been converted to benzophenone to the extent of 97%. Distillation gave 9.1 g. of product which analyzed (polarograph) 88% benzophenone. Benzophenone, m. p. 46–47°, was obtained from the crude product by recrystallization from alcohol.

Diphenylcarbinol (10 g.), cyclohexanone (16 g.) and the alkoxide (13 g.) in toluene (60 ml.) were allowed to stand at 20–25° for a week. Polarographic determinations upon the reaction mixtures showed that the alcohol had been converted to benzophenone to the extent of about 90%. Benzophenone (8 g.) was also obtained when the same reactants were held at 56° for three hours. 2-Cyclohexylidene-cyclohexanone was isolated in a yield of about 20% from the reaction carried out at 20–25°.

Diphenylcarbinol (10 g.), isobutyrophenone (40.3 g.) and the alkoxide (13.4 g.) were refluxed in toluene (105 ml.) for forty-two hours. A polarographic analysis indicated that 81% of the alcohol was oxidized. The amount of benzophenone recovered was 68% of the theoretical. Benzaldehyde (18 g.) in 100 ml. of benzene was added during one and one-half hours to a solution at 55–56° of 10 g. of diphenylcarbinol and 13 g. of alkoxide in 100 ml. of benzene. After reaction for one hour, 10 g. of a sample, 91% pure, of benzophenone was obtained.

2-Ethylcyclohexanol (15 g.), *p*-benzoquinone (65 g.) and aluminum *t*-butoxide (14.8 g.) in a liter of toluene were allowed to stand at 20–25° for eight days. After the removal of aluminum hydroxide, the toluene solution was washed with a 5% solution of sodium hydroxide and with water. After distillation and fractionation through a modified Widmer column 11.4 g. of 2-ethylcyclohexanone, b. p. 178–182° (738 mm.), $n^{25}\text{D}$ 1.4500, identified as its semicarbazone, m. p. 160–161° (from benzene), was obtained.[11] The sample of ketone was shown to contain no more than 3% of 2-ethylcyclohexanol.

Cholesterol (7.5 g.) in 100 ml. of methyl ethyl ketone with 7 g. of aluminum *t*-butoxide in 50 ml. of benzene was refluxed for eight hours. The crude product (8.4 g.) after recrystallization from equal parts of acetone and methanol gave 6.2 g. of cholestenone, m. p. 78–79°, or an 84% yield.

Cholesterol was oxidized with acetone as by Oppenauer,[6,12] and with cyclohexanone as by Butenandt[13] and others. The results obtained were similar to those previously reported.

Summary

Some of the factors governing the choice of a ketone and experimental conditions for the oxidation of an alcohol with a ketone in the presence of aluminum *t*-butoxide have been considered.

[11] Bartlett and Berry, THIS JOURNAL, **56**, 2683 (1934).

[12] Cason and Fieser, "Organic Syntheses," John Wiley and Sons, Inc., New York, N. Y., Vol. XXI, 1941.

[13] Butenandt, Schmidt-Thome and Weisz, *Ber.*, **72**, 423 (1939).

MADISON, WISCONSIN RECEIVED JUNE 9, 1941

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, DUKE UNIVERSITY]

The Activated Complex Theory Applied to Fast Reactions. The Reaction of Aldchlorimines with Bases[1]

BY W. E. JORDAN,[2] H. E. DYAS AND D. G. HILL

There are two theories currently in use to explain the mechanism by which chemical reactions attain their measured rates. One, generally known as the collision theory, was first applied to reactions in solution by Moelwyn-Hughes.[3] It treats reactions in solution by the methods of gas reactions, and uses the fundamental equation $k' = PZe^{-E/RT}$ in which k' is the rate constant, Z is the collision number calculated as if the reactants were gas molecules, P is a probability factor, and E the Arrhenius activation energy. Moelwyn-Hughes has shown that for many reactions, the P factor has the order of magnitude of unity and that the treatment has considerable application. The cases where P is far from unity, however, are also numerous, and the explanation of this fact is somewhat unsatisfactory. Particularly is this true for reactions in which P is greater than unity, in which case the practice seems to be to assign it to some ill-defined "internal degrees of freedom," borrowing the term from the theory of unimolecular gas reactions.

