester synthesis from 1-bromododecane by the usual procedure [18]. Recrystallization of the crude product from benzene, then glacial acetic acid, then benzene yielded a pure sample with melting point 121.0°C (corr.). According to eq. (12) there should be 6 molecules of substrate in the substrate–catalyst complex for this reaction (step 1). Assuming 2 molecules of catalyst in the complex (step 2), the total number of atoms in the complex contributed by both substrate and catalyst molecules [eq. (7)] turns out to be 130 (step 3). This yields a value of 27,300 cal/mole for the heat of activation of this reaction by use of eq. (5) (step 4). If the isokinetic temperature of the reaction series is equal to the melting point of the *n*-dodecylmalonic acid (121.0°C), and if the $\Delta G^{\ddagger}_0$ value is equal to 29,000 cal/mole, the entropy of activation of the reaction calculated by means of eq. (12) turns out to be -4.313 eu/mole (step 5). Substituting these values in eq. (12), the free energy of activation of this reaction at 110.30°C is found to be 28,954 cal/mole (step 6). When this value is substituted in eq. (11), the calculated specific reaction velocity constant turns out to be 0.0002514 sec^{-1}. The experiment was thereafter carefully conducted using a sample of *n*-dodecylmalonic acid weighing 0.2992 g in 80 ml of freshly distilled reagent grade heptanol-1 at 110.30°C (corr.). The observed rate constant turned out to be 0.0002511 sec^{-1}.

Conclusion

The above described technique for predicting rate constants rests on the assumption that the enthalpy of activation of a reaction is a function of the number of atoms associated substrate and solvent molecules contribute to a hypothetical substrate–catalyst complex. In the case of the reaction in question, namely, the decarboxylation of malonic acid and its *n*-alkyl derivatives taking place in amines, it is assumed that this complex contains only one molecule of solvent, for reaction in alcohols it is assumed that there are two molecules of solvent in the complex. Studies on the decarboxylation of malonic acid in quinoline–dioxane mixtures [8,2] have shown that the reaction is first order with respect to the amine. The fact that the base ionization constants for quinoline and aniline are of the same order of magnitude (for quinoline it is 6.3×10^{-10}, for aniline 3.83×10^{-10}) lends support to the assumption that the reaction involving malonic acid and aniline is also first order with respect to the amine. The basis for the assumption that the reaction involving malonic acid and normal alkanols is second order with respect to the solvent is the fact that the decrement in $\Delta H^{\ddagger}$ per methylene group added to the hydrocarbon chain of the solvent molecule is twice as great for the reaction in alcohols as it is for the reaction in amines. The fact that a number of other heterolytic reactions involving hydroxylic solvents have been shown to exhibit second-order dependence on the solvent [11–15] lends further support to this assumption. A stronger case for these two assumptions might be made by conducting studies in an inert solvent involving the respective pairs of reactants. Additional studies directed toward obtaining evidence in support of the reality of the postulated substrate–catalyst complex also are indicated. Continuing work on this problem is in progress in this laboratory.

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