THE INFLUENCE OF PRESSURE ON THE KINETICS OF THE ALKALINE HYDROLYSIS OF ESTERS AND AMIDES

By K. J. Laidler and David Chen

Dept. of Chemistry, University of Ottawa, Canada

The rates of the alkaline hydrolysis of methyl acetate, ethyl acetate, acetamide and propionamide have been measured in aqueous solution over a range of hydrostatic pressures from atmospheric pressure to 15,000 lb/in.^{2}. Activation energies for the two ester hydrolyses were also determined. The results obey van't Hoff's law, the logarithm of the rate constant varying linearly with the pressure. From the slopes of the lines values of ΔV^* were calculated; they fell in the range of -10 to -17 cm^3/mole. These negative volumes of activation are to be correlated with the negative entropies of activation for the reactions. It is suggested that the results may be explained in terms of the hypothesis that the activated complex is much more polar than the reactants, there being an ionization of the carbonyl bond during the course of activation. Some of the implications of this hypothesis are discussed.

————————

As a general rule reactions between ions and neutral molecules in aqueous solution have frequency factors that may be described as " normal ", in that they agree approximately with the kinetic theory of collisions. It is probable that if there are no important electrostatic effects involved in a reaction in solution the frequency of collision is close to that predicted by the kinetic theory. In reactions between ions and neutral molecules there are usually no large electrostatic effects, and the normal frequency factors are to be understood on this basis. For reactions between ions of the same sign or of opposite signs abnormal frequency factors are often obtained, and can generally be explained in terms of electrostatic effects. Some support for these explanations has been provided by studies of the effects of hydrostatic pressure on reaction rates,[1-4] and it has been noted [3] that the volumes of activation and entropies of activation are to some extent related to one another.

There are, however, certain reactions, involving an ion and a neutral molecule, for which the frequency factors are very much lower than predicted by the kinetic theory of collisions. These are the hydrolyses of substances containing a carbonyl group, such as esters, amides and anilides. For these reactions the frequency factors are always several powers of ten lower than predicted by collision theory, and theories that consider merely the electrostatic interactions between the reactants can give no satisfactory interpretation of this result; the electrostatic interaction between an ion and a dipole is much too small to account for the low frequency factors. The effects of solvents on reactions of this type have been shown [5] to lead to the conclusion that there is a large dipole moment in the activated complexes, and a theory in terms of these dipole moments agrees quantitatively with the experimental results using mixed solvents. Unfortunately, however, a satisfactory theoretical treatment of frequency factors along the same lines has not yet been formulated. If there is indeed a large increase of dipole moment when the activated complex is formed there will be an increased electrostriction of solvent molecules, and consequently a loss of entropy. At the same time there will be a contraction resulting from this electrostriction, and an increase in velocity with increasing pressure is to be expected. Studies of the effect of hydrostatic pressure should therefore contribute to an understanding of the exact nature of reactions

of this type, and may eventually lead to a more detailed formulation of the structure of the activated complex.

The present work has been carried out with this object in view. An investigation has been made of the alkaline hydrolyses of four carbonyl compounds, over a range of pressures from atmospheric to 15,000 lb/in.². In order to avoid the complications arising from the use of mixed solvents the work was done in pure aqueous solutions, enough of each substance being soluble to allow satisfactory rate measurements to be made. The four compounds employed were methyl acetate, ethyl acetate, acetamide and propionamide. Activation energies were also determined for the first two compounds, but for the amides the values recently obtained by Willems and Bruylants [6] have been employed. The results did show a marked decrease in volume during the formation of the activated complex, and the significance of this is discussed in more detail at the end of the paper.

EXPERIMENTAL

MATERIALS

The methyl acetate was purified by refluxing for 6 h with acetic anhydride and was then fractionally distilled, the distillate passing at 56° to 57° being collected. The distillate was shaken with anhydrous potassium carbonate, filtered and redistilled. The procedure with ethyl acetate was similar, but the refluxing was done with both acetic anhydride and a few drops of sulphuric acid.

Acetamide was washed in a mixture of benzene and ethyl acetate (50 : 15 by volume) and recrystallized from methyl alcohol. Propionamide was used as a crystallized Eastman Organics product.

HIGH-PRESSURE TECHNIQUE

The reaction vessel used for the study of the reactions at high pressures is shown in fig. 1, which is largely self-explanatory. The vessel is constructed of stainless steel and has a maximum working pressure of 20,000 lb/in.². The pressure is generated by an electrically-operated pump.