The activated complex theory as developed by Eyring, Wynne-Jones and Eyring, and Evans and Polanyi[4] has been applied particularly to very "fast" reactions. The equation derived from statistics is $k' = \frac{kT}{h} e^{-\Delta F^*/RT}$. This was shown by Stearn and Eyring[5] to explain several very rapid reactions and to ascribe the very large rate to a gain in entropy in the formation of the

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[1] This paper is in part taken from a thesis submitted by H. E. Dyas to the Graduate School of Arts and Sciences of Duke University, Durham, North Carolina, in partial fulfillment of the requirements for the degree of Doctor of Philosophy, June, 1941.

[2] Associate Professor of Chemistry, North Carolina State College, Raleigh, North Carolina.

[3] Moelwyn-Hughes, "The Rate of Chemical Reactions in Solution," Clarendon Press, Oxford, England, 1933.

[4] H. Eyring, *J. Chem. Phys.*, **3**, 107 (1935); Wynne-Jones and Eyring, *ibid.*, **3**, 492 (1935); Evans and Polanyi, *Trans. Faraday Soc.*, **21**, 875 (1935); see also Faraday Soc., Discussion on Reaction Kinetics, Sept., 1937.

[5] Stearn and Eyring, *J. Chem. Phys.*, **5**, 113 (1937).

activated complex. Further work on reactions in which this might be expected seems desirable.

Studies in this Laboratory by Hauser and his students[6] established that the reaction of several chlorimines with bases went quantitatively at easily measurable speeds in spite of a rather high activation energy (20,000 cal.). These authors were not interested in the absolute rates, but rather in the changes in rate when different groups were substituted in the molecule, and the application of these relative rates to the elucidation of organic mechanisms. We have calculated the absolute rates in the cases in which data at several temperatures were available, and find them all much too rapid for the collision theory (see Table I). Since the reaction is one which lends itself to accurate measurements, we have extended the measurements to several bases and solvents not previously used in the hope of identifying the entropy and free energy of activation with some other properties of the reactants or solvent.

The reaction of chlorimines with bases was shown by Hauser and his co-workers to be a general one brought about by a number of bases, and to proceed according to the bimolecular equation. Their data show the effect of various substituents upon the rate, and establish that the Arrhenius activation energy is essentially unchanged by such substitution even though the absolute rate changes several fold. The reaction may be represented as $R—CHNCl + B = RCN + HB^+ + Cl^-$, where B represents the base, which may or may not bear a charge, and R is an aromatic radical with the various substituents. Hauser suggests that the reaction occurs in two steps

$$R—CHNCl + B = R{=}CNCl^- + HB^+$$
$$R—CNCl^- = RCN + Cl^-$$

in which the second step is rapid, compared with the first. However, as he states, the kinetics would be identical if the second step were slow, and the first a reversible acid–base equilibrium, or even, which is perhaps more probable, if the two processes were simultaneous. In terms of the activated complex hypothesis, the rate depends on the formation of a complex between the chlorimine and the base, and whether the next step is simple or complex would not affect the conclusions.

The reaction thus is a neutralization in which the chlorimine plays the part of an extremely weak acid. A neutralization of a very weak acid would be expected to be slow, and since we can feel fairly sure of the mechanism of this type of reaction, the data should be of interest.

Experimental

The chlorimines were prepared by the method of Hauser, Gillaspie and Lemaistre[7] by treating the proper aldehyde, either *p*-chloro- or *p*-methoxybenzaldehyde, with monochlorimine, freshly prepared from sodium hypochlorite and ammonium hydroxide. The chlorimine precipitated, since it was insoluble in water. It was washed with ice water and twice recrystallized by diluting an alcoholic solution with water until it became turbid, and then cooling to 0°. The chlorimine was dried over sodium hydroxide in a desiccator, but was never kept more than one day before use. It has been shown that chlorimines decompose slowly upon standing, particularly in the presence of acid, to give hydrogen chloride and a nitrile, but apparently by a different mechanism than in solution. The chlorimine as prepared might contain some nitrile (which would be the product of the reaction to be studied), and even some unchanged aldehyde, but Hauser has shown that neither has any effect on the rate.

