554. *The Kinetics of the Decomposition of the Addition Compounds formed by Sodium Bisulphite and a Series of Aldehydes and Ketones. Part I.*

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In aqueous solution sodium bisulphite reacts reversibly with an aldehyde or ketone to form an addition compound. The kinetics of the decomposition of a series of such compounds have been studied. The reaction is of the first order with respect to the addition compound, and the rate increases with the pH of the solution. The energy of activation and the frequency factor are reported for each compound, the series as a whole being built up by progressive substitution of formaldehyde, the simplest reactant. The results indicate that the rate of the reaction is influenced very little by electronic effects but that two steric effects are in operation. One of these effects operates by reducing the activation energy with increasing bulk of substituent whereas the other acts in the opposite sense. In both cases there is evidence for an accompanying change in frequency factor tending to offset, in some measure, the change in rate which the change in activation energy would otherwise cause.

Stewart and Donnally [1] observed that in acid solution the decomposition in presence of iodine of the addition compound formed by sodium bisulphite and benzaldehyde is of the first order with respect to the addition compound and independent of the amount of iodine present. The iodine simply oxidises the free bisulphite as it is formed and allows the decomposition to proceed to completion instead of to the equilibrium:

$$\text{Addition Compound} \rightleftharpoons \text{Free Bisulphite} + \text{Free Aldehyde}$$

The present investigation of a series of these addition compounds was designed to yield information about the influence of structure on reactivity.

Experimental

The aldehydes and ketones came from a variety of sources. Liquids were purified by distillation under suitable pressures, and certain of the solids were recrystallised, although the preparation of a bisulphite compound itself constitutes purification. *o*-Propoxybenzaldehyde was prepared by a variant of Buu-Hoï's method for the preparation of *o*-butoxybenzaldehyde.[2] 18 g. of rapidly crushed potassium hydroxide pellets were added to 26 ml. of salicylaldehyde and 70 ml. of propyl iodide (both freshly distilled), and the mixture was gently refluxed for 15 hr. with constant stirring. When cool the mixture was extracted with dry ether, which was later removed by gentle warming. The remaining propyl iodide was distilled off at 8 mm. and the product was fractionated through a short column at <1 mm.

The procedure for the preparation of a bisulphite addition compound was as follows.[3] A suitable volume of saturated aqueous sodium bisulphite was prepared at room temperature and 70% of its own volume of ethanol was added. Enough water to clear the solution was then added with constant stirring, followed by the aldehyde or ketone in suitable amount relative to the volume of bisulphite solution. The solution became hot and the addition compound was precipitated at once or on cooling. Stirring was continued for 30 min. after which the precipitate was filtered off, washed with a little alcohol, and dried in a vacuum desiccator ($CaCl_2$) for at least 3 days. The basic procedure was varied when necessary: chloral hydrate, for example, was dissolved in a very little hot water before addition of bisulphite solution, and in the preparation of the acetaldehyde compound it was best to omit the alcohol in the first

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[1] Stewart and Donnally, *J. Amer. Chem. Soc.*, 1932, **54**, 2333, 3555, 3559.

[2] Buu-Hoï, *Compt. rend.*, 1945, **221**, 202.

[3] Vogel, " A Textbook of Practical Organic Chemistry," Longmans, Green and Co. Ltd., London, 1948, p. 340.

stage and precipitate the product finally by a large excess of alcohol. The addition compounds obtained by this method may contain some free bisulphite or perhaps a little aldehyde if this is solid at room temperature. It will be shown that these impurities would not interfere with the rate determinations.