At the top of the apparatus there is a double-walled glass bulb, and water from the constant temperature bath is constantly circulated through the jacket. The mercury level is brought up to the bottom of this bulb, and the reaction mixture is then introduced into the bulb and into the pressure vessel. The high-pressure valve is then closed, and the desired pressure applied by means of the pump. When samples are required for analysis the pressure is released, and a sample of solution forced into the upper bulb. A sample is then pipetted off, and the remainder introduced again into the pressure vessel and the pressure applied. This procedure is carried out at various stages during the course of the reaction. The time taken for these procedures is only a small fraction of the total duration of the experiment, and the correction necessary is therefore very small.

FIG. 1.—Schematic drawing of the high-pressure reaction vessel. The inside diameter is 2·5 in., the outside 4·93 in.; overall length 14·75 in. Approximately 100 ml can be introduced into the inner compartment.

The compression of the reaction system brings about a rise in temperature. In order to minimize this the vessel was " conditioned " before the beginning of each run; this was done by pumping to the pressure of the experiment, allowing temperature equilibrium
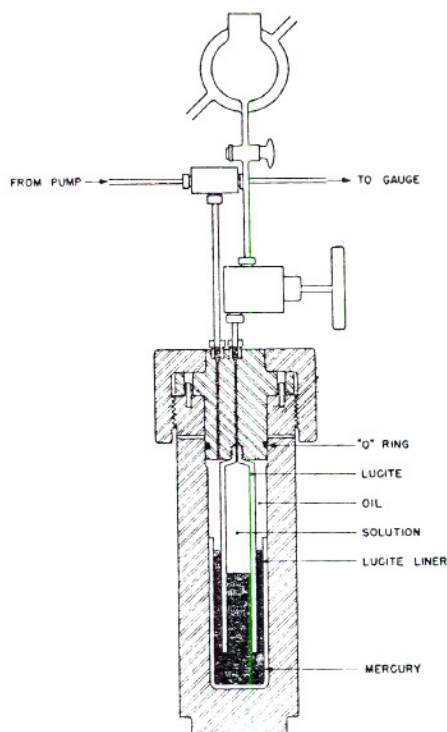
to be established, and then releasing the pressure. The resulting cooling fairly accurately compensates for the temperature rise at the beginning of the experiment.

KINETIC PROCEDURE

For the determination of the energy of activation of the alkaline hydrolyses of methyl acetate and ethyl acetate the reactions were carried out in flasks maintained in the constant temperature water-bath. A mixture was made of 25 ml each of 0·1 M sodium hydroxide and the ester, and 5 ml samples were removed at various intervals and mixed with 5 ml of 0·1 M hydrochloric acid. The excess acid was titrated with 0·1 N $Ba(OH)_2$ solution from a microburette, using phenolphthalein as indicator.

The high-pressure runs were carried out at 25°C in the vessel in the manner indicated above. In order to slow down the reactions for the high-pressure work the solutions were used at lower concentrations than above. In the ester hydrolyses 25 ml each of 0·01 M NaOH and ester solutions were mixed and introduced into the vessel. 5 ml samples were taken at about 800-sec intervals and added to 5 ml of 0·01 M HCl. The excess acid was titrated with 0·01 N $Ba(OH)_2$, using phenolphthalein as indicator.

For the hydrolyses of the amides 10 ml each of 2 M NaOH and amide solution were mixed and introduced into the pressure vessel. 1 ml samples were taken at about 1000-sec intervals, added to 2 ml of 2 N H_2SO_4, and diluted to 100 ml. 10 ml aliquots were delivered into a Nessler tube and diluted to 25 ml. 10 ml 2 N H_2SO_4 followed by 15 ml Nessler reagent were then added. After thorough mixing the solutions were examined in a photoelectric colorimeter.

RESULTS

All of the reactions studied were kinetically of the second order, and the rate constants were determined by plotting $x/a(a - x)$ against time, and measuring the slope of the straight line.

