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Kinetics of Reactions of Amines with Alkene Oxides

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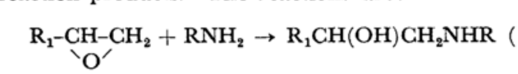
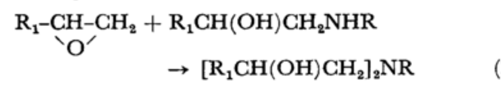
A variety of amines such as piperazine, pyrrolidine, morpholine, dialkyl amines, alkanolamines *etc.* were reacted with ethylene-, propylene-, and 1,2-butylene oxides in aqueous medium. Most of the experiments were made at 20°C. For some typical amines kinetic runs were made over a wide temperature range to obtain values of activation energy. Theoretical aspects of the reaction are discussed. It is shown that the method suggested by Swain and Scott could be used to correlate the rate constants. A close relationship exists between the relative rates of reaction of amines with CO_2, COS, CS_2 and alkene oxides.

The reaction of an amine with an alkene oxide results in the formation of an alkanolamine. The first addition to the epoxide is followed by one or more secondary additions of the epoxide to the reaction products. The reactions are:

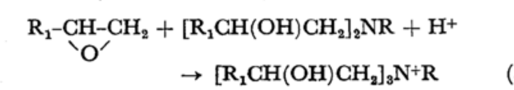


$$R_1\text{-}\underset{\diagdown O \diagup}{CH\text{-}CH_2} + RNH_2 \rightarrow R_1CH(OH)CH_2NHR \quad (1)$$



$$R_1\text{-}\underset{\diagdown O \diagup}{CH\text{-}CH_2} + R_1CH(OH)CH_2NHR \rightarrow [R_1CH(OH)CH_2]_2NR \quad (2)$$

which may be followed by



$$R_1\text{-}\underset{\diagdown O \diagup}{CH\text{-}CH_2} + [R_1CH(OH)CH_2]_2NR + H^+ \rightarrow [R_1CH(OH)CH_2]_3N^+R \quad (3)$$

which occurs very slowly at a very late stage in the reaction.

Sharma[1] and Kothari and Sharma[2] have studied the kinetics of reactions between a variety of primary and secondary amines and CO_2, COS and CS_2 and have found close relationships in their rates of reactions *e.g.*:

$$\log_{10} k_{\text{Am-CS}_2} \approx \log_{10} k_{\text{Am-CO}_2} - 4.3 \quad (4)$$

where k is the second order rate constant. It is likely that there also exists a close relationship between the rates of reactions of amines with CO_2, COS, CS_2 and alkene oxides.

Experimental Methods, Analytical Techniques and Theoretical Aspects

Many methods have been reported in the literature for following the amine-alkene oxide reactions: the distillation method, conductivity method, dialatometric method, polarimetric method and the gas chromatographic method. Hansson[3] in his extensive series of reactions between amines and alkene oxides had adopted the "distillation method," which does not appear to be sound. Here an aliquot of the reaction mixture was taken at appropriate times and was subjected to vacuum. *n*-Octadecyl alcohol was added to the flask in which the aliquot of the reaction mixture was taken to reduce foaming on application of vacuum. It was supposed by Hansson that on application of vacuum to the aliquot of the reaction mixture, none of the reaction product (that is, the alkanolamine which was thought to be nonvolatile) was lost and what was distilled off was only the relatively more volatile reactants in the reaction mixture. The material left in the flask after application of vacuum for sufficient length of time was titrated directly with a standard mineral acid. The supposition that no reaction product distilled off is not valid. Hansson had realized that some alkanolamine is likely to be lost and he therefore, applied a 'correction' factor. His method of correcting for the loss of the alkanolamine is theoretically unsound.

Known and appropriate amounts of freshly estimated epoxide[4] and amine[5] were taken separately in two 250 m*l* iodination flasks and brought to the experimental temperature in a thermostatic bath where the temperature could be controlled to ±0.05°C of the desired temperature. The reactants were mixed at a known time and aliquots of the reaction mixture were withdrawn at known intervals of time and added to sufficient quantity of dilute sulphuric acid taken in a 100 m*l* conical flask to arrest the reaction. The volatile epoxide (*i.e.* ethylene- or propylene oxide) was removed by the application of vacuum. In the case of 1,2-butylene oxide the reaction sample withdrawn was analysed immediately after adding it to sulphuric acid with the minimum lapse of time——this being necessitated due to its relative nonvolatility (bp 63.2°C/760 mmHg)

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[1] M. M. Sharma, *Trans. Faraday Soc.*, **61**, 681 (1965).

