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The Kinetics and Carbon-13 Isotope Effect in the Decomposition of Substituted Ureas[1,2]

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The rate constants for the decomposition in propionic acid of urea, *sym*-dimethylurea, phenylurea, *sym*-diphenylurea and 3,3'-dimethylcarbanilide have been measured at various temperatures and the carbon-13 isotope effect has been determined for these reactions. All the reactions were first order except that of urea, which exhibited second-order kinetics with respect to the urea. The first-order activation energies and the isotope effects can be explained on the basis of resonance in the activated complex.

The work of Daniels and co-workers[3] on the isotope effect in the rate of hydrolysis of urea and the studies of Mukaiyama, *et al.*,[4-6] on the thermal dissociation of substituted ureas in various carboxylic acids with evolution of carbon dioxide led to the present investigation. It was hoped that a variation in the isotope effect with different substituents would help to elucidate the mechanism of these reactions and that the application of present theories would provide information concerning the activated complex involved.

Since the experimental method used for determining the isotope effect provides, at the same time, values of the rate constants, an independent check can be made of the values reported by Mukaiyama and co-workers.

The rate constants for the dissociation in propionic acid of *sym*-dimethylurea, phenylurea, *sym*-diphenylurea, 3,3'-dimethylcarbanilide and urea have been measured at various temperatures and the C^{13}-isotope effect has been determined.

Experimental

Mallinckrodt A. R. grade urea was used both without purification and with purification by recrystallization from 95% ethanol. The melting point in both cases was 132.7°. The *sym*-dimethylurea was Eastman yellow label and was purified by recrystallization from acetone–ether mixture by cooling with ice. The melting point was 106°. Phenylurea and *sym*-diphenylurea were prepared from urea and aniline.[7] The phenylurea was recrystallized three times from hot water and had a melting point of 147°. The *sym*-diphenylurea was purified by recrystallization using ethyl acetate, and its melting point was 237°. The 3,3'-dimethylcarbanilide was Eastman white label grade and was recrystallized from ethyl acetate, giving a melting point of 225°. Both Fisher certified and Matheson propionic acid were purified by distillation. Linde high-purity tank nitrogen was used and any water and carbon dioxide were removed by passing the nitrogen through magnesium perchlorate and ascarite.

The method used for following the reaction was similar to that previously developed in this Laboratory,[3] but it included certain modifications. An oil-bath with a mercury thermoregulator and relay maintained a constant temperature. An iron–constantan thermocouple calibrated with a platinum resistance thermometer which in turn had been calibrated by the Bureau of Standards was employed for temperature measurements.

In the experiments with urea, phenylurea and *sym*-dimethylurea, approximately 0.01 mole of the urea was accurately weighed, dissolved in propionic acid, and diluted to 10 ml. Either 25 or 50 ml. of propionic acid was placed in the reaction flask in the bath. Nitrogen was run in at a constant rate of 20–60 cc. per min. through the purification tubes, then through a glass spiral inserted in the thermostat to heat the nitrogen to the thermostat temperature. The nitrogen bubbled through the propionic acid with the help of a fritted glass tube and escaped through a condenser. Though most of the propionic acid was returned to the reaction flask, a small amount was carried away by the nitrogen. The escaping acid was removed in a Dry Ice trap.

After approximately 30 min., 5 ml. of the urea solution was added to the reaction flask and the exit-nitrogen passed through a fritted tube into a standardized carbonate-free $Ba(OH)_2$ solution. After about 10% of the reaction had taken place, the flow was switched to another tube containing $Ba(OH)_2$. The removal of fractions at intervals of 10% of complete reaction was continued until 6 or 8 samples had been collected. The $BaCO_3$ formed was allowed to settle and most of the solution was poured off. The $BaCO_3$ was removed by centrifugation and washed with CO_2-free water. The excess of $Ba(OH)_2$ was back-titrated with standard HCl. The C^{13}/C^{12} ratios for the successive samples of CO_2 were obtained with a mass spectrometer as previously reported.[3a]

A blank run showed that all CO_2 and solvent acid had been removed from the nitrogen stream and several experiments, carried to essentially 100% completion, showed that all CO_2 from the reaction was being recovered.