HYDROLYSIS OF ESTERS

The results obtained for the alkaline hydrolyses of methyl and ethyl acetate at atmospheric pressure and at four different temperatures are shown in table 1, and the corresponding Arrhenius plots are shown in fig. 2. The activation energies calculated from these
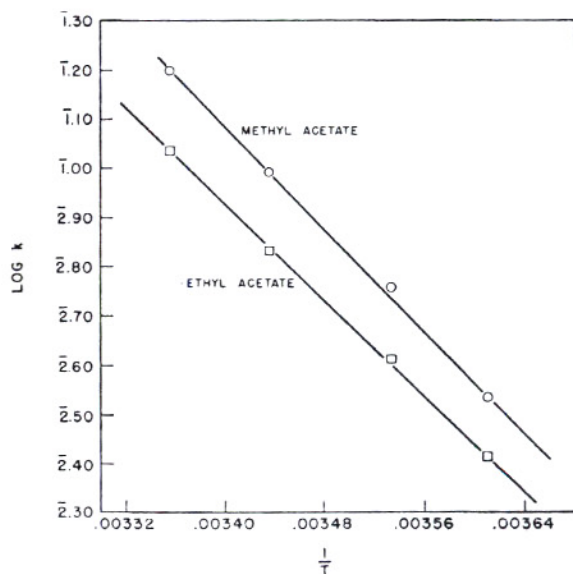

FIG. 2.—Arrhenius plots for the alkaline hydrolyses of methyl and ethyl acetates.

plots are 11·95 and 11·55 kcal/mole respectively. Potts and Amis [7] have given a value of 11·66 for ethyl ester, in good agreement. Values of 11·21 and 11·22 kcal for the two esters have been quoted by Moelwyn-Hughes [8] who, however, gives no reference to the original source. The frequency factors and entropies of activation for the reactions are shown in table 1.

TABLE 1.—RATE CONSTANTS FOR THE ALKALINE HYDROLYSIS OF METHYL
AND ETHYL ACETATES AT DIFFERENT TEMPERATURES

Concentration of both reactants after mixing = 0·05 M ;
rate constants in l. mole^{-1} sec^{-1}

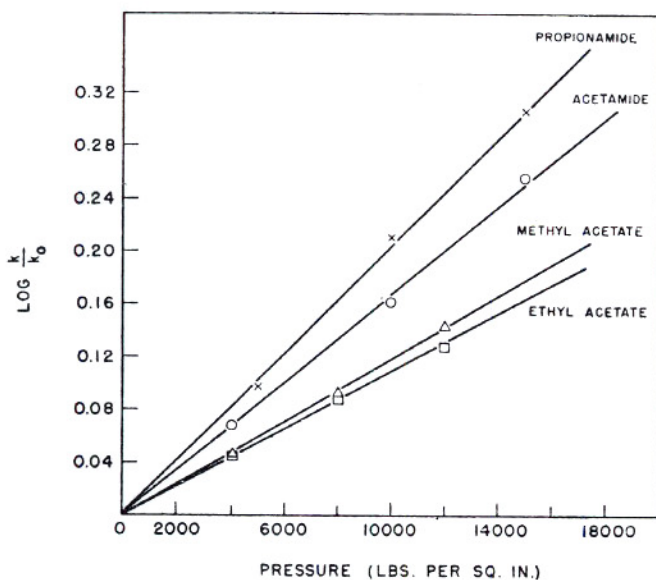|	rate constants for	
temp. (°C)	methyl acetate	ethyl acetate
4·0	0·0343	0·0258
10·0	0·0573	0·0410
18·0	0·0982	0·0680
25·0	0·158	0·1080
activation energy (kcal/mole)	11·95	11·55
frequency factor (l. mole^{-1} sec^{-1})	$9·28 \times 10^7$	$3·23 \times 10^7$
entropy of activation (cal/mole deg.)	− 24·1	− 26·2

FIG. 3.—Van't Hoff plots for the alkaline hydrolyses of the esters and amides.

Table 2 shows the rate constants obtained for the alkaline hydrolyses of the two esters for a range of pressure up to 12,000 lb/in.^{2}. Fig. 3 shows a plot of the logarithm of k/k_0 against the pressure ; k_0 is the rate constant at zero pressure, here assumed to be the

TABLE 2.—RATE CONSTANTS FOR THE ALKALINE HYDROLYSES OF
METHYL AND ETHYL ACETATES AT DIFFERENT PRESSURES

Concentration of both reactants after mixing = 0·005 M ;
rate constants in l. mole^{-1} sec^{-1} ; $T = 25·0$°C

	rate constants for	
pressure (lb in.$^{-2}$)	methyl acetate	ethyl acetate
14·7	0·146	0·080
4,000	0·163	0·089
8,000	0·181	0·098
12,000	0·203	0·107
ΔV^* (cm^3 mole^{-1})	− 9·93	− 8·77

same as at atmospheric pressure.   The van't Hoff law

$$\ln k = \ln k_0 - (\Delta V^* p / RT)$$

is seen to be obeyed accurately with ΔV^* constant, and from the slope of the curves the values of ΔV^* have been calculated; these are shown in table 2.   It is to be noted that in tables 1 and 2 there is a slight difference between the rates at atmospheric pressure and 25°, and this is attributed to the differences in concentration; there is a small ionic strength effect for these reactions.