[2] P. J. Kothari and M. M. Sharma, *Chem. Engng. Sci.*, **21**, 391 (1966).

[3] J. Hansson, *Sevensk Kem. Tidskr.*, **67**, No. 5, 263 (1955).

[4] W. C. J. Ross, *J. Chem. Soc.*, **1950**, 2257.

[5] S. Siggia, "Quantitative Organic Analysis *via* Functional Groups," III Ed., John Wiley & Sons Inc., New York (1963), p. 423.

and the difficulty in removing it by the application of vacuum. In this case the analysis was carried out quickly so as to reduce to a minimum any possibility of reaction of the protonated amine with the epoxide.

Most of the reactions were studied at 20°C in aqueous medium. However, in some typical cases, experiments were made upto 40°C to obtain values of activation energy.

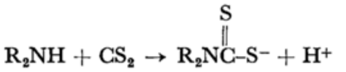
In most of the cases secondary amines were reacted with an epoxide and in a few cases when primary amine-epoxide reactions were studied, the relative amine concentration in the reaction mixture was taken at least four times that of the epoxide so that the secondary reactions are either obviated or reduced to a minimum. Similarly when a secondary amine is reacted with an epoxide the product of the reaction is a tertiary amine and the complications due to its reaction with another molecule of the epoxide to form a tetra-alkyl ammonium hydroxide (in the presence of a hydrogen ion from the solvent) are insignificant.

Analytical Techniques

Primary Amine-Epoxide Reactions. The analysis involving the separation of the primary amine and the product (a secondary amine) was effected by the Schiff's reaction of salicylaldehyde in 1:1 ethylene glycol, isopropanol solvent with the primary amine and the potentiometric titration of the unreacted secondary amine with hydrochloric acid in the same prescribed solvent:[6,7] The method depends upon the fact that salicylaldehyde reacts quantitatively with primary amines to form compounds of decreased basicity capable of being differentiated from the secondary amine in a non-aqueous potentiometric titration.[7]

It was found that the above method was suitable only for studying the reactions between alkene oxides and amines like cyclohexyl-, and benzylamines, the products of reactions of which had steric resistance and were likely to react sluggishly, if at all, with salicylaldehyde under normal conditons. However, this method failed to differentiate between simple amines like *n*-butylamine and its product with ethylene oxide-butylaminoethanol or that with propylene oxide, butylaminoisopropanol.

Secondary Amine-Epoxide Reactions. This involved an estimation of the secondary amine in the presence of the tertiary amine. An aliquot of the reaction mixture withdrawn in an excess of sulphuric acid was subjected to vacuum to remove the volatile epoxide. The solution was then neutralized with alkali using thymolphthalein indicator after running in 30—40 m*l* of isopropanol. An excess of CS_2 was then added to convert the secondary amine to the dithiocarbamic acid which was only 90—95 per cent complete. It was forced to completion by a standard sodium hydroxide titrant to a first blue or blue green end point. The amount of the standard sodium hydroxide titrant gave a direct measure of the secondary amine present. The reactions involved are:



$$R_2NH + CS_2 \rightarrow R_2N\overset{\overset{S}{\|}}{C}\text{-}S^- + H^+ \qquad (6a)$$

and $$OH^- + H^+ \rightarrow H_2O \qquad (6b)$$

This method of the estimation of secondary amine[8] is specific as only the secondary amine can react with carbon disulphide; the tertiary amine does not have a labile hydrogen atom to react with carbon disulphide. In this method only amines that are highly branched in the 2-position, like diisopropylamine, tertiary butylamine, *etc.* do not react quantitatively with CS_2 under the conditions used.

Materials

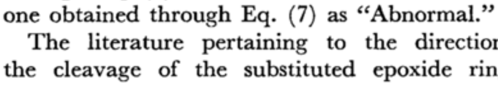
All the chemicals used were, in general, technical grade. The materials were purified whenever necessary and estimated before using them for experimental work.