Since *sym*-diphenylurea and 3,3'-dimethylcarbanilide are not very soluble in propionic acid at room temperature, it was necessary to introduce the solids mechanically into the reaction tube. The reaction tube was then placed in the bath and allowed to come to the thermostat temperature. The first sample of CO_2, generated under uncertain temperature conditions, was not used except to determine the "initial" amount of urea present.

Results

First-order kinetics were obtained for all reactions except that of urea. Figure 1 is an example of the first-order plots found in the determination of the rate constants. When more than one experiment was carried out at the same temperature, the values of k were averaged and the averages are given in Table I.

The activation energy for the decomposition of *sym*-dimethylurea agrees well with the value which has been reported for the reaction in butyric acid,[4b] but the activation energy of *sym*-diphenylurea is lower than that previously reported for this substance in propionic acid.[4a]

Experiments with urea did not produce first-order kinetics but a second-order plot fits the data well. Figure 2 shows the graphs for both first- and second-order reactions, and Table II gives the values of the second-order constants which were thus obtained.

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[1] Presented at the 129th National meeting of the American Chemical Society, Dallas, Texas, April 10, 1956.

[2] From a thesis submitted for the partial fulfillment of the degree of Doctor of Philosophy at the University of Wisconsin, 1956.

[3] (a) J. A. Schmitt, A. L. Myerson and F. Daniels, *J. Phys. Chem.*, **56**, 919 (1952); (b) J. A. Schmitt and F. Daniels, THIS JOURNAL, **75**, 3564 (1953).

[4] (a) T. Hoshino, T. Mukaiyama and H. Hoshino, *ibid.*, **74**, 3097 (1952); (b) *Bull. Chem. Soc. Japan*, **25**, 392 (1952).

[5] T. Mukaiyama and T. Matsunaga, THIS JOURNAL, **75**, 6209 (1953).

[6] T. Mukaiyama, S. Ozaki and T. Hoshino, *Bull. Chem. Soc. Japan*, **27**, 578 (1954).

[7] T. L. Davis and K. C. Blanchard, "Organic Syntheses," Col. Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1941, p. 453.

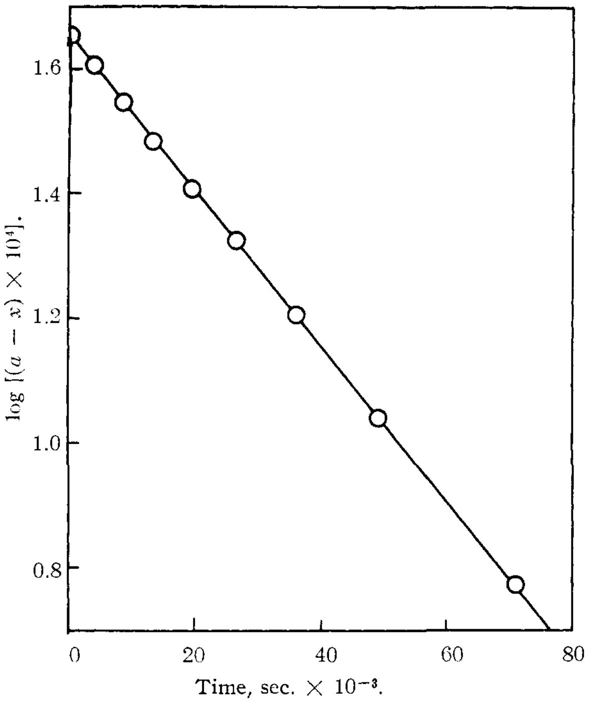

Fig. 1.—First-order plot of the decomposition of *sym*-dimethylurea at 126°.