Cohen and Kaiser [9] have studied the effect of pressure on the alkaline hydrolysis of ethyl acetate at 2·4°C using 0·01 M solutions, and from their results we calculate a ΔV^* value of $-$ 4·8 cm^3/mole.   The much smaller value obtained by them is attributed to the much lower temperature they employed.
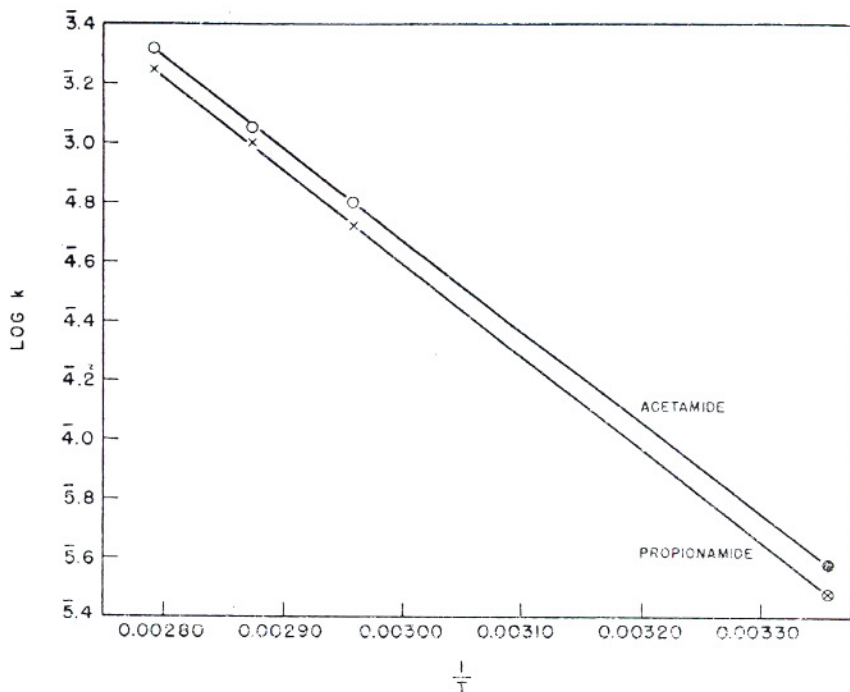

FIG. 4.—Arrhenius plots for the alkaline hydrolyses of acetamide and propionamide; the open circles and crosses are the results of Willems and Bruylants, the other points our own.

ALKALINE HYDROLYSIS OF AMIDES

Since accurate values of activation energies for the amide hydrolyses have recently been determined by Willems and Bruylants [6] we did not carry out a measurement of these quantities.   Table 3 shows the rate constants at the various pressures, and the

TABLE 3.—RATE CONSTANTS FOR THE ALKALINE HYDROLYSES OF ACETAMIDE AND PROPIONAMIDE AT DIFFERENT PRESSURES

Concentrations of both reactants after mixing = 1 M; rate constants in l. mole^{-1} sec^{-1}; $T = 25 \cdot 0$ C

	rate constants for	
pressure	acetamide	propionamide
14·7	$3 \cdot 77 \times 10^{-5}$	$3 \cdot 00 \times 10^{-5}$
4,000	$4 \cdot 44 \times 10^{-5}$	—
5,000	—	$3 \cdot 75 \times 10^{-5}$
10,000	$5 \cdot 47 \times 10^{-5}$	$4 \cdot 86 \times 10^{-5}$
15,000	$6 \cdot 80 \times 10^{-5}$	$6 \cdot 07 \times 10^{-5}$
ΔV^* (cm^3 mole^{-1})	$- 14 \cdot 2$	$- 16 \cdot 9$

corresponding van't Hoff plots are included in fig. 3. The volumes of activation are shown in table 3. Fig. 4 shows an Arrhenius plot for the data of Willems and Bruylants and ourselves; our own rates at 25°C are seen to be consistent with theirs at the higher temperatures. The activation energies and entropies are included in table 4.