Propylene- and 1,2-butylene oxides were obtained as liquids and were sufficiently pure to be used as such without further purification. Ethylene oxide was available in cylinders and an aqueous solution was prepared for reactions immediately prior to use. All the three epoxides were estimated prior to use in aqueous solution by Ross method[4]——by estimating the total amount of hydroxide ion liberated in the reaction between the epoxide and an excess of thio-sulphate anion in a 50 per cent aqueous acetone solution, by using a standard acetic acid solution.

Methylaminoethanol, ethylaminoethanol, butylaminoethanol and methylaminoisopropanol were synthesized by reacting the relevant epoxide and the amine; the amount of the amine being at least five times the concentration of the epoxide. The alkanolamines were recovered in aqueous solutions from the synthetic mixture (after allowing it to stand for sufficient length of time) by removing the relatively more volatile amine used, by application of vacuum.

Discussion of the Reactions

The primary reactions are:



$$R_1\text{-}\underset{\diagdown O \diagup}{CH\text{-}CH_2} + RNH_2 \begin{cases} \nearrow R_1CH(OH)\text{-}CH_2NHR & (1) \\ \searrow R_1\underset{\underset{NHR}{|}}{CH}\text{-}CH_2OH & (7) \end{cases}$$

which can give rise to one or both possible isomers, with the exception of ethylene oxide or symmetrically substituted alkene oxides. In accordance with the general practice and also the rule summarized from the work of Krassusky[9] product obtained through Eq. (1) will be termed "Normal" and the one obtained through Eq. (7) as "Abnormal."

The literature pertaining to the direction of the cleavage of the substituted epoxide ring is extensive and various hypotheses to explain the observed isomer distribution have been considered by various workers. It may be summarized that the reactions between amines and alkene oxides

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[6] Ref. 5, p. 450.

[7] C. D. Wagner, R. H. Brown and E. D. Peters, *J. Am. Chem. Soc.*, **69**, 2661 (1947).

[8] F. E. Critchfield and J. B. Johnson, *Anal. Chem.*, **28**, 430 (1956).

[9] K. A. Krassusky and V. D. Kutzenos, *Ukrain Khem. Zhur. Sci.*, Pt. 4, 75 (1929) cited from *Chem. Abstr.*, **24**, 1083 (1930).

give predominantly the "Normal" isomer under neutral or basic conditions. Since the reactions studied here are all under basic conditions reaction (7) could be neglected.

When primary amine reactions are studied complications arise due to the consecutive and competitive reaction of the product amine with the epoxide. The same could be avoided or reduced to a minimum by taking high ratios of the amine to the alkene oxide as pointed out earlier. In the case of secondary amine the reactions become reasonably free of complications as the reaction rate of the tertiary amine product will be very small compared to the secondary amine used due to the steric inhibition.

Another important factor to be considered is the solvolysis of the epoxide. In the case of water (and even alcohol) the solvolysis does not disturb the main reaction of addition of amine to the alkene oxide as the solvolysis rates are of no significance till almost the very end of the reaction. This becomes important however, when rather slow reactions, as those between sterically hindered amines and epoxides are studied as the rate constant for the primary reactions may be affected appreciably due to the side reaction.

Results

The reactions between amines and alkene oxides were found to follow a second order rate equation:

$$\frac{dx}{dt} = k(a-x)(b-x) \tag{8}$$

giving,

$$\log_{10}\frac{(a-x)}{(b-x)} = \frac{k_2(a-b)}{2.303}t - \log_{10}\frac{b}{a} \tag{9}$$

where,

a = the initial concentration of the epoxide
and b = the initial concentration of the amine.

The values of the second order rate constants k_2 were obtained graphically by plotting $\log_{10}\frac{(a-x)}{(b-x)}$ against t, the slope of the line being $\frac{k_2(a-b)}{2.303}$. The points fell on good straight lines. A good portion usually 5—75 per cent of the reaction was followed and all the runs were done at least in duplicate. There was always a good agreement between the duplicate runs.

The rate constants for the reactions between amines and alkene oxide in water at 20°C are presented in Table 1.