The rate of the reaction could be measured over the range where the pseudo-first order rate constant, k, was between 10^{-1} sec.$^{-1}$ and 10^{-5} sec.$^{-1}$. Since the bisulphite ions liberated in the decomposition are oxidised to bisulphate ions by iodine, reaction mixtures of high buffer capacity are needed to maintain the correct pH. Rather concentrated buffers were therefore used and the reaction mixtures were only 0·01 molar with respect to the addition compound. The buffer solutions were made up as follows, reagents of " AnalaR " quality being used as in the preparation of iodine solutions: for pH 3, 0·1200M in potassium hydrogen phthalate and 0·04878M in hydrochloric acid; for pH 5, 0·1192M in sodium acetate and 0·04972M in acetic acid. The pH was measured with a glass electrode before, during, and after trial runs at each pH and the buffer solutions were found to be satisfactory. At pH 5 the buffer showed signs of failing as the reaction proceeded but not enough for rate constants based on the early part of the reaction to be seriously in error.

Activation energies were calculated by the method of least squares from rate constants at five or six different temperatures. For solutions of pH 3 the range was generally from about 20° to 40° and at pH 5 either from 5° to 25° or from 20° to 40°. These temperature ranges are such that no significant change in pH was produced by a change in dissociation constant of the weak acid used in the buffer, the dissociation constants of acetic acid and phthalic acid varying with temperature in such a way that the pH change is less than 0·04 unit over the whole range of either buffer used in the experiments.[4] The only possible " buffer error " is therefore a systematic one because the actual pH might have been a little above or a little below that indicated by the glass electrode. This error, however, would be the same for all compounds studied.

The rate of reaction was measured by the following method. 50 ml. of the appropriate buffer solution and 1 ml. of starch indicator were placed in a 250-ml. conical flask and immersed in a thermostat for at least 30 min. before the start of the run. At room temperature or above water thermostats maintaining the temperature constant to within ±0·05° were used and below room temperature a refrigerated thermostat was used giving control to within ±0·15°. Enough of the bisulphite addition compound to make 50 ml. of approximately 0·01M solution was weighed accurately in a small wide-mouthed glass tube and a suitably small volume, say 0·5 ml., of approximately 0·01M-iodine solution was added to the mixture. The bisulphite compound was then added together with the containing tube, time " zero " being generally taken to be the moment of addition since the addition compounds dissolved in a few seconds. The time at which the blue colour disappeared was noted and gave the time for an amount of reaction corresponding to the iodine first added. A further small volume of iodine was at once added and the sequence was repeated. The amount present had no effect at all on the rate of the reaction, the iodine simply removing one product as fast as it was formed. In all experiments below room temperature the iodine solutions were chilled to the temperature of the thermostat. The reaction vessels were always kept stoppered between additions to prevent loss of iodine as vapour.

" End-points " were obtained by the following procedure. In buffer solution of pH 6·7 (42·981 g. of disodium hydrogen phosphate dodecahydrate and 10·887 g. of potassium dihydrogen phosphate per litre of solution) the rate of decomposition of every addition compound studied was extremely great and it was therefore possible to titrate small weighed amounts in 50 ml. of buffer against iodine solution. Several small amounts of each compound (greater, less, and equal to the amount required to make 50 ml. of 0·01M-solution) were weighed out and titrated with iodine in this way at pH 6·7. The results gave the linear relations between volume of iodine required for complete reaction and weight of bisulphite compound used. All end-point volumes for the compound could then be read off the graph since the amount used in each run was accurately known. Both the calibration and the corresponding runs were done on the same day with the same iodine solution. The vast majority of the aldehydes and ketones liberated by the decomposition of the addition compounds reacted much too slowly with iodine for their own secondary reaction with it to be a source of error in the rate measurements, but

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[4] Robinson and Stokes, " Electrolyte Solutions," Butterworths Scientific Publications, London, 1955, p. 496.

calibration titrations with the acetaldehyde compound had to be carried out rather quickly, slow fading after the first end-point being ignored. With propionaldehyde it was impossible for this reason to do more than estimate the rate very roughly at pH 3.

The presence of a little free carbonyl compound has no effect on the rate of reaction. Traces of bisulphite are easily allowed for as follows. Free bisulphite reacts instantaneously with iodine at any pH and therefore makes its presence known by giving the reaction a very fast start. One pilot run for each compound is sufficient to establish the amount, if any, of this " fast reaction " corresponding to a known weight of addition compound and in all subsequent runs the first addition of iodine can be augmented by the amount required to neutralise the free bisulphite. The iodine thus added is subtracted from the end-point volume and the time zero is moved to the first disappearance of the blue colour.