Commercial absolute methanol was refluxed with magnesium and distilled.

Triethylamine was obtained from Eastman Kodak Co., dried with Drierite, and distilled in a good column. It boiled within 0.02° at 89.4°.

Kahlbaum benzene was dried with sodium and distilled.

Sodium alcoholate was prepared from sodium and the absolute alcohol already prepared. It was presumably not entirely dry, although care was used to free the sodium from as much oxide and hydroxide as possible. The experiments to be given show that the small trace of water that could be present would have no measurable effect on the rate, for the effect of 5% is small. The sodium alcoholate was prepared fresh for each run.

Temperatures of 0° were obtained by immersing the flasks in a mixture of ice and water. For the other temperatures, a thermostat was used, in which the temperature was measured by a thermometer calibrated against a Bureau of Standards thermometer, and was maintained constant to 0.01°.

For each run, approximately the desired amount of chlorimine was weighed into a flask and made up to 250 ml. with the solvent. The desired amount of base, always slightly in excess, was also made up to 250 ml. and both solutions allowed to come to the reaction temperature. The solutions were then mixed, and a sample taken at once with a pipet for analysis. This was necessary to establish the initial concentration, due to the possible impurities already mentioned. Further samples were taken from time to time, and the reaction stopped by allowing the pipet to drain into a known excess of standard acetic acid. The time was taken as that of half drainage of the pipet, and was measured by pressing the stems of two stopwatches simultaneously, starting one at the instant the other stopped. Since the constants obtained at the start of a run agreed well with those later on, it is believed that

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[6] Hauser, Lemaistre and Rainsford, THIS JOURNAL, **57**, 1056 (1935).

[7] Hauser, Gillaspie and Lemaistre, *ibid.*, **57**, 567 (1935).

the heat of mixing is too small to cause any appreciable error.

In analyzing the samples, the chlorimine was treated with excess potassium iodide, and the iodine titrated with standard sodium thiosulfate. One-half mole of iodine is set free by one mole of chlorimine immediately upon adding it to an acid solution of potassium iodide. The base subsequently was determined in the same solution by back titrating the excess of standard acid originally added with standard alkali. Methyl orange was used as indicator when alcoholate ion had been the base, and brom phenol blue for the reaction with triethylamine. The titrations in benzene solution were carried out easily by adding a large amount of alcohol to the acid before the chlorimine sample was added. A homogeneous solution resulted, in which the titrations could be carried out with aqueous reagents, although the end-points were not quite as satisfactory. It was found better to omit starch in the thiosulfate titration.

The base concentration was not determined throughout all the runs, for it was found that it ran strictly parallel to the chlorimine, and therefore need only be measured for the initial concentration.

Two runs were made in which large amounts of triethylammonium chloride, one of the products of reaction, were added to the reaction mixture in absolute methyl alcohol and no effect on the rate was observed.

An attempt was made to study the salt effect by adding known quantities of lithium chloride to *p*-chlorobenzalchlorimine in absolute methanol and treating the mixture with sodium methylate. The expected linear primary salt effect was not found, the plot of the rate constant against the ionic strength showing a pronounced curvature. However, the effect of added salt was to decrease the rate, which is in accord with the mechanism suggested. The failure to obtain a straight line is ascribed to the low activity of lithium chloride in methanol, and to its nonlinear change with concentration at the comparatively high concentrations (0.8 *N*) which had to be used if the change of rate were to be measurable.

Attempts were made to extend the reaction to other solvents and other bases than are reported here, but these did not succeed. The high oxidizing power of all chlorimines eliminates such bases as CN^-, which is alcohol soluble, and limits the choice of amines to tertiary ones. Only bases which differ markedly in strength will give results of interest.