In Tables 2 and 3 are presented the rate constants for the reactions of some typical amines with propylene oxide and ethylen oxide, respectively, at different temperatures along with the values of the activation energies evaluated from the slopes of the Arrhenius plots.

TABLE 1. RATE CONSTANTS FOR THE REACTIONS BETWEEN AMINES AND ALKENE OXIDES IN WATER
Temperature = 20°C k_2 in l mol^{-1}min^{-1}

No.	Amine	Ethylene oxide	Propylene oxide	1,2-Butylene oxide
	Group I			
1	Piperazine	0.215	0.141	—
2	Pyrrolidine	0.146	0.103	0.094
3	Piperidine	0.157	0.110	0.073
4	Morpholine	0.068	0.051	0.031
	Group II			
5	Dimethyl-	0.207	0.134	—
6	Diethyl-	0.042	0.021	0.014
7	Di-*n*-butyl-	0.033	0.018	—
8	Di-*n*-propyl-	0.031	0.016	—
	Group III			
9	Methylaminoethanol	0.103	—	—
10	Ethylaminoethanol	0.032	—	—
11	Butylaminoethanol	0.027	—	—
12	Methylaminoisopropanol	—	0.047	—
13	Diethanol-,	0.015	0.011	—
	Group IV			
14	Benzyl-	0.037	0.015	—
15	Cyclohexyl-	0.028	0.031	—

TABLE 2. REACTION RATES AND THE ENERGIES OF ACTIVATION FOR THE REACTION OF SOME TYPICAL AMINES WITH PROPYLENE OXIDE
k_2 in l mol^{-1} min^{-1}

No.	Amine	20°C	30°C	35°C	40°C	$E\,\frac{\text{kcal}}{\text{gmol}}$
1	Piperazine	0.141	0.275	—	—	12.18
2	Piperidine	0.110	0.222	0.328	0.432	12.43
3	Morpholine	0.051	0.103	—	—	13.22
4	Di-*n*-propyl	0.016	0.036	—	0.079	14.76

TABLE 3. REACTION RATES AND THE ENERGIES OF ACTIVATION FOR THE REACTION OF PIPERIDINE AND DIETHYLAMINE WITH ETHYLENE OXIDE
k_2 in l mol^{-1} min^{-1}

No.	Amine	20°C	30°C	35°C	39.6°C	$E\,\frac{\text{kcal}}{\text{gmol}}$
1	Piperidine	0.157	0.345	0.489	—	13.75
2	Diethyl	0.042	0.097	—	0.204	14.55

Discussion

The reactions of amines with alkene oxides follow a second order rate equation and follow the S_N2 mechanism, the rate being proportional to the concentration of both the nucleophilic reagent and the substrate.[10]

The rates of the reactions of amines with the alkene oxides (see Table 1) show a close relationship. A plot of logarithms of the rate constants of the amines for one epoxide say ethylene oxide with the same parameter for another epoxide say propylene oxide shows a linear free energy relationship (see Figs. 1 and 2). The relationships are:

$$\log_{10} k_{\text{Am-Propylene oxide}} \approx \log_{10} k_{\text{Am-Ethylene oxide}} - 0.17 \qquad (10)$$

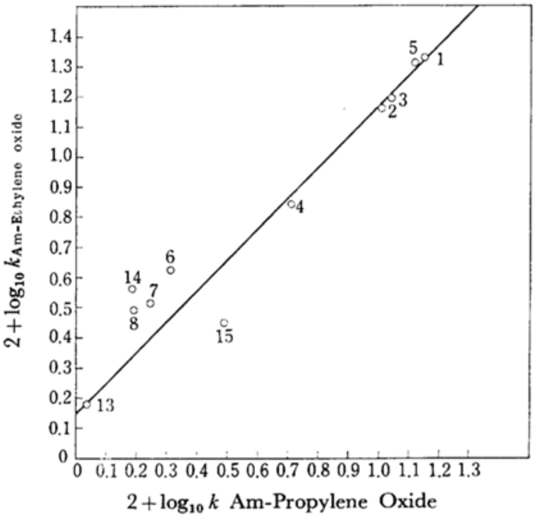


Fig. 1. Plot of rate constans of amines with ethylene oxide against rate constants for propylene oxide.