RESULTS

A pseudo-unimolecular rate constant, k (sec.$^{-1}$), was calculated for each run from the good first-order plots given by the experimental data, and reproducibility was satisfactory. Table 1 gives the principal experimental data for all the compounds studied; k and A are in sec.$^{-1}$. The general results may be summarised as follows.

TABLE 1. *Decomposition of bisulphite addition compounds in aqueous solution at 20°.*

	pH 3				pH 5			
Compound	5 + $\log_{10} k$	E (cal.)	ΔE (cal.)	$\log_{10} A$	5 + $\log_{10} k$	E (cal.)	ΔE (cal.)	$\log_{10} A$
PhCHO	1·19	17,750	—	9·44	2·89	14,550	—	8·77
o-Cl-	1·20	17,850	+ 100	9·48	—	—	—	—
o-NO_2-	1·15	18,200	+ 450	9·70	—	—	—	—
o-MeO-	1·07	19,050	+1300	10·2	2·74	16,150	+1600	9·79
o-EtO-	0·98	19,250	+1500	10·3	2·67	17,000	+2450	10·4
o-PrO-	0·95	19,700	+1950	10·6	2·56	18,000	+3450	11·0
p-NO_2-	1·25	17,550	− 200	9·33	—	—	—	—
p-Cl-	1·28	17,550	− 200	9·37	2·94	14,250	− 300	8·57
p-Me-	1·28	17,850	+ 100	9·59	3·05	16,500	+1950	10·3
m-NO_2-	1·28	18,100	+ 350	9·76	—	—	—	—
p-Me_2N-	1·32	19,850	+2100	11·1	—	—	—	—
p-MeO-	1·41	17,150	− 600	9·19	3·16	15,550	+1000	9·77
p-HO-	1·43	17,850	+ 100	9·73	3·24	17,800	+3250	11·5
o-HO-	2·10	15,300	−2450	8·53	3·91	15,350	+ 800	10·4
CCl_3·CHO	2·55	19,600	+1850	12·1	—	—	—	—
$COMe_2$	0·82	18,850	+1100	9·87	2·69	19,600	+5050	12·3
$CH_2<[CH_2]_4>CO$	0·45	20,950	+3200	11·0	2·12	17,850	+3300	10·4
EtCHO	≃0·1	—	—	—	—	—	—	—
MeCHO	−0·46	21,650	+3900	10·7	1·40	19,400	+4850	10·9
HCHO	—	—	—	—	−0·26	22,350	+7800	11·4

(1) The reaction is invariably faster at the higher pH and the activation energy is generally lower. A temperature of 20° has been selected for comparing rates and the benzaldehyde compound is used as the reference standard. At each pH $\Delta \log k$ is calculated for all compounds relative to benzaldehyde and the results appear in Fig. 1. It is immediately obvious that all manifestations of substituent effects are pH independent or nearly so.

(2) In view of the inherent uncertainty about the precise absolute value of the pH in the buffer solutions it is not possible to do more than estimate the order of the reaction with respect to hydroxyl-ion concentration. It would, however, appear that the true order is less than, or equal to, but never greater than unity.

(3) Figs. 2 and 3 show the result of plotting $\log_{10} k$ against energy of activation, E (kcal.), at pH 3 and at pH 5, respectively. (Several compounds were studied at one pH only, generally the lower one.) The lines are of slope $-1/2{\cdot}303\boldsymbol{R}T$ as required by the Arrhenius equation, $k = A \exp(-E/\boldsymbol{R}T)$, if A is constant for a series of reactions. It is immediately obvious that for the most part A is not constant, but varies markedly in such a way as to reduce the changes in rate which would otherwise follow the changes in the activation energy. This compensation effect is in some cases so marked that compounds of high activation energy actually decompose faster than those of low activation energy.