Hauser, Lemaistre and Rainsford[6] showed that the reaction was quantitative when sodium ethylate was the base, and 92.3% alcohol the solvent. We have established that it is also essentially quantitative in absolute methyl alcohol, using triethylamine as the base. *p*-Chlorobenzalchlorimine was allowed to stand in absolute methyl alco-

TABLE I

Chlorimine	Base	Solvent	Temp., °C.	k'	E	PZ	ΔF^*	ΔS^*
p-Chloro	NaOEt	EtOH 95%	30	1.8	20090	1.4×10^{15}	18773	+ 4.6
p-Chloro	NaOEt	EtOH 95%	0	0.050			18726	
p-Chloro	NaOEt	EtOH (abs.)	30	1.4	17400	1×10^{13}	18926	− 4.8
p-Chloro	NaOEt	EtOH (abs.)	0	0.060			18717	
p-Chloro	NaOMe	MeOH 95%	30	.177			20185	
p-Chloro	NaOMe	MeOH 95%	10	.0182	20150	1.7×10^{14}	20066	0
p-Chloro	NaOMe	MeOH (95)	0	.0051			20654	
p-Chloro	NaOMe	MeOH (abs.)	30	.159			20250	− 2.1
p-Chloro	NaOMe	MeOH (abs.)	10	.0161	19550	4.7×10^{13}	20165	
p-Chloro	NaOMe	MeOH (abs.)	0	.0045			20127	
p-Chloro	Et_3N	MeOH (abs.)	40	.00017	17600	3.5×10^{8}	24950	−22.1
p-Chloro	Et_3N	MeOH (abs.)	25	.000040			23965	
p-Chloro	Et_3N	C_6H_6	40	.000044	11900	1.5×10^{4}	25995	−44.5
p-Chloro	Et_3N	C_6H_6	30	.000025			25525	
p-OMe	NaOEt	EtOH 95%	30	.18	19940	1.04×10^{14}	20181	− .6
p-OMe	NaOEt	EtOH 95%	0	.0047			20099	
p-OMe	NaOEt	EtOH (abs.)	30	.15	17015	6.1×10^{11}	20273	− 6.9
p-OMe	NaOEt	EtOH (abs.)	0	.0049			19893	
p-OMe	NaOMe	MeOH 95%	30	.0271			21305	
p-OMe	NaOMe	MeOH 95%	0	.00056	21320	4.7×10^{14}	21248	0
p-OMe	NaOMe	MeOH (abs.)	30	.0227			21423	
p-OMe	NaOMe	MeOH (abs.)	10	.00207	20620	4.3×10^{14}	21320	− 2.4
p-OMe	NaOMe	MeOH (abs.)	0	.000353			21281	

TABLE II

BASE = OEt; SOLVENT = EtOH 92.5%

Chlorimine	Temp., °C.	k'	E	PZ	ΔF^*	ΔS^*
Benzal	30	0.62	19800	1.2×10^{14}	19400	+1.3
	0	.017			19413	
Cinnamic	30.5	.23	20100	1.8×10^{14}	20000	−0.3
	0	.0058			19987	
3,4-Methylenedioxy	30	.277	20400	1.5×10^{14}	19916	−1.6
	0	.007			19909	

hol with excess triethylamine, and the solution after reaction treated to recover *p*-chlorobenzonitrile, the expected product; 90.7% of the desired product was obtained. The reaction is believed to be perfectly general.

Table I gives the rate constants calculated according to the usual bimolecular equation in liters per gram molecule per second. The values given for the constants at each temperature have been rounded off so that they are accurate to one or two units in the last figure. The data of Hauser have been recalculated to the same units and are given in Table II. *E*, the Arrhenius activation energy, and *PZ* follow in the next two columns.