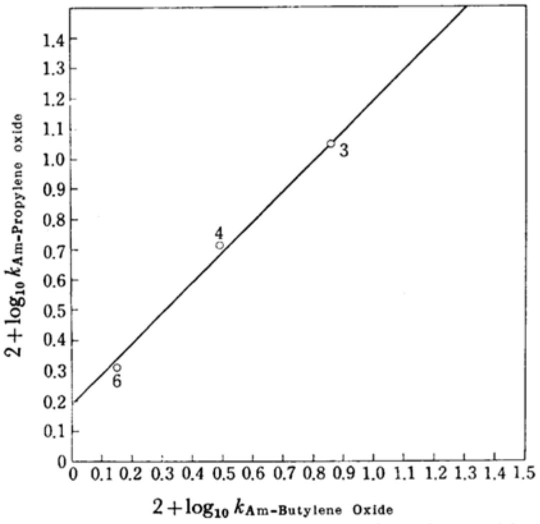
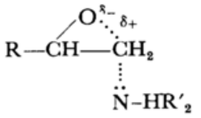


Fig. 2. Plot of rate constants of amines with propylene oxide against rate constants for 1,2-butylene oxide.

$$\log_{10} k_{\text{Am-Butylene oxide}} \approx \log_{10} k_{\text{Am-Propylene oxide}} - 0.19 \qquad (11)$$

so that with the same amine on passing from ethylene-, propylene-, to 1,2-butylene oxide the rate goes on decreasing approximately in the ratio 1 : 0.67 : 0.44.

A similar trend has been observed in the results obtained by Hansson[11] and other workers,[12] where ethylene oxide was found to react faster than propylene oxide and epichlorohydrin even faster than ethylene oxide. This behaviour could be understood by considering the transition state

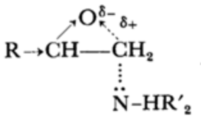


$$R\text{—CH—CH}_2\text{(}O^{\delta-}\text{, }\delta+\text{)}\cdots\ddot{N}\text{-HR}'_2 \qquad (I)$$

supposed to involve the attack of the nucleophile on the methylene group of the epoxide ring, with a simultaneous displacement of the ring oxygen atom in the opposite direction.[13]

The presence of the substituent R in the epoxide acts as an impediment for the approach of the reactant and hence the reaction will be slower the larger the size of this substituent R. Thus the increasing size of the alkyl substituent group in propylene oxide ($R=CH_3$) and 1,2-butylene oxide ($R=CH_3CH_2$), explains the decreasing rate of reaction.

However, if the positive inductive effect of the alkyl groups is considered simultaneously, the transition state could be represented by:



$$R\rightarrow\text{CH—CH}_2\text{(}O^{\delta-}\text{, }\delta+\text{)}\cdots\ddot{N}\text{-HR}'_2 \qquad (II)$$

The density of electrons at the CH-carbon atom will increase due to the presence of the electron repelling group R.[14] Consequently, the demand for the electron shift from the methylene carbon atom (CH_2 carbon) will be lowered resulting in a smaller positive charge on it and a lower reaction rate. Thus the dual effect of the alkyl groups, one steric and the other polar (with a positive inductive effect) act in the same direction as to inhibit the reaction.

Similar reasoning accounts for the much higher reactivity of epichlorohydrin[12] when compared to the other epoxides. In this instance it appears

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[10] L. F. Fieser and M. Fieser, "Organic Chemistry," III Ed., Reinhold Publishing Corp., New York (1958), p. 337.

[11] J. Hansson, "A Kinetic Study of the Addition of Amines to Propylene Oxide," Lindstedts. Lund (1955), and earlier papers.

[12] L. Smith, S. Mattsson and S. Andersson, Lunds Univ. Arsskr., Nr. 7, 1 (N. F.) (1946).

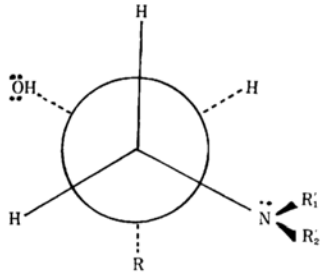
[13] R. E. Parker, N. B. Chapman and N. S. Issaacs, *J. Chem. Soc.*, **1959**, 1925.