(4) If the substituted benzaldehydes are considered as a group related to the unsubstituted compound as a reference standard the following observations can be made:

(*a*) With the exception of an *ortho*-hydroxy-group all *ortho*-substituents reduce the rate slightly, the effect increasing with increasing size of substituent. The rates are, however, not reduced by anything approaching the factor expected on the basis of constant entropy of activation. There is in fact marked " compensation."

FIG. 1. *Comparison of substituent effects at* pH 3 *and* pH 5.

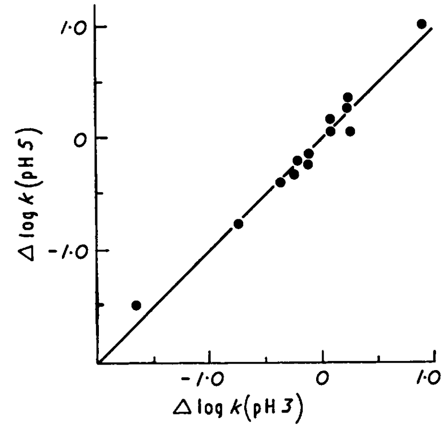


FIG. 2. *Relation between rate and activation energy at* pH 3.

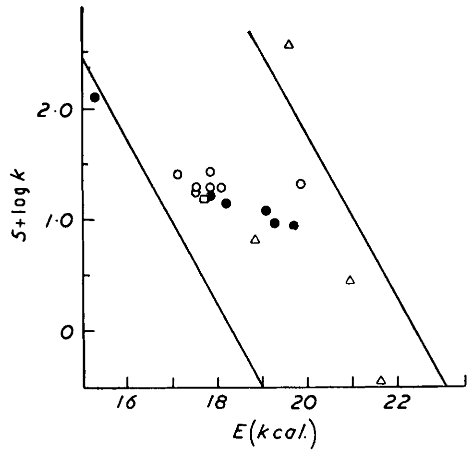
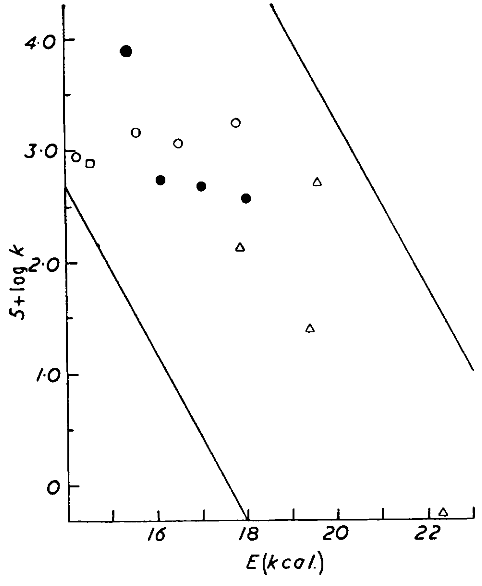


FIG. 3. *Relation between rate and activation energy at* pH 5.



□ *Benzaldehyde.*
○ *Benzaldehyde with* meta- *or* para-*substituent.*
● *Benzalde with* ortho-*substituent.*
△ *Other aldehydehydes and ketones.*

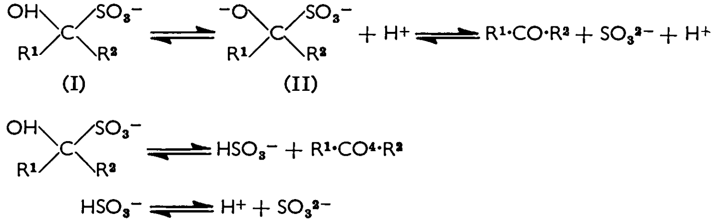
(*b*) Without exception *meta*- and *para*-substituents increase the rate slightly despite the fact that most of them raise the activation energy. There is again marked, but less regular compensation.

(*c*) An *ortho*-hydroxy-substituent has a greater effect on the rate than any other substituent in any position. At the upper pH this is due to increased entropy of activation and at the lower pH to reduced energy of activation.