Discussion

The experiments in 92.5 or 95% ethyl or methyl alcohol all show the same *E* within experimental error, even though there is a large variation in their absolute rates, as was pointed out by Hauser. The *PZ* term for all these is greater by a factor of from 10 to 1000 than would be predicted on the collision theory, 2×10^{11}. When triethylamine is used as the base in either methyl alcohol or benzene, the value of *E* is much less, as is that of *PZ*. Thus it should fall in the class of "slow" reactions. Since the reaction is essentially the same, such a change from fast to slow is not easily explained.

The column headed ΔF^* gives the free energy of activation calculated from Eyring's equation. Regularities are at once apparent. ΔF^* depends markedly on the base used, somewhat on the chlorimine, and to a very slight extent on the solvent. Not only does the addition of a few per cent. of water to absolute alcohol seem to be without effect, but the change from methyl alcohol to benzene as solvent raises ΔF^* by only 1000 cal.

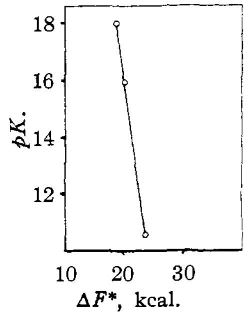

Fig. 1.

The relationship between ΔF^* and the strength of the base used is seen if ΔF^* is plotted against some measure of the basic strength. The most convenient is the *pK* of the acids corresponding to each base, *i. e.*, CH_3OH, C_2H_5OH and Et_3NH^+. The values are 16, 18 and 10.7, respectively. That for Et_3NH^+ is taken from the "I. C. T." value for the ionization constant of triethylamine, and the others from the table of McEwen.[8] Figure 1 shows the plot of these values against ΔF^* for the reaction of *p*-chlorobenzalchlorimine with the three bases. A straight line is obtained. This is to be expected if the reaction is an acid–base reaction, for ΔF^* is derived from the equilibrium constant for the formation of the activated complex, and this constant should be proportional to the activity of the base, or inversely to the ionization constant of the acid. This relationship is often expressed in terms of the Brönsted Catalytic Law, $k' = AK^x$. From the slope of the line in our plot, the value of *x* in this form of the law is 0.54.

A similar comparison is not possible with the chlorimine structure, since there is no information about the strength of these compounds as acids. However, a rough comparison may be made with the strength of the carboxylic acids in which the aromatic radical is the same, *i. e.*, *p*-chlorobenzoic acid instead of *p*-chlorobenzalchlorimine. Table II gives the ionization constants of these acids taken from "I. C. T." Figure 2 is a plot of the free energy of activation against the *pK* of this somewhat analogous acid.

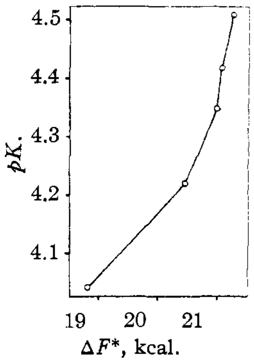

Fig. 2.

TABLE III

Acid	Ionization const. ($\times 10^5$)	*pK*
p-Methoxybenzoic	3.1	4.51
Cinnamic	3.8	4.42
3,4-Methylenedioxybenzoic	4.5	4.35
Benzoic	6.1	4.22
p-Chlorobenzoic	9.1	4.04

This curve is not a straight line such as is found in the plot of the three bases. The accuracy of the ionization constants may be at fault; however, the positive slope of the line is that expected if the reaction is a neutralization, and if the free energy of activation is inversely proportional to the acid strength of the chlorimines (directly proportional to their *pK*).

The entropy of activation is calculated from the free energy of activation and from the Arrhenius energy of activation, which is nearly identical with the heat of activation in Eyring's formulation, $\Delta S^* = (E - \Delta F^*)/T$.

The entropies of activation are included in the table for the sake of completeness. So far it has not proved possible to correlate them with any

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[8] W. K. McEwen, This Journal, 58, 1124 (1936).

property of the reacting system. However, it should be pointed out that the large positive entropies which Stearn and Eyring found for fast reactions do not appear in the present investigation. Quite possibly, the reaction under consideration is not fast enough for a large entropy of activation. In any case, the accuracy of ΔS^* as the difference between two large numbers is small enough that speculation seems fruitless.