[14] D. Swern, G. N. Billen and H. B. Knight, *J. Am. Chem. Soc.*, **71**, 1152 (1949).

that the increased size of the substituent in the epoxide from CH_3 (in propylene oxide) to $ClCH_2$ (in epichlorohydrin) does not have as much effect in retarding the reaction rate as the acceleration of the rate due to the negative inductive character of the chloromethyl group.

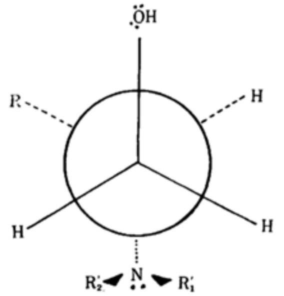
Normal and Abnormal Reactions. The attack of the epoxide by the nucleophile on the terminal methylene carbon atom (CH_2) bearing a positive charge and having less steric hindrance is much easier than the attack on the CH carbon atom. Moreover the secondary amines themselves show appreciable primary steric effects. All these factors contribute to the preferential formation of the normal rather than the abnormal products of the reactions considered.

Conformational Analysis. Conformational analysis as to the relative stabilities of the normal isomer (a) and the abnormal isomer (b) (see Fig. 3) also favours the formation of the former rather than the latter.



Normal isomer $R\text{-}CH(OH)\text{-}CH_2\text{-}N\begin{matrix}\diagup R'_1\\ \diagdown R'_2\end{matrix}$

(a)



Abnormal isomer $R\text{-}\underset{\displaystyle N\begin{matrix}\diagup R'_1\\ \diagdown R'_2\end{matrix}}{\underset{|}{C}H}\text{-}CH_2OH$

(b)

Fig. 3. Projection formulae of normal and abnormal Isomers

Of the various rotational isomers possible for the normal and the abnormal isomers (a) and (b) represent the most stable conformation in each set. The relative stabilities of the above two structures will determine as to which isomer is formed predominantly, if at all. In the formula (b) the groups R'_1 and R'_2 are situated very close to the hydrogen atoms and the conformation though not exactly, is similar to an eclipsed one. These two "almost eclipsed" interactions combined with the strong skew interaction between groups R and $\ddot{\underset{..}{O}}H$ and the probable R–R'_2 interaction make the molecule very constrained and of much higher energy content than (a) where there are two mild interactions between $\ddot{\underset{..}{O}}H$ and H, R'_1 and H, and R and $\ddot{\underset{..}{N}}$. But the sum of these interactions should be much smaller than that of (b). These indicate that the isomer (b) is under great strain and of higher energy content and hence the predominance, if not the exclusive formation of the isomer (a), in most of the reactions.

In view of the above considerations, it may be inferred that the greater the size of the alkyl group R and also the greater the branching of the chains present in the alkyl groups R'_1 and R'_2, the more difficult should be the formation of the isomer (b).

Reactivities of Heterocyclic Amines. The heterocyclic amines pyrrolidine, piperidine, *etc.* (See Table 1) react markedly faster compared to most of the amines listed. Pyrrolidine reacts with ethylene oxide about 3.5 times as fast as diethylamine and about 5 times as fast with propylene oxide. Similarly, the reactivity of morpholine (pK_a at 25°C[15]=8.36) is about 4—5 times that of diethanolamine (pK_a at 25°C[16]=8.88) though the former is the weaker base.

The structures of pyrrolidine and morpholine could be obtained from those of diethyl- and diethanolamines respectively with a little distortion and this results in the high increase in the reaction rates.

The relative rates of reactions of morpholine and diethanolamine with CO_2 and COS are about 13.5 and 20 respectively as shown by the work of Sharma.[1] Pyrrolidine reacts about 5 times as fast as diethylamine with COS.[1] The rate of reactions with CS_2 also follow a similar trend—pyrrolidine reacting about 6 times as fast as diethylamine and morpholine about 10 times as fast as diethanolamine.[2] Further at 25°C, pyrrolidine and morpholine react with 4-nitrofluoro-benzene[17] about 90 times as fast as diethylamine and diethanolamine respectively. The increased reactivity of the heterocyclic amines is due to the restriction of the free play of the alkyl groups about the nitrogen atom about the ring.