(5) If benzaldehyde itself is chosen to represent the benzaldehyde group the order of increasing rate through the whole series of compounds is as follows: formaldehyde, acetaldehyde, propionaldehyde, *cyclo*hexanone, acetone, benzaldehyde, and chloral. The entropy of activation decreases somewhat in the progression, formaldehyde, acetaldehyde, *cyclo*hexanone, but is markedly reduced in the case of benzaldehyde, and quite appreciably increased in the case of chloral. Acetone seems to occupy an anomalous position.

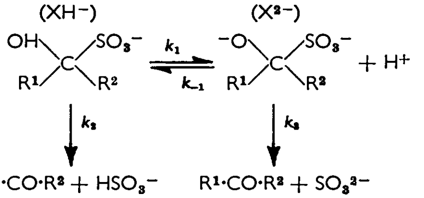
DISCUSSION

(1) *General Mechanism.*—The addition compounds formed by alkali bisulphites and aldehydes or ketones are α-hydroxy-sulphonates and not hydroxy-sulphite esters.[5, 6] The addition compound is therefore the salt of a strong acid and is assumed to exist in solution as the singly charged anion (I). This anion is itself a weak acid and will enter into an equilibrium with a doubly charged anion (II). In time, equilibrium would also be established with free bisulphite and free aldehyde or ketone as shown in the scheme:



When iodine is present all free bisulphite is removed from the solution, making its elimination irreversible.

The kinetic picture of the decomposition of an addition compound may therefore be represented as follows:



$$K = \frac{k_1}{k_{-1}} = \frac{[H^+][X^{2-}]}{[XH^-]}$$

Rate of reaction (rate of appearance of bisulphite) $= k_2[XH^-] + k_3[X^{2-}]$.

On the assumption that the concentration of doubly charged ions reaches a small stationary value, we may write

$$k_1[XH^-] = k_{-1}[X^{2-}][H^+] + k_3[X^{2-}].$$

Hence

$$[X^{2-}] = \frac{k_1[XH^-]}{k_{-1}[H^+] + k_3}$$

and by substitution we obtain

$$\text{rate} = k_2[XH^-] + \frac{k_1k_3[XH^-]}{k_{-1}[H^+] + k_3}$$

From the experimental data the reaction proved to be of the first order with respect to the addition compound and dependent on the hydroxyl-ion concentration to a power equal to or rather less than unity. The above rate expression gives a satisfactory account

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[5] Caughlan and Tartar, *J. Amer. Chem. Soc.*, 1941, **63**, 1265.

[6] Shriner and Land, *J. Org. Chem.*, 1941, **6**, 888.

of these requirements, although for the power to be not much less than unity the first term must make only a small contribution to the observed rate and for most purposes it can probably be neglected.

The simplified rate expression

$$\text{rate} = \frac{k_1k_3[\text{XH}^-]}{k_{-1}[\text{H}^+] + k_3} \quad (= Kk_3[\text{XH}^-]/[\text{H}^+] \text{ if } k_{-1}[\text{H}^+] \gg k_3)$$

must now be discussed in the light of substituent effects.

(2) *Substituent Effects.*—It is convenient to begin with a consideration of electronic effects in the light of the proposed reaction scheme and Table 2 shows the probable effect of different substituents on the rate constant k_1, k_{-1}, and k_3.

The substituted benzaldehydes form a fairly large group and are discussed first. The effect of *meta-* and *para*-substituents on the rate of reaction is surprisingly small, as shown below. (*ortho*-Substituents do of course exert electronic influences but these are combined with typically " *ortho* "-effects.)

Substituent	p-NO$_2$	m-NO$_2$	p-Cl	p-Me	p-Me$_2$N	p-MeO	p-OH
$\Delta \log k$ (pH 3)	+0·06	+0·09	+0·09	+0·09	+0·13	+0·22	+0·24

The results strongly suggest a large-scale cancellation of electronic effects within the molecule and this indeed follows from the proposed reaction scheme where the rate constants are affected in opposite senses (Table 2) by a given substituent and the interplay of changes in these constants will certainly minimise changes in the observed rates. Electron-withdrawing groups have least effect and further ring deactivation would presumably lead to a reduction in the rate since there is no obvious reason why the large-scale annulment of electronic effects should always result in a small net increase in rate for every possible substituent or combination of substituents. There is of course the possibility that any substituent, whatever its affinity for electrons, somehow disturbs the solvation pattern round the reactant molecule. This important and probably rather general effect will be discussed in Part II.