In the case under consideration we seem to have a reaction which exhibits both the anomalies of the collision theory, that is, it may be either too fast or too slow for the simple theory. The changes when the base of the chlorimine is varied are very great, and difficult of explanation, since the type of reaction is essentially unchanged. When the activated complex concept is applied, the anomalies disappear, and instead regularities appear which are in accord with such other data as can be found. It would appear, then, as though the activated complex approach were the more fruitful attack in explaining the rate of reactions, at least those that deviate from the normal.

Conclusion

The rates of reaction of several chlorimines with various bases in several solvents have been measured, and the results calculated according to the two alternative procedures for explaining the dependence of rate on temperature. The activated complex explanation seems to be the more successful, admitting of several correlations with other data which do not appear in the collision theory.

DURHAM, NORTH CAROLINA RECEIVED JUNE 23, 1941

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, COLUMBIA UNIVERSITY]

Effect of Structure on Reactivity of Carbonyl Compounds; Temperature Coefficients of Rate of Formation of Several Semicarbazones[1]

BY FRASER P. PRICE, JR., AND LOUIS P. HAMMETT

The reaction of ketones and aldehydes with typical carbonyl reagents such as hydroxylamine, hydrazine, and semicarbazide shows a dependence of reaction rate upon the structure of the carbonyl compound with which existing theory is in no way competent to deal yet which is of large magnitude and is a characteristic concomitant of all reactions of this type.[2] Thus the lengthening of the carbon chain in an aliphatic ketone in proceeding from acetone to diethyl ketone lowers the rates of these reactions by an order of magnitude or so, yet cyclohexanone is considerably more reactive than acetone while cyclopentanone is only slightly more reactive than diethyl ketone.

In approaching a phenomenon as challenging as this, it is important to remember that the effect of a change in structure of reactant upon rate of reaction can be explained in terms of internal electron displacements or of external electrical fields due to a substituting group, in terms that is of potential energies alone, only when there is a cancellation of other effects due to the internal kinetic energies of the reactants[3]; further that the criterion of this cancellation is that the quantity

$$\Delta S_1^{\ddagger} - \Delta S_2^{\ddagger} = \frac{\partial}{\partial T}\left(RT \ln \frac{k_1}{k_2}\right) \qquad (1)$$

shall vanish (the subscripts 1 and 2 refer to two different reactants, k is specific reaction rate, $\Delta S^{\ddagger}$ is entropy of activation). The study of temperature coefficients of reaction rate is therefore prerequisite to a serious investigation of such a problem as the one in question, and the present paper furnishes the necessary data for the reaction of a variety of carbonyl compounds with semicarbazide in a phosphate buffer of pH 7.0. The stoichiometric equation for the reaction is

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(1) Dissertation submitted by Fraser Pierpont Price, Jr., in partial fulfilment of the requirements for the degree of Doctor of Philosophy in the Faculty of Pure Science, Columbia University.

(2) Among the more important papers on this subject are: (a) Westheimer, THIS JOURNAL, **56**, 1962 (1934); (b) Conant and Bartlett, *ibid.*, **54**, 2881 (1932); (c) Ölander, *Z. physik. Chem.*, **129**, 1 (1929); (d) Ardagh and Williams, THIS JOURNAL, **47**, 2976, 2983 (1925); (e) Bodforss, *Z. physik. Chem.*, **109**, 223 (1924); (f) Michael, THIS JOURNAL, **41**, 393 (1919); (g) Acree, *Am. Chem. J.*, **39**, 300 (1908); (h) Barrett and Lapworth, *J. Chem. Soc.*, **93**, 85 (1908); (i) Acree and Johnson, *Am. Chem. J.*, **38**, 308 (1907); (k) Stewart, *J. Chem. Soc.*, **87**, 410 (1905); (l) Petrenko-Kritschenko, *et al.*, *Ann.*, **341**, 150 (1905); *Ber.*, **34**, 1702 (1901); **39**, 1452 (1906).

(3) Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, pp. 118–120.