If the same analogy is applied in the case of dimethylamine and ethylenimine, it would be con-

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[15] H. K. Hall, Jr., *J. Am. Chem. Soc.*, **79**, 5441 (1957).

[16] V. E. Bower, R. A. Robinson and R. G. Bates, *J. Res. Nat. Bur. Stand.*, **A66**, 71 (1962).

[17] H. Suhr, *Ann. Chem.*, **689**, 109 (1965).

cluded that ethylenimine should be a very highly reacting species as even dimethylamine is a fast reacting compound. Some preliminary experiments showed that ethylenimine was reacting so slow as to be termed "almost inert" when compared to the other amines listed. In agreement with the above observation, the reactivity of dimethylamine with 4-nitrofluoro-benzene is seen to be 156 times as great as that of ethylenimine.[17] The "inert" character of ethylenimine is probably due to the aromaticity or electron delocalization of the three membered ring.[18] The fact that ethylenimine is a base (pK_a at 25°C[19]=8.04) even weaker than ammonia (pK_a at 25°C[15]=9.21) is also due to the same reason.

Steric and Inductive Effects. The relative rates of reactions of dimethyl-, diethyl-, di-*n*-propyl-, and di-*n*-butylamines with propylene oxide are seen to be 8.60 : 1.32 : 1.00 : 1.13. The same order of reactivity is maintained in their reactions with ethylene oxide, with a minimum in the rate in case of di-*n*-propylamine. But then to di-*n*-butylamine there is a slight but a definite increase in the rate. This may be explained by considering the simultaneous operation of two effects——the rate decreasing steric effect and the rate increasing positive inductive character of the alkyl groups attached to the amino nitrogen.

It appears that from dimethyl-, to di-*n*-propylamine the steric effect outweighs the inductive effect but from di-*n*-propyl- to di-*n*-butylamine, the effect of the increase in the inductive character is a little more than that of the increase in the size of the alkyl groups, giving rise to the observed minimum at the di-*n*-propylamine.

Amine Reactivities and pK_a Values. No correlation between the reactivities of amines with the epoxides, with the pK_a values of the amines is found.

It may be that the steric arrangements of the amines are such that the different groups attached to the amino nitrogen are not effective in preventing a hydrogen ion in combining with it in the equilibrium reaction:

$$RNH_2 + H^+ \rightleftarrows RNH_3^+ \qquad (12)$$

on which the basicity of the amine depends, but offering strong resistance to the transition state formation with a bulkier substrate like an epoxide.

The non-dependence of the basicities of the substituted ammonium ions on the steric factors is reflected in the fact that *n*-, *s*-, and *t*-butylamines have practically the same basicities (pK_a's 10.5 at 25°C[15]).

The importance of steric and inductive factors is evident from the following examples in the reactions of amines with ethylene oxide:

1) piperazine (pK_{a_1}=9.81[20]) and dimethylamine (pK_a=10.64[15]) react almost with the same velocity.

2) dimethylamine (pK_a=10.64[15]) reacts more than six times as fast as di-*n*-butylamine (pK_a= 11.25[15])

3) methylaminoethanol (pK_a=9.70[21]) reacts more than three times as fast as ethylaminoethanol (pK_a=9.80[21]) and

4) morpholine (pK_a=8.36[15]) reacts more than four times as fast as diethanolamine (pK_a=8.80[16]).

Similarly with CO_2, *n*-butylamine and isobutylamine (pK_a=10.42 at 25°C[22]) show practically the same rate of reaction, but *s*-butylamine reacts at one third this rate; *t*-butylamine, where the steric factors are likely to be most important, reacts at about only a tenth of that for *n*- and isobutylamine.[1]

Similarity of Structures and Reactivities. The rate constant in the case of ethylaminoethanol (containing one ethyl and one hydroxy-ethyl groups) is about the mean of the rate constants of diethylamine (containing two ethyl groups) and diethanolamine (containing two hydroxyethyl groups). A similar relation in the case of methylaminoethanol with that of dimethyl- and diethanolamines is also seen to exist.