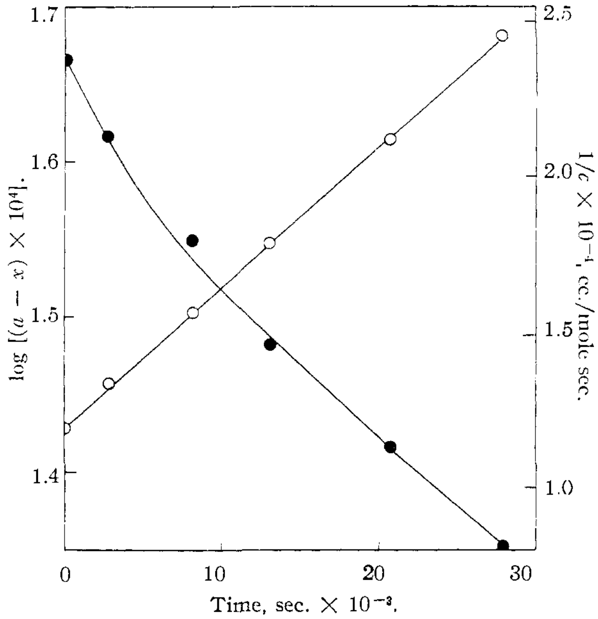

Fig. 2.—Decomposition of urea at 122°: ●, first-order plot; ○, second-order plot.

The ratios of k_{12}/k_{13} were calculated using an equation derived by Downes[8]

$$\log (C^{13}/C^{12}) = (k_{13}/k_{12} - 1) \log (1 - f) + (k_{13}/k_{12}) \log N_x^0 \quad (1)$$

The ratio C^{13}/C^{12} is the ratio determined for one sample, f is the fraction of material reacted, and N_x^0 is a constant. A plot of $-\log C^{13}/C^{12}$ *vs.* $-\log(1 - f)$ gives a straight line; and from the slope values of k_{12}/k_{13} may be calculated. It should be noticed that the slope is the difference between k_{13}/k_{12} and unity. This gives quite an accurate value for k_{13}/k_{12}. Figure 3 is an example of such a plot for one experiment while Table III gives the ratios of k_{12}/k_{13} which were found for the various reactions. The values in Table III are averages of several experiments and although some of the values used for averaging were obtained at different temperatures, no temperature effect was

TABLE I

RATE CONSTANTS k, ACTIVATION ENERGIES E_a AND FREQUENCY FACTORS s, OF FIRST-ORDER DECOMPOSITIONS

Reactant	T°, A.	k, sec.⁻¹ × 10³	E_a, kcal.	s, sec.⁻¹
sym-Dimethylurea	399.3	3.09[a]		
	409.1	8.3	33	5 × 10¹³
Phenylurea	393.0	3.85		
	406.9	13.2		
	409.5	14.8	27	6 × 10¹⁰
sym-Diphenylurea	392.7	6.32		
	403.7	14.0		
	407.9	18.8	23	4 × 10⁸
3,3′-Dimethylcarbanilide	380.9	2.95		
	392.3	7.16		
	400.1	11.1[b]	20	10⁷

[a] Average of 4 experiments (±0.05). [b] Average of 2 experiments (±0.05).

TABLE II

SECOND-ORDER RATE CONSTANTS AND ACTIVATION ENERGY E_a FOR UREA DECOMPOSITION

T°, A.	k, cc. mole⁻¹ sec.⁻¹	E_a, kcal.
395.2	0.453	
404.4	.804	
410.6	1.44	29

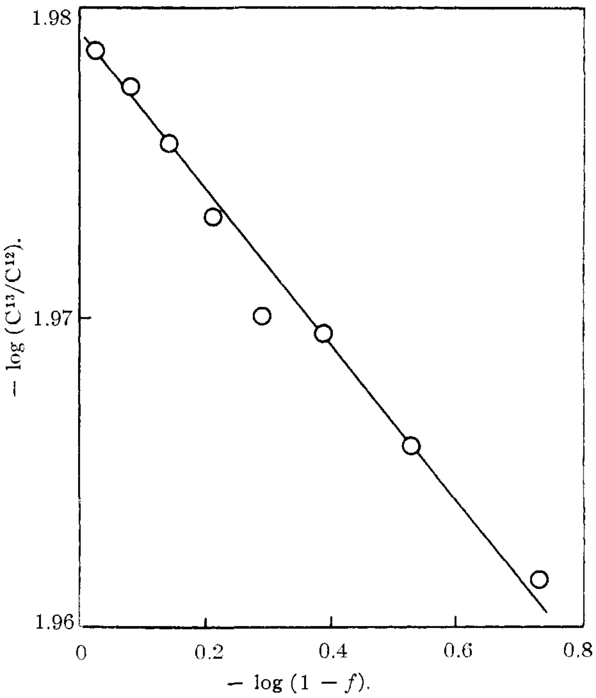

Fig. 3.—Isotope effect in the decomposition of *sym*-dimethylurea.