TABLE 2.

Process	Electron-attracting substituent	Electron-repelling substituent
Ionisation (k_1)	Proton held less firmly. k_1 increased.	Proton held more firmly. k_1 reduced.
Elimination of SO$_3{}^{2-}$ (k_3)	Negatively charged groups held more firmly. k_3 reduced.	Negatively charged group tends to be forced out. k_3 increased.
Protonation of doubly charged ion (k_{-1})	Proton attracted less strongly. k_{-1} reduced.	Proton attracted more strongly. k_{-1} increased.

With one conspicuous exception *ortho*-substituents tend to reduce the rate in a regular way (Figs. 2 and 3).

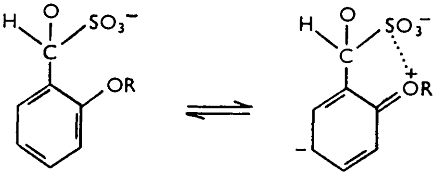
Substituent	o-OH	o-Cl	o-NO$_2$	o-MeO	o-EtO	o-Pr^{n}O
$\Delta \log k$ (pH 3)	+0·91	+0·01	−0·04	−0·12	−0·21	−0·24
,, (pH 5)	+1·02	—	—	−0·15	−0·22	−0·33

It would appear that the general trend of the results is determined by some special " *ortho* " effect exerted by these substituents rather than by their purely electronic effect. The nature of the effect is discussed later. A characteristic feature is that it is associated with large, regular energy–entropy compensation effects of a rather striking nature, the actual rate of the reaction being in fact little reduced by quite large increases in activation energy.

Thus far the results have been explained in terms of (*a*) a neutralisation of electronic influences and (*b*) a special " *ortho* " effect. All the compounds so far discussed have, however, belonged to the sub-group of substituted benzaldehydes. In their relations with other compounds they may now be represented by benzaldehyde itself.

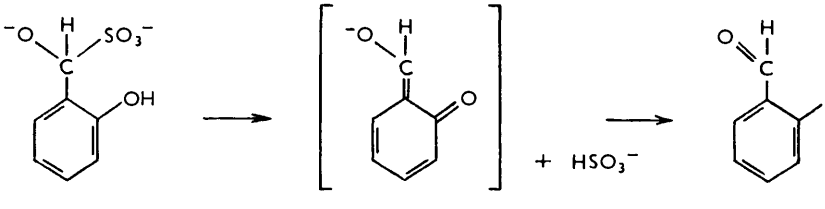
Over the whole series the total spread of rates and activation energies is very much greater than in the sub-group and there is, moreover, over this whole range a less regular compensation effect. Now the mechanism already developed depends on the neutralisation of electronic effects and there is no reason to suppose that this neutralisation ceases to operate outside the benzaldehyde sub-group. It is in fact impossible to attribute the spread in rates to electronic effects because the observed order does not follow variations in the electron affinities of the substituents. There is thus evidence for another kind of steric effect, different from the " *ortho* " effect and causing large changes in activation energy without regular energy–entropy compensation associated with the latter. This new effect is more understandable in the light of information concerning the formation of bisulphite compounds. Benzophenone does not form an addition compound and acetophenone forms one with difficulty and in small amount. If the difficult formation is a manifestation of steric hindrance to the entry of the bisulphite group it may well be matched by a pressure in the compound tending to facilitate the ejection of the bisulphite. The general order and distribution of points on the graph of $\log_{10} k$ against E is therefore understandable in terms of a rather large steric effect depending on the bulk of the groups causing it. Deviations from the general trend are presumably due to special effects, in which the degree of solvation might well be an important factor.