DISCUSSION

Table 4 shows the main results of the present investigation, together with, for comparison, certain additional data. The values for the last four reactions listed in the table are taken from Burris and Laidler.[3] The corrected ΔS^* values shown in table 4 are the values of the entropy of activation that do not include the "cratic" terms; these are the intrinsic entropy losses when two molecules become one in the activated state. The significance of those cratic terms was first pointed out by Gurney [10] and further discussed by Burris and Laidler.[3]

TABLE 4.—SUMMARY OF RESULTS

Reaction	E (kcal/mole)	A	ΔS^* (cal/mole deg.)	ΔS^*corr. (cal/mole deg.)	ΔV^* (cm³/mole)
methyl acetate + OH⁻	12·0	$9·3 \times 10^7$	− 24·1	− 16·2	− 9·9
ethyl acetate + OH⁻	11·6	$3·2 \times 10^7$	− 26·2	− 18·3	− 8·8
acetamide + OH⁻	14·2	$9·5 \times 10^5$	− 33·5	− 25·6	− 14·2
propionamide + OH⁻	14·6	$1·5 \times 10^6$	− 32·6	− 24·7	− 16·9
$CH_2BrCOO^- + S_2O_3^{2-}$	13·3	$1·64 \times 10^9$	− 17·0	− 9·1	− 4·8
$CH_2ClCOO^- + OH^-$	22·7	$5·74 \times 10^{10}$	− 11·6	− 3·7	− 6·1
$CH_2BrCOOCH_3 + S_2O_3^{2-}$	17·2	$1·0 \times 10^{14}$	− 5·7	2·2	3·2
$Co(NH_3)_3Br^{2+} + OH^-$	23·6	$5·0 \times 10^{17}$	21·7	29·6	8·5

It is to be noted that there is some correlation between the entropies of activation and the volumes of activation. This is shown in fig. 5, in which the volumes of activation have been plotted against the uncorrected entropies of
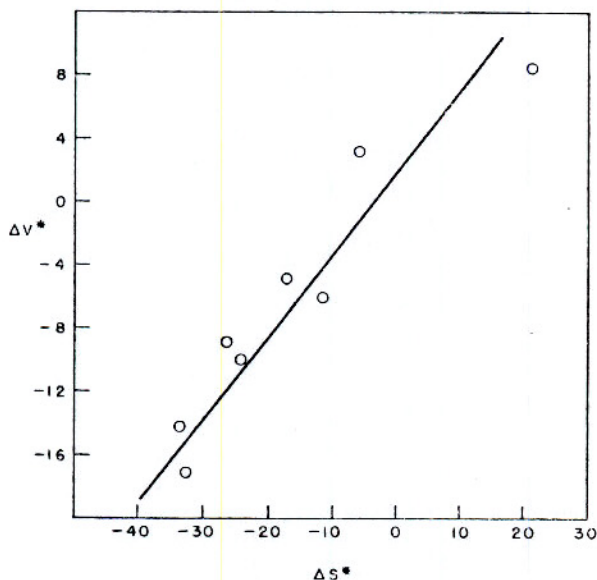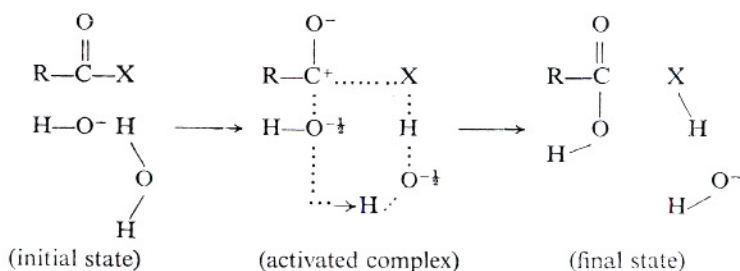

FIG. 5.—Plots of ΔV^* against ΔS^* for the eight reactions listed in table 4.

activation. The corrected entropies and volumes are seen from table 4 to be of the same sign in all cases. A rough correlation of this kind is to be expected in view of the fact that the charges and charge distributions on the reacting molecules

and the activated complexes influence both the entropies and the volumes. However, as has recently been discussed in some detail,[4, 11] an exact correlation between entropies and volumes of activation is not to be expected in view of the fact that entropies and volumes do not depend upon these charges and charge distributions in exactly the same manner; volumes in fact depend upon the first power of the charge [12] and entropies upon the square of the charge.[13]