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[8] A. M. Downes, *Aust. J. Sci. Research*, **5**, 521 (1952).

noticeable in the short temperature intervals covered.

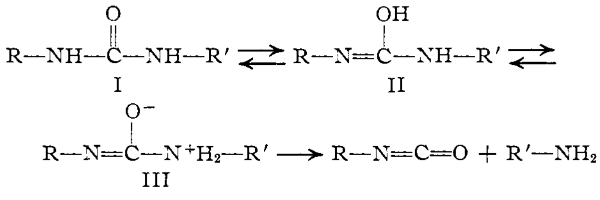
TABLE III

ISOTOPE EFFECTS AND DIFFERENCES IN $G(u_i)\,\Delta u_i$ BETWEEN REACTANTS AND COMPLEX

Reactant	No. of expt.	Av. k_{12}/k_{13}	$[(k_{12}/k_{13})/(m_{13}^{\ddagger}/m_{12}^{\ddagger})]-1$
sym-Dimethylurea	3	1.0269 ± 0.001	0.006
Phenylurea	2	1.016 ± .004	− .005
sym-Diphenylurea	2	1.0076 ± .001	− .013
3,3′-Dimethylcarbanilide	3	1.0071 ± .003	− .014
Urea	1	1.021	.000

Discussion

A mechanism has been proposed[4–6] for the decomposition of ureas in carboxylic acids in which the rate-determining step is $RNHCONHR' \rightleftarrows RNCO + R'NH_2$. Furthermore, as has been pointed out,[4b] a possible path for this first step may consist of



$$\underset{\text{I}}{R{-}NH{-}\overset{\overset{\large O}{\|}}{C}{-}NH{-}R'} \rightleftarrows \underset{\text{II}}{R{-}N{=}\overset{\overset{\large OH}{|}}{C}{-}NH{-}R'} \rightleftarrows \underset{\text{III}}{R{-}N{=}\overset{\overset{\large O^-}{|}}{C}{-}N^+H_2{-}R'} \longrightarrow R{-}N{=}C{=}O + R'{-}NH_2$$

where III may be thought of as the activated complex, since only a rearrangement of charge distribution is necessary for dissociation.

Another possibility is that III is formed directly from I,[9] but for the purposes of calculating a rate constant by absolute reaction rate theory, there is no difference between the two possibilities.[10]

A structure such as III for the activated complex seems probable since the conjugation which results when one or more of the substituted groups is a phenyl group would cause resonance in the structure.

The effect of resonance in the activated complex on the rate of reaction has been explained.[11] Resonance leads to a strengthening of the bonds in the activated complex. This increase of strength lowers the potential surface with respect to the normal molecule and hence decreases the energy of activation. At the same time, however, the increase in the bond strength lowers the entropy of the activated complex. Thus the frequency factor in the Arrhenius equation is smaller also. The decrease in both entropy and energy of activation tend to cancel in the final expression for the rate constant.