In the above case, the groups mentioned are similarly linked with the reaction centre both in the compounds considered for isolating the combined contribution of the polar and steric effects of each group and also in the compounds for which the estimations of the rates are made in addition to the mechanism of the reactions as well as the substrate being the same in all the cases. However, it is unlikely that general group contribution values could be assigned to various functional groups.

Swain-Scott Correlation. Plots of the values of n[23] the nucleophilic constants of the amines against their respective logarithms of rate constants with alkene oxides are found to give approximate linear plots (Fig. 4) showing that the nucleophilic reactivities of aliphatic amines towards varied substrates can be correlated by the four parameter equation proposed by Swain and Scott.[24] The correlation of course is not exact as indicated by the scatter of the points.

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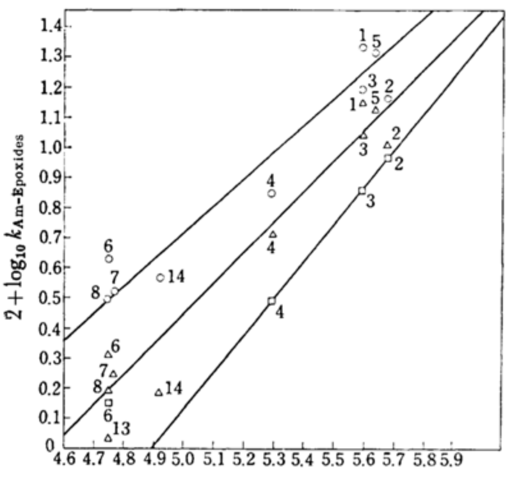

Fig. 4. Plot of logarithms of the rate constants of amines with alkene oxides against the nucleophilic constant, n, of the amines.

○ Ethylene oxide, △ Propylene oxide,
□ 1,2-Butylene oxide

The values of n are found to be higher for the faster reacting amines and *vice-versa*. Thus the values of n are found to give the quantitative measures for the reactivities of different nucleophiles.

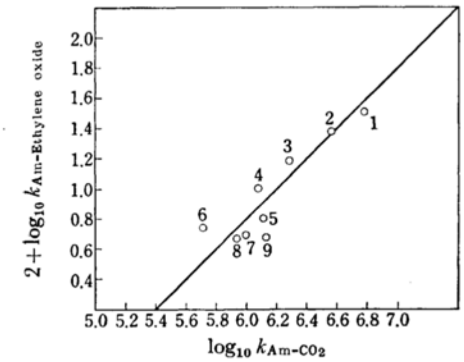

Fig. 5. Plot of rate constants of amines with ethylene oxide against rate constants for CO_2.

Linear Free Energy Relationship. An attempt was made to see whether a linear free energy relationship exists between the reactions of a variety of amines with ethylene oxide and CO_2. The values of the logarithms of the rate constants of amines with ethylene oxide at 25°C (obtained from the respective rates at 20°C using a value of activation energy of 14 kcal/g mol) were plotted against the logarithms of the rate constants of the amines with CO_2[1) at 25°C (Fig. 5). Although there is some scatter of data, the following relation is likely to hold:

$$\log_{10} k_{\text{Am-Ethylene oxide}} \approx \log_{10} k_{\text{Am-CO}_2} - 7.20 \qquad (13)$$

Conclusions

1) The rate constant for a given reaction is found to be a function of (i) steric and (ii) polar factors: (i) For a specified amine, the rate constant for ethylene oxide is significantly greater than that for propylene- and 1,2-butylene oxides; (ii) In the case of dialkylamines the rate constant decreases from dimethyl- to di-*n*-propylamine and then there is a nominal increase in the rate when higher di-*n*-alkylamines are used.

2) The "Normal" addition of amines to epoxides could be explained on the basis of conformational analysis.

3) Heterocyclic amines react faster than the other related amines probably due to structural factors.

4) For all classes of amines there is no general relationship between their basicities and rate constants.

5) In general, the rate constants for a variety of amines can be correlated by the Swain-Scott equation.

6) Linear free energy relationships exist between the rates of reactions of a variety of amines with ethylene-, propylene-, 1,2-butylene oxides, CO_2, *etc.*

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