It is now of interest to consider on what basis we may interpret the values of the volumes of activation that have been obtained for the esters and amides; the values have been seen to fall in the range of -10 to -17 cm^3/mole. The work on the hydrolysis of esters and amides in mixed solvents [5] has suggested that the alkaline hydrolyses may be represented according to the mechanism

$$
\begin{array}{ccc}
\underset{\text{(initial state)}}{
\begin{array}{c}
\text{O} \\
\parallel \\
\text{R—C—X} \\[4pt]
\text{H—O}^-\text{ H} \\
\quad \diagdown \\
\qquad \text{O} \\
\qquad \diagup \\
\qquad \text{H}
\end{array}}
&
\longrightarrow
\quad
\underset{\text{(activated complex)}}{
\begin{array}{c}
\text{O}^- \\
\mid \\
\text{R—C}^+\cdots\cdots\text{X} \\[4pt]
\text{H—O}^{-\frac{1}{2}}\quad\text{H} \\
\vdots \\
\qquad \text{O}^{-\frac{1}{2}} \\
\cdots\!\rightarrow\!\text{H}
\end{array}}
&
\longrightarrow
\quad
\underset{\text{(final state)}}{
\begin{array}{c}
\text{O} \\
\parallel \\
\text{R—C}\qquad\text{X} \\
\mid \qquad \diagdown \\
\text{O}\qquad\quad\text{H} \\
\text{H}\diagup \\
\qquad\qquad \text{O}^- \\
\qquad\quad \text{H}\diagup
\end{array}}
\end{array}
$$

The principle on which the ionization of the activated complex has been formulated is that by the time the activated state has been reached the charge transfers have occurred to just one-half of the extent to which they occur in the complete reaction. This type of activated complex has been seen to provide an adequate interpretation of the effects of solvents on the rates.

The empirical equation obtained by Couture and Laidler [12] indicates that a unit charge in aqueous solution brings about a diminution of volume of 26 cm^3/mole as a result of the electrostriction effect. Considering the hydroxide ion in the initial state of the reaction, we may therefore say that there will be a volume diminution of 26 cm^3. For the activated complex, contributions must be assigned to the individual charges. The oxygen atom of the carbonyl group bears a full negative charge, and if it were completely surrounded by water a contribution of -26 would be obtained. The rest of the molecule, however, occupies perhaps one-quarter of the volume, and a reasonable estimate is therefore three-quarters of -26, i.e. approximately -18. For the carbon atom in the carbonyl group a reasonable estimate is that three-quarters of the surroundings are occupied by the activated complex itself, and a contribution of one-quarter of -26, namely -6, may be taken. Two other oxygen atoms bear half-charges and in both cases the environs may be said to be occupied to approximately half of the extent by complex, and half by water; a contribution of about one-quarter of -26, namely -6, will therefore be taken in both cases. The total diminution in volume in the activated state, due to electrostriction, is therefore roughly equal to $-18-6-6-6$, i.e., -36. As a result of the electrostatic effects alone, therefore, there has been a change of volume from -26 to -36, i.e., a decrease in volume of 10 cm^3. Structural effects are not likely to be important in this addition of the hydroxide ion to an ester, and the electrostatic effects are probably the main ones. The theory, although crude, therefore appears to give an adequate interpretation of the volume changes taking place in these reactions.

1 Buchanan and Hamann, *Trans. Faraday Soc.*, 1953, **49**, 1425.
2 David and Hamann, *Trans. Faraday Soc.*, 1954, **50**, 1188.
3 Burris and Laidler, *Trans. Faraday Soc.*, 1955, **51**, 1497.
4 Laidler, *Faraday Soc. Discussions*, 1956, **22**, 88.
5 Laidler and Landskroener, *Trans. Faraday Soc.*, 1956, **52**, 200.
6 Willems and Bruylants, *Bull. Soc. Chim. Belg.*, 1951, **60**, 191.
7 Potts and Amis, *J. Amer. Chem. Soc.*, 1949, **71**, 2112.
8 Moelwyn-Hughes, *Kinetics of Reactions in Solution* (Clarendon Press, Oxford, 1947), p. 324.
9 Cohen and Kaiser, *Z. physik. Chem.*, 1915, **89**, 338.
10 Gurney, *Ionic Processes in Solution* (McGraw-Hill Book Co., New York, 1953), p. 89.
11 Laidler, *J. chim. phys.*, 1957, **54**, 485.
12 Couture and Laidler, *Can. J. Chem.*, 1956, **34**, 1209 ; 1957, **35**, 207.
13 Laidler, *Can. J. Chem.*, 1956, **34**, 1107. Laidler and Pegis, *Proc. Roy. Soc. A*, 1957, **241**, 80. Couture and Laidler, *Can. J. Chem.*, 1957, **35**, 202.