As can be seen from Table I, there is a decrease in activation energy and frequency factor on going from *sym*-dimethylurea to the aryl ureas. The 10 kcal. difference in the activation energies of *sym*-dimethylurea and *sym*-diphenylurea may be compared to the resonance energy of styrene in excess of that of the benzene ring. This excess resonance energy has been calculated to be 7 kcal./mole.[12]

With the usual form of the absolute rate theory, it is difficult to calculate the change in the isotope effect when different ureas are decomposed, since calculation of the partition function for the activated complex offers serious difficulties. If there were no change in the entropy of activation on substitution of different groups, it could be assumed that the decrease in activation energy would result in a decrease in the isotope effect for those reactions where resonance is possible in the activated complex and not in the normal molecule. Where the entropy of activation changes appreciably with different substituents, as in the present work, the above assumption cannot be made with such certainty. A modification of the absolute rate theory[13,14] has resulted in a more useful form for obtaining information from isotope effects. The equation obtained is

$$\frac{k_{12}}{k_{13}} = \frac{s_1 s_2^{\ddagger}}{s_2 s_1^{\ddagger}} \frac{K_{12}}{K_{13}} \left(\frac{m_{13}^{\ddagger}}{m_{12}^{\ddagger}}\right)^{1/2} \left[1 + \sum_{i}^{3n-6} G(u_i)\,\Delta u_i - \sum_{i}^{3n'-7} G(u_i^{\ddagger})\Delta u_i^{\ddagger}\right] \qquad (2)$$

and the terms have been previously defined.[13] In the urea molecules the carbon atom of interest occupies a central position and substitution of C^{13} would make the symmetry numbers, s_1 and s_2, equal. It is difficult to imagine a configuration of the activated complex whose symmetry number would change on substitution of C^{13} for the C^{12}. The ratio of transmission coefficients, K_{12}/K_{13}, should be very close to one, while the ratio of effective masses, $m_{13}^{\ddagger}/m_{12}^{\ddagger}$, should not change on substitution of different groups on the nitrogen atom. Variation of the isotope effect must arise then from those terms in the brackets of eq. 2. The functions $G(u_i)$ are functions only of the vibrational frequencies and increase with increasing frequency. Stronger bonds due to resonance in the transition state would result in higher frequencies and an increase in the $G(u_i^{\ddagger})$ term and a decrease in the ratio k_{12}/k_{13}. From Table III it may be seen that the isotope effect for *sym*-diphenylurea, 3,3′-dimethylcarbanilide and phenylurea is much less than that for *sym*-dimethylurea. This fact gives added support to a complex with resonance.

A value of 1.021 may be calculated for the ratio $(m_{13}^{\ddagger}/m_{12}^{\ddagger})^{1/2}$ using a theorem by Slater[15] if it is assumed that a C–N bond is breaking in the activated complex. If it is assumed that the activated complex has the same empirical formula as the reacting molecule and is non-linear, then the sum $\sum_{i}^{3n'-7} G(u_i^{\ddagger})\Delta u_i^{\ddagger}$ has one less term than the sum for the reacting molecule. The ratio of $(k_{12}/k_{13})/(m_{13}^{\ddagger}/m_{12})^{1/2}$ gives the term in brackets in (2) and this ratio minus 1 is the difference of the $G(u_i)\Delta u_i$ for the reacting molecule and the ac-

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[9] A. A. Frost and R. G. Pearson, "Kinetics and Mechanism," John Wiley and Sons, Inc., New York, N. Y., 1953, p. 261.

[10] S. Glasstone, K. J. Laidler and H. Eyring, "The Theory of Rate Processes," McGraw-Hill Book Co., Inc., New York, N. Y., 1941, p. 99.

[11] A. E. Remick, "Electronic Interpretations of Organic Chemistry," 2nd ed., John Wiley and Sons, Inc., New York, N. Y., 1950, p. 221.

[12] L. Pauling, "The Nature of the Chemical Bond," 2nd ed., Cornell University Press, Ithaca, N. Y., 1948, p. 137.

[13] J. Bigeleisen and M. Wolfsberg, *J. Chem. Phys.*, **21**, 1972 (1953).

[14] J. Bigeleisen, *ibid.*, **17**, 675 (1949).

[15] N. B. Slater, *Proc. Roy. Soc.* (*London*), **194**, 113 (1948).

tivated complex. The values calculated for this difference are given in col. 3 of Table III. The magnitude of the differences in the $G(u_i)\Delta u_i$ terms can best be appreciated when it is realized that the value of this term for a C–N bond with a vibrational frequency of 1000 cm.$^{-1}$ is 0.018 at 136°. It is evident that there is some strengthening of the bonding of the activated complex in the case of *sym*-dimethylurea and even much more in the phenylureas.