The *ortho*-effect may, under certain conditions, be partly due to the presence of an electrostatic bond. Such a bond would have a retarding influence on the reaction and could be quite strong since an electron-repelling substituent has a full positive charge in three of the four resonance structures



and two equivalent forms.

The apparently anomalous effect of an *ortho*-hydroxy-group is understandable since unlike any other substituent it can be involved chemically in the stages of the reaction. The following is one of several possibilities leading to a large but quantitatively unpredictable increase in the rate of the reaction.



It must be emphasised that the present results manifest once more the tendency for energies and entropies of activation to compensate one another in a series of chemical reactions when certain factors, as yet undefined, come into play. The other substituents in the benzaldehyde sub-group provide a particularly regular case of such compensation. The fact that the measured rate constant is compounded of three separate rate constants in no way reduces the significance of the results. The reason for the compensation effect and its ubiquity will be discussed in Part II (following paper) but at this stage it is important to indicate clearly the specifications to which any data must conform before they can provide real evidence for its existence.

A " correlation " between frequency factor and activation energy may in fact be completely spurious and nothing more than a by-product of errors in the measured activation energies. Warnings [7] have not been completely successful in underlining the hazards of comparing activation energies which come rather close together. The logarithm of the frequency factor has to be calculated from the rate at a given temperature and the activation energy which depends upon measurements over a range of temperatures.

$$\log_{10} A = \log_{10} k + E/2{\cdot}303\boldsymbol{R}T$$

The rate constant is always known to a much higher degree of accuracy than the activation energy and the error in $\log_{10} A$ is therefore directly proportional to the error in the measured activation energy. Suppose a series of reactions gives rise to a series of closely similar experimental rate constants at a given temperature because both energy of activation and frequency factor hardly vary over the series. Experimental errors in the separate activation energies produce, however, corresponding errors in the frequency factors and in fact a very good linear plot of $\log_{10} A$ against E will be obtained. This type of spurious correlation can be easily recognised: a narrow band (of experimental error dimensions) of activation energies coupled with virtually identical rate constants leads to a line of slope $1/2{\cdot}303\boldsymbol{R}T$ on the graph of $\log_{10} A$ against E. With certain assemblies of experimental data the " correlation " slope proves to be the " error " slope. A few " error slopes " are given for purposes of comparison (E in kcal.).

Temperature	0°	10°	20°	40°	60°	100°
" Error slope "	0·80	0·77	0·75	0·70	0·66	0·59

The likelihood of interpreting the results correctly in other cases may now be considered. (i) $\log_{10}$ A *constant,* $\log_{10}$ k *determined by changes in* E. Unless the spread of activation energies is extremely small there is little difficulty in recognising the constancy of the frequency factor. Experimental errors in the activation energy simply scatter the results about the line of constant $\log_{10} A$ on the graph of $\log_{10} A$ against E. (ii) E *constant,* $\log_{10}$ k *determined by changes in* $\log_{10}$ A. If the rate constants are noticeably different then the frequency factors will also differ. Errors in the activation energies will simply scatter the results about the line of constant E on the graph of $\log_{10} A$ against E. (iii) $\log_{10}$ k *determined by simultaneous* (*compensation*) *changes in* E *and* $\log_{10}$ A. The very presence of a compensating effect reduces the spread of the rate constants and great care must be exercised but nevertheless a genuine correlation can be identified provided that (*a*) the activation energies are spread over a sufficiently wide range or (*b*) the rates are spread over a narrower range than the activation energy would indicate.

On the basis of the foregoing observations the data presented in this paper seem to be suitable for inclusion in a general survey of compensation effects. The maximum % error in k is estimated at 5% and is generally a good deal less. Similarly the maximum error in E is about ± 250 cal. Part II (following paper) seeks to fit the results presented in Part I into a more general picture of the extremely varied instances of energy–entropy correlations.

Physical Chemistry Laboratory, Oxford University. [*Received, February* 27*th*, 1958.]

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[7] Purlee, Taft, and De Fazio, *J. Amer. Chem. Soc.*, 1955, **77**, 837.