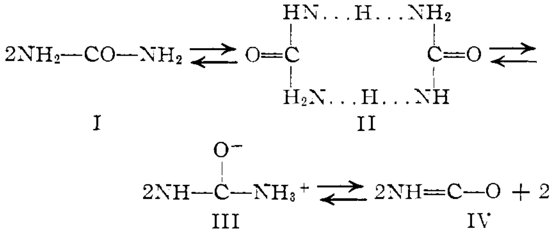
The large difference in the isotope effect for the different ureas points out the fact that care must be exercised in drawing conclusions concerning mechanisms from isotope effects. The usual approximation that only the bond being broken need be considered in the *a priori* calculation of the isotope effect is shown to be very inaccurate when resonance occurs in the activated complex, but is absent in the normal molecule. Such a large resonance effect probably would not be found if the normal molecule and the activated complex had the same structural formula.

Since phenylurea is unsymmetrical, there should be two paths of decomposition with different activation energies. These two paths represent formation of ammonia and phenyl isocyanate in the first step in one case and aniline and isocyanic acid in the other case. At high temperatures, the path with the high activation energy should predominate, while at low temperatures, more of the reaction would occur by the path of a lower activation energy. If a wide enough temperature range were covered, the two activation energies could be separated from each other. In this work only a relatively short range of temperature was covered.

Table I shows that the value of the activation energy for phenylurea falls between that of *sym*-dimethylurea and *sym*-diphenylurea. Table III shows that the isotope effect for phenylurea falls between the two values of the dimethyl- and diphenylureas. If conjugation of the double bond with the phenyl group accounted for all the difference between the rates and isotope effects of *sym*-dimethylurea and the aryl ureas, then one would expect the rate constants and isotope effects for phenylurea and *sym*-diphenylurea to be the same. Two possible explanations exist for the difference of these values for the two phenylureas.

According to one hypothesis, the second phenyl group in the *sym*-diphenylurea could increase the resonance stability of the activated complex. This increased stability would then make the activation energy smaller for the diphenylurea than for the phenylurea. The extra stability would also decrease the isotope effect. According to a second hypothesis, the phenylurea is decomposing by the two paths mentioned above and the rate constants and ratio of rate constants found are weighted averages of the values for the two paths. A large temperature dependence of the activation energy or isotope effect would indicate that this second explanation is the correct one. The temperature range of the present measurements is too small for this evaluation.

A reaction path which could give second-order kinetics for the urea decomposition is suggested. This path consists of the steps



$$\underset{\text{I}}{2NH_2{-}CO{-}NH_2} \rightleftharpoons \underset{\text{II}}{\begin{array}{ccc} & HN\cdots H\cdots NH_2 & \\ O{=}C & & C{=}O \\ & H_2N\cdots H\cdots NH & \end{array}} \rightleftharpoons$$

$$\underset{\text{III}}{2NH{-}\overset{O^-}{C}{-}NH_3^+} \rightleftharpoons \underset{\text{IV}}{2NH{=}C{-}O} + 2NH_3$$

If II is the activated complex, then second-order kinetics would be observed. This mechanism is similar to that outlined above, but involves an intermolecular proton transfer instead of the intramolecular one previously assumed.

No explanation has been found for the disagreement in the second-order kinetics of the urea decomposition in carboxylic acids found here and the first-order kinetics previously reported.[5] In water solutions the urea decomposition seems to be definitely first order.[16] The mechanism involved in the decomposition of urea in water solutions differs from that in propionic acid as shown by a comparison of the isotope effect for the decomposition of urea found here and the effect previously reported for the decomposition in aqueous solution.[2] Schmitt and Daniels found a value for $(k_{12}/k_{13} - 1)$ of 0.055. This effect is over twice as large as that found here for the urea reaction in propionic acid. It seems improbable that such a large difference in the isotope effect could be due to solvent alone. Further work on both urea and phenylurea would be desirable.

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[16] W. H. R. Shaw and J. J. Bordeaux, THIS JOURNAL, **77**, 4729 